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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020

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:	Trading Symbol	Name of each exchange on which registered:
Common Stock, $0.001 par value	CTSO	**The Nasdaq Stock Market LLC (Nasdaq Capital Market)**

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically 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 ☐ No

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 ☐
Non-accelerated Filer ☑ Smaller reporting company ☑
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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C.7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☑

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

The aggregate market value of the common stock of the registrant held by non-affiliates as of June 30, 2020 was approximately $306,285,000 based upon the closing price reported for such date on the Nasdaq Capital Market. As of March 9, 2021, there were outstanding 43,263,772 shares of the registrant's common stock.

Documents incorporated by reference:

Portions of the registrant's 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 of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. Forward-looking statements discuss matters that are not historical facts. Because they discuss future events or conditions, forward-looking statements may include words such as "anticipate," "believe," "estimate," "intend," "could," "should," "would," "may," "seek," "plan," "might," "will," "expect," "predict," "project," "forecast," "potential," "continue," negatives thereof or similar expressions. These forward-looking statements are found at various places throughout this Report and include information concerning possible or assumed future results of our operations; business strategies; future cash flows; financing plans; plans and objectives of management; any other statements regarding future operations, future cash needs, business plans and future financial results, and any other statements that are not historical facts. Unless otherwise indicated, the terms "CytoSorbents," "Company," "we," "us" and "our" refer to CytoSorbents Corporation.

From time to time, forward-looking statements also are included in our other periodic reports on Forms 10-Q and 8-K, in our press releases, in our presentations, on our website and in other materials released to the public. Any or all of the forward-looking statements included in this Report and in any other reports or public statements made by us are not guarantees of future performance and may turn out to be inaccurate. These forward-looking statements represent our intentions, plans, expectations, assumptions and beliefs about future events and are subject to risks, uncertainties and other factors. Many of those factors are outside of our control and could cause actual results to differ materially from the results expressed or implied by those forward-looking statements. In light of these risks, uncertainties and assumptions, the events described in the forward-looking statements might not occur or might occur to a different extent or at a different time than we have described. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of 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®, ECOS-300CY®, VetResQ®, BetaSorb™, HemoDefend™, K^{+}ontrol™,and DrugSorb™, 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 an 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, we received a label expansion for CytoSorb covering use of the device for the removal of bilirubin and myoglobin in the treatment of liver disease and trauma, respectively. In January 2020, we received CE-Mark label expansion for CytoSorb covering the use of the device for the removal of the anti-platelet agent, ticagrelor, in patients undergoing surgery requiring cardiopulmonary bypass. In April 2020, the United States Food and Drug Administration (the "FDA") granted Breakthrough Designation to CytoSorb for the removal of ticagrelor in a cardiopulmonary bypass circuit during emergent and urgent cardiothoracic surgery. In April 2020, we announced that the FDA has granted Emergency Use Authorization ("EUA") of CytoSorb for use in patients with COVID-19 infection. In May 2020, we received a CE-Mark label expansion for CytoSorb for the removal of rivaroxaban during cardiothoracic surgery requiring cardiopulmonary bypass. 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. We believe 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 121,000 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. . The technology is protected by 16 issued U.S. patents and multiple international patents, with applications pending both in the U.S. and internationally. We have numerous product candidates under development based upon this unique blood purification technology, 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 known as cytokine storm. Left unchecked, this cytokine storm can lead to 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.

As part of the CE Mark approval process, we completed our randomized, controlled, European Sepsis Trial amongst 14 trial sites in Germany in 2011, with enrollment of 100 patients with sepsis and respiratory failure. The trial established that CytoSorb was sufficiently safe in this critically-ill population, and that it was able to broadly reduce key cytokines in the blood of these patients.

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, the expansion of which we officially completed in June 2018. Upon expanding our facility we quadrupled our manufacturing capacity and 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 2020, 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 E.U. were expanded to include the removal of bilirubin in liver disease, and the removal of myoglobin in trauma.

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 the third quarter of 2019, we established CytoSorbents UK Limited, a wholly-owned subsidiary of CytoSorbents Medical, Inc., to manage our clinical trial activities in the United Kingdom.

In August 2019, we announced that CytoSorb had received renewal of its European Union CE Mark through May 2024 and ISO 13485:2016 Full Quality Assurance System certification of its manufacturing facility through September 2022.

In January 2020, we received CE-Mark label expansion approving the use of CytoSorb to remove the anti-platelet agent, ticagrelor, in cardiac patients during surgery requiring cardiopulmonary bypass.

In April 2020, the Company announced that the FDA granted EUA of CytoSorb for use in critically-ill patients infected with COVID-19. Under the EUA, the Company can make CytoSorb available, through commercial sales, to all hospitals in the United States for use in patients, 18 years of age or older, with confirmed COVID-19 infection who are admitted to the intensive care unit (ICU) with confirmed or imminent respiratory failure who have early acute lung injury or acute respiratory distress syndrome (ARDS), severe disease, or life-threatening illness resulting in respiratory failure, septic shock, and/or multiple organ dysfunction or failure. The CytoSorb device has neither been cleared nor approved for the indication to treat patients with COVID-19 infection. The EUA will be effective until a declaration is made that the circumstances justifying the EUA have terminated or until revoked by the FDA.

In April 2020, the Company also announced that the FDA had granted Breakthrough Designation to CytoSorb for the removal of ticagrelor in a cardiopulmonary bypass circuit during emergent and urgent cardiothoracic surgery. The Breakthrough Devices

Program provides for more effective treatment of life-threatening or irreversibly debilitating disease or conditions, in this case the need to reverse the effects of ticagrelor in emergent or urgent cardiac surgery that can otherwise cause a high risk of serious or life-threatening bleeding. Through Breakthrough Designation, the FDA intends to work with CytoSorbents to expedite the development, assessment, and regulatory review of CytoSorb for the removal of ticagrelor, while maintaining statutory standards of regulatory approval (e.g., 510(k), *de novo* 510(k) or premarket approval) consistent with the FDA's mission to protect and promote public health.

In May 2020, we received CE-Mark label expansion approving the use of CytoSorb for the removal of rivaroxaban, a widely-used Factor Xa inhibitor and novel oral anticoagulant, during cardiothoracic surgery requiring cardiopulmonary bypass. With this announcement, and the E.U. approval earlier this year to remove ticagrelor, for the same indication, CytoSorb is providing cardiac surgeons and perfusionists an easy-to-use and rapid new treatment option to help reduce the risk of serious and potentially fatal perioperative bleeding complications caused by these two drugs, in separate categories of blood thinners.

In addition, we now have more than 50 investigator-initiated studies and additional Company sponsored trials that are currently planned, enrolling or completed in Europe and elsewhere outside of the United States. We believe that these trials, which are conducted and supported by what we believe to be well-known university hospitals and KOLs, are the equivalent of Phase 3 and Phase 4 clinical studies. We believe they will provide invaluable information regarding the success of the device in the treatment of sepsis, cardio-pulmonary bypass surgery, liver failure, and many other indications, and if successful, may be integral in helping to drive additional usage and adoption of CytoSorb.

As of March 1, 2021, our European commercialization team included 93 people.

We have complemented our direct sales efforts with sales to distributors and/or strategic corporate partners. For more information regarding our distributors and strategic partners, refer to the Sales and Marketing section in item 1 of this report.

We continuously evaluate other potential distributor and strategic partner networks in other countries where we are approved to market the device.

Overall, we have established either direct sales or distribution (via distributors or strategic partners) of CytoSorb in 67 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 has distribution in Turkey, India, Sri Lanka, Australia, New Zealand, Russia, Serbia, Norway, Vietnam, Malaysia, Hong Kong, Chile, Panama, Costa Rica, Colombia, Brazil, Mexico, Argentina, Perú, Guatemala, Ecuador, Bolivia, the Dominican Republic, El Salvador, Iceland, Israel, UAE, Iran, Saudi Arabia and other Middle Eastern countries, 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. For example, in December 2019, we discontinued our distributor relationship with Dr. Reddy's in South Africa due to lack of market adoption. We continuously evaluate other potential distributor and strategic partner networks in other countries that accept CE Mark approval.

In February 2020, we announced an agreement with China Medical System Holdings Limited ("CMS"), a well-established, innovation-driven specialty pharma with a focus on sales and marketing in China and Asia, to bring CytoSorb to mainland China to treat critically-ill patients with COVID-19 (fka Wuhan or 2019-nCoV) coronavirus infection. Under the terms of the agreement, CytoSorbents and CMS agreed to partner together to earn regulatory clearance to import CytoSorb into China under the "fast-track" review process established by the National Medical Products Administration of the People's Republic of China (NMPA) to respond to the 2019 novel coronavirus (COVID-19) pandemic. CytoSorbents donated the initial CytoSorb devices and provided product, training, and support to CMS to introduce CytoSorb initially into four hospitals in the Wuhan, China area. The therapy was used and will be evaluated in severe COVID-19 coronavirus patients with a systemic inflammatory response being treated with either continuous renal replacement therapy (CRRT) or extracorporeal membrane oxygenation (ECMO). The use of CytoSorb for the treatment of patients with severe COVID-19 coronavirus infection is considered exploratory in nature in China, and is currently not yet approved for commercial purposes in mainland China.

In addition to our direct and distributor commercial channels, we have a number of strategic partners to market and distribute CytoSorb. These partners include Biocon Biologics Limited, Fresenius Medical Care AG, B. Braun Avitum AG, Aferetica s.r.l., and Terumo Cardiovascular Group. For detailed information regarding these partnerships, see the section entitled “Commercial and Research Partners” in item 1 of this report.

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 responsible for an estimated one in every five deaths worldwide. Sepsis 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 and regulatory submissions.

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. These additional dosing data were used to support the label expansion to increase treatment time from 6 hours, the initial approval, to 24 hours of treatment. This study also provided additional treatment options for CytoSorb, helped to support the positive clinical data from our first European Sepsis Trial, and helped to 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 former market for leukoreduction filters in cardiac surgery that attempt to indirectly reduce cytokines by capturing cytokine-producing leukocytes – an inefficient and suboptimal approach.

The Company is currently conducting the following clinical trials:

Country	Trial Name	Indication
United States	REFRESH 2-AKI	Post-Cardiac Surgery AKI
United States	CTC Registry	Real world outcomes in COVID-19 patients under the EUA
Germany	CYTATION	Ticagrelor Removal During Cardiac Surgery
United Kingdom	TISORB	Ticagrelor Removal During Cardiac Surgery
Europe	STAR Registry	Real world outcomes in antithrombotic removal

The Company is also providing an update on the following investigator initiated clinical trial:

Germany	REMOVE	Infective Endocarditis

For further detailed information regarding our clinical trial strategy, see the section entitled “Clinical Studies” of this Item 1 of this Report.

Even though we have obtained CE Mark approval for CytoSorb, 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, 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.

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%. 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 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 $214 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.

July 24, 2020 Offering

On July 24, 2020, the Company closed an underwritten public offering of 6,052,631 shares of its common stock at a public offering price of $9.50 per share (the "Offering"). The Company completed the Offering pursuant to the terms of an Underwriting Agreement, dated as of July 21, 2020, by and among the Company and Cowen and Company, LLC and SVB Leerink LLC, as representatives of the several underwriters named therein. The Company received gross proceeds of approximately $57.5 million from the Offering. After deducting the underwriting discounts and commissions and fees and expenses payable by the Company in connection with the Offering, the Company received net proceeds of approximately $53.8 million.

Shelf Registration

On July 26, 2018, the Company filed a 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.

Open Market Sale Agreement with Jefferies LLC and B. Riley FBR, Inc.

On July 9, 2019, the Company entered into an Open Market Sale Agreement (the “New Sale Agreement”) with Jefferies LLC and B. Riley FBR, Inc. (each an “Agent” and, together, the “Agents”), pursuant to which the Company may sell, from time to time, at its option, shares of the Company’s common stock having an aggregate offering price of up to $25,000,000 through the Agents, as the Company’s sales agents. All shares of the Company’s common stock offered and sold, or to be offered and sold under the New Sale Agreement were or will be issued and sold pursuant to the Company’s 2018 Shelf by methods deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, in block transactions or if specified by the Company, in privately negotiated transactions.

On April 20, 2020, the Company and the Agents entered into an amendment to the New Sale Agreement (the “Amendment”) to provide for an increase in the aggregate offering amount under the New Sales Agreement, such that as of April 20, 2020, the Company may offer and sell Shares having an additional aggregate offering price of up to $50 million under the New Sale Agreement, as amended by the Amendment (the “Amended Sale Agreement”).

Subject to the terms of the Amended Sales Agreement, the Agents are required to use their commercially reasonable efforts consistent with their normal sales and trading practices to sell the shares of the Company’s common stock from time to time, based upon the Company’s instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company is required to pay the Agents a commission of up to 3.0% of the gross proceeds from the sale of the shares of the Company’s common stock sold thereunder, if any. The Company has also agreed to provide the Agents with customary indemnification rights. The offering of the shares of the Company’s common stock under the Amended Sales Agreement will terminate upon the earliest of (a) the sale of the maximum number or amount of the shares of the Company’s stock permitted to be sold under the Amended Sale Agreement and (b) the termination of the Amended Sale Agreement by the parties thereto. During the year ended December 31, 2019, the Company sold 191,244 shares pursuant to the Amended Sale Agreement, at an average selling price of $4.11 per share, generating net proceeds of approximately $762,000. During the year ended December 31, 2020, the Company sold 4,110,625 shares pursuant to the Amended Sale Agreement, at an average selling price of $6.64 per share, generating net proceeds of approximately $26,476,000. In the aggregate, the Company has sold 4,301,869 shares pursuant to the Amended Sale Agreement, at an average selling price of $6.53 per share, generating net proceeds of approximately $27,238,000. In addition, during the year ended December 31, 2020, the Company paid approximately $49,000 in expenses related to the Amended Sale Agreement.

Research and Development

We have been engaged in research and development since inception. Since 2012, we have been awarded an aggregate of approximately $28.4 million in grants, contracts, and other non-dilutive funding 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, $1.1M 2nd Phase II), the U.S. Air Force $3.0M Rapid Innovation Fund, the Congressionally Directed Medical Research Program Office, (“CDMRP”, $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 STTR; $2.9M Defense Health Agency, US Army and CDMRP Phase III STTR; $4.4M US Army and CDMRP Rapid Innovation Fund; and a $1.1M US Army contract), New Jersey Technology Business Tax Certificate Program for research related expenses ($5.9M), and others 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 helps 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, ECOS-300CY, and other product candidates under development, including CytoSorb XL, BetaSorb, ContrastSorb, DrugSorb, HemoDefend-RBC, HemoDefend-BGA, K^+ontrol,and others 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 2020, the Company received CE-Mark label expansions for CytoSorb to remove the anti-platelet agent ticagrelor and the direct oral anticoagulant rivaroxaban in patients undergoing cardiac surgery on cardiopulmonary bypass.

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. A 2020 study published in The Lancet estimated that there were 49 million new cases of sepsis globally, killing 11 million people every year. The researchers estimate that 1 in every 5 deaths worldwide is due to sepsis. Data released by the Healthcare Cost and Utilization Project (H-CUP) identified approximately 1.6 million cases of sepsis each year in the U.S. 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, COVID-19 coronavirus, and others.

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. In recognition of this, in 2016 the 3rd International Consensus Definition Task Force re-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 adsorber 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 experimental therapies has been discontinued, including Eritoran from Eisai, CytoFab from BTG/Astra Zeneca, Talactoferrin from Agennix, tranexemic acid from Leading Biosciences, and others.

For more information regarding our competitor's clinical trials, see the section entitled "Competition" in Item 1 of this report.

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 Biologics Limited, India's largest biopharmaceutical company, for exclusive distribution of CytoSorb in India, Sri Lanka, and other select emerging markets. In March 2021, we announced a strategic partnership with B. Braun Avitum AG, and the launch of a global co-marketing agreement to promote the use of CytoSorb with B Braun's latest OMNI® continuous blood purification platform and OMNIset® Plus bloodline set (set version 3.0 or higher). 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 67 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. there are an estimated 1.6 million cases of sepsis, while the European Sepsis Alliance estimates 3.4 million individuals in Europe become septic each year. In Germany alone, according to the Center of Sepsis Control and Care, there are approximately 175,000 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 cardiac surgery procedures performed on cardiopulmonary bypass annually in the U.S., another 500,000 in the EU, and approximately a total of 1.5 million procedures worldwide. These include relatively common procedures including coronary artery bypass graft surgery, valve replacement surgery, heart and lung transplantation, aortic reconstruction, congenital heart defect repair, and LVAD placements 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 plus first year expenses total $1.2 million in the U.S. Valve replacement surgery for infective endocarditis is poorly reimbursed and may cost up to $150,000-$250,000 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 adsorber can be easily incorporated in the heart-lung machine circuit without the need for a separate pump, a unique competitive advantage over other technologies. After the surgery, CytoSorb can continue to be used similarly to dialysis on patients that develop a severe post-operative inflammatory response with hemodynamic instability. 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.

Removal of Antithrombotic Drugs in Cardiac Patients During Surgery Requiring Cardiopulmonary Bypass

The role of antithrombotics, a category that includes both antiplatelet and anticoagulant drugs in cardiovascular medicine is constantly growing. Antiplatelet drugs are routinely used in patients with atherosclerotic cardiovascular disease such coronary disease, vascular disease or stroke. In the acute management of these patients especially when they need interventional procedures such as stent placement therapy is escalated using two antiplatelet drugs (dual antiplatelet therapy - DAPT). Ticagrelor (Astra Zeneca - Brilinta(R), Brilique(R)) is considered best in class and is one of the most commonly used anti-platelet drugs to reduce the risk of cardiac death, heart attacks, and strokes in patients with either a history of a heart attack, or those actively undergoing percutaneous coronary intervention (PCI) with stent placement for acute coronary syndrome or heart attack. On the other hand, patients with atrial fibrillation or venous thrombosis require chronic anticoagulation. A new category of drugs called Direct Oral Anticoagulants (DOAC) is now the new standard of care with tens of millions of patients relying on them for lifelong protection. The two leaders in the category,Apixaban (Bristol Myers Squibb - Eliquis(R)) and rivaroxaban (Janssen and Bayer - Xarelto(R)) aare estimated to reach 40 billion USD in sales by 2026.

There is a clear and large unmet medical when patients on these antithrombotic agents need to undergo surgery due to the very high risk of bleeding. Specifically, in patients on these drugs requiring urgent or emergent cardiac surgery the risk of major fatal/life-threatening bleeding has been reported to be as high as 65%. This scenario is most common in patients presenting with an acute coronary syndrome (ACS). In the US alone there are approximately 1.1 million ACS hospital admissions annually. CytoSorb is able to very efficiently remove ticagrelor and DOACs from blood. The use of CytoSorb during emergency coronary artery bypass surgery (CABG) in patients on ticagrelor or rivaroxaban significantly reduced post-operative bleeding complications in a landmark observational study and had projected cost savings of approximately $5,000 per patient, including the cost of the device. Every year there are approximately 400,000 CABG procedures performed in the US and 250,000 CABG procedures in the EU with nearly 100,000 in Germany alone.

Acute Respiratory Distress Syndrome

Acute lung injury (“ALI”) and acute respiratory distress syndrome (ARDS) are two of the most serious conditions on the continuum of respiratory failure when both lungs are compromised by inflammation and fluid infiltration, severely compromising their 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 ARDS in the U.S. each year, with even more cases in the EU. During the COVID-19 pandemic in 2020-2021, ALI and ARDS were responsible for more than 500,000 deaths in the U.S. alone. Patients with ALI and ARDS typically require mechanical ventilation, and sometimes extracorporeal membrane oxygenation (ECMO) 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 towards benefit. Future, prospectively defined, larger studies are required to confirm these findings. Although a number of therapies have been tried such as nitric oxide, surfactant therapy, and others, only corticosteroids, such a dexamethasone or methylprednisolone, have demonstrated mortality benefit in patients with ARDS. For example, in critically ill COVID-19 patients on mechanical ventilation, the RECOVERY study demonstrated use of once daily dexamethasone led to a reduction in mortality from 41.4% control to 29.3% treatment. 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, we believe 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 approximately $2 billion for the U.S and EU combined.

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 at 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. 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, ARDS preventing adequate oxygenation of blood, capillary leakage resulting in tissue edema and intravascular depletion, hypermetabolism leading to massive protein degradation and catabolism and is also associated with 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 up to $600 million for the U.S. and EU combined.

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 in cytokine production or cytokine storm. In trauma, cytokine storm contributes to the systemic inflammatory response syndrome triggering 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 ALI and ARDS 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.

Trauma patients on antithrombotic drugs represent an especially challenging cohort since any necessary surgery would be associated with very high bleeding risk. The ability of CytoSorb to efficiently remove some of the most popular antithrombotic drugs may represent an additional mode of benefit to improve clinical outcomes in trauma patients.

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 and cytokines 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 many 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.

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. CytoSorb has been used successfully in many 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. In early 2020, the first two case reports of CRS successfully treated with the adjunctive use of CytoSorb were published.

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.

Organ Transplant and 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.

In October 2020, CytoSorbents announced the EU approval of the ECOS-300CY cartridge for the removal of inflammatory mediators during ex vivo organ perfusion, with the goal of either preserving organ function in healthy organs, or rehabilitating dysfunctional organs that would otherwise have been discarded. We believe the ECOS-300CY cartridge has the potential to expand the organ donor pool. According to Eurotransplant, there were approximately 6,400 transplants from deceased donors and roughly 14,000 patients on waiting list for organs in Europe last year. In the United States, UNOS cites 39,035 organ transplants in 2020, with approximately 108,000 patients on the waiting list. This represents a US and European total addressable market for the ECOS-300CY device of approximately $400-600 million.

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, and a number of other inflammatory mediators that accumulate in transfused blood products during storage. Leukoreduction can remove the majority of white cells that can produce new cytokines but cannot eliminate those cytokines already in blood, and cannot otherwise remove other causative agents such as free hemoglobin and antibodies. Automated washing of pRBC is effective but is impractical due to the time, cost, and logistics of washing each unit of blood. The HemoDefend platform is a potentially superior alternative to purify blood transfusion products to these methods. The total addressable market for HemoDefend is more than $500 million for pRBCs alone. 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. According to the American Red Cross, nearly 10,000 units of plasma are needed daily in the United States, or more than 3.5 million units a year. The World Health Organization (WHO) reports that plasma is transfused at a rate of 2.2 – 18.9 units per 1,000 population (median 7.7 units) globally. In westernized countries alone, with a population of 1.5 billion, there are approximately 12 million units of plasma administered each year. The total addressable market for HemoDefend-BGA in transfusion medicine in westernize countries alone is an estimated $400 million to $600 million, and represents a fraction of the global market.

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 invasive and interventional cardiovascular procedures 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 500,000 patients in the U.S. currently receiving chronic dialysis and more than 3.0 million worldwide. Approximately 66% of patients with chronic kidney disease are treated with hemodialysis. One of the problems with standard high-flux dialysis is the limited ability to remove certain mid-molecular weight toxins such as β_2 -microglobulin. Over time, β_2 -microglobulin can accumulate and cause amyloidosis in joints and elsewhere in the musculoskeletal system, leading to pain and disability. Our BetaSorb device has been designed to remove these mid-molecular weight toxins when used in conjunction with standard dialysis. Standard dialysis care typically involves three sessions per week, averaging approximately 150 sessions per year.

Products

The polymer adsorbent technology used in our products can remove middle molecular weight toxins, such as cytokines, from blood and physiologic fluids. All of the potential applications described below (i.e., the adjunctive treatment and/or prevention of sepsis; the adjunctive treatment and/or prevention of other critical care conditions such as acute respiratory distress syndrome, burn injury, trauma and pancreatitis; the prevention of damage to organs donated by brain-dead donors prior to organ harvest; the prevention of post-operative complications of cardiopulmonary bypass surgery; the prevention of kidney injury from IV contrast; and the treatment of chronic kidney failure) share in common high concentrations of toxins in the circulating blood. However, because of the limited studies we have conducted to date, we are subject to substantial risk that our technology will have little or no effect on the treatment of any of these indications. In 2011, we completed our European Sepsis Trial of our CytoSorb device. The study was a randomized, open label, controlled clinical study in 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 a recent 2020 The Lancet study, the worldwide incidence is estimated to be 49 million cases annually, accounting for 1 in every 5 deaths globally. 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® did not have a statistically significant mortality benefit, and Eli Lilly withdrew 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 121,000 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 27 countries of the EU, the United Kingdom 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 67 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 has distribution in Turkey, India, Sri Lanka, Australia, New Zealand, Russia, Serbia, Norway, Vietnam, Malaysia, Hong Kong, Chile, Panama, Costa Rica, Colombia, Brazil, Mexico, Argentina, Perú, Guatemala, Ecuador, Bolivia, the Dominican Republic, El Salvador, Iceland, Israel, UAE, Iran, Saudi Arabia and other Middle Eastern countries, 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 2022.

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, 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. In addition, CytoSorb can remove certain anti-thrombotics such as ticagrelor and rivaroxaban during cardiopulmonary bypass in patients requiring urgent or emergent surgery. 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;
- reduce the total cost of patient care;and
- reduce the risk of post-operative bleeding complications such as need for blood and platelet transfusions, rethoracotomy, and death

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.

CytoSorb was recently approved to remove the anti-platelet agent, ticagrelor, during cardiac surgery involving cardiopulmonary bypass via label expansion of its CE Mark. Ticagrelor (Brilinta®, Astra Zeneca) is a widely-used anti-platelet agent used to decrease cardiovascular risk and risk of stroke in patients with a known history of heart disease or heart attack. It is also widely used during dual-anti platelet therapy in patients with acute coronary syndrome undergoing percutaneous coronary intervention and stent placement. However, when patients on ticagrelor require emergent or urgent cardiac surgery, up to 65% of patients will have severe or massive peri-operative bleeding complications that contributes to a high risk of death and major costs to the healthcare system. CytoSorb has already demonstrated the ability to remove ticagrelor rapidly and efficiently from human blood *in vitro*. Meanwhile, a retrospective case series reported by clinicians at Asklepios Klinik St. Georg in Hamburg, Germany on the investigational use of CytoSorb to reverse the effects of ticagrelor during emergency cardiac surgery demonstrated a greatly reduced risk of bleeding complications and the need for repeat surgery to explore the source of bleeding, with extrapolations showing projected cost savings of £3,982, or approximately $5,000 USD, per patient in a U.K. based study.

Projected Timeline: Cardiac surgeons, cardiac perfusionists, and cardiothoracic ICU intensivists in Germany, Austria, and other countries have now used CytoSorb intra-operatively and post-operatively in more than 40,000 treatments in cardiac surgery patients. This application is also the focus of number of planned and enrolling company-sponsored and investigator-initiated studies in the United States and Europe.

CytoSorb is the subject of a pivotal, 400-patient randomized controlled trial in the United States called the REFRESH 2-AKI trial. Two CytoSorb cartridges are being used intraoperatively to reduce activated complement, free hemoglobin, and other inflammatory toxins that are generated during valve replacement surgery as well as aortic reconstruction with hypothermic cardiac

arrest, with the goal of reducing the risk of acute kidney injury. Acute kidney injury following cardiac surgery is associated with an increased risk of death in the first 5 years after surgery. The trial has enrolled more than 150 patients to date. The Company has been undertaking multiple activities in preparation to resume the study, which is estimated to take place in the first half of 2021. If the study is successful, we plan to submit a PMA application to the FDA in 2023 for U.S. regulatory approval.

The 250-patient randomized controlled REMOVE infective endocarditis trial was completed in January 2020. The COVID-19 pandemic has caused delays in data monitoring and data analysis. Topline data are expected to be reported in the first half of 2021 with full data presentation at a major international conference also in 2021.

We are currently conducting the 30-patient, single arm trial in the United Kingdom called the TISORB trial, obtaining more country-specific data to support the use of CytoSorb to remove ticagrelor in emergent or urgent cardiac surgery to reduce perioperatively bleeding complications. Due to the COVID-19 pandemic, the execution of the TISORB trial has been greatly impacted and ongoing national restrictions in the UK on the conduct of non-COVID clinical studies add further uncertainty to TISORB.

For further detailed information regarding our clinical trial strategy, see the section entitled "Clinical Studies" of this Item 1 of this Report.

APPLICATION : *Maintaining or improving the quality of solid organs harvested from donors for organ transplant*

Potential Benefits:

ECOS-300CY: Solid organ transplant is very costly, and the success of the transplant is heavily dependent upon the health and quality of the harvested organs. ECOS-300CY was designed to maintain or improve the quality of these organs prior to transplant in an ex vivo perfusion system, and may have the benefit of improving outcomes in organ transplant and also increasing the availability of organs by rehabilitating organs that would have otherwise been discarded.

CytoSorb : By preventing or reducing 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: ECOS-300CY: The ECOS-300CY was approved in the E.U. for the removal of inflammatory mediators during ex vivo organ perfusion under CE Mark designation in 2020. CytoSorbents announced a partnership with Aferetica srl to provide the ECOS-300CY cartridge under the exclusive trade name, PerSorb™, that is compatible with Aferetica's PerLife™ ex vivo organ perfusion system, recently approved in the E.U. as well.

CytoSorb for brain dead organ donors: 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 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 RBC 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 3% to 5%), the sheer number of blood transfusions is so large, that the number of transfusion reactions, ranging from mild to life-threatening, is substantial, ranging from several hundreds of thousands to millions of reactions each year. In critically-ill patients, the risk of transfusion reactions is significantly higher than in the general population and can increase the risk of death because their underlying illnesses have depleted protective mechanisms and have primed their bodies to respond more vigorously to transfusion-associated insults.

A number of retrospective studies have also suggested that administration of older blood leads to increased adverse events and even increased mortality, compared with blood recently harvested. Biological studies have demonstrated the accumulation of erythrocyte storage lesions that compromise the function and structural integrity of packed red blood cells and have also demonstrated the accumulation of substances during blood storage that can lead to transfusion reactions. Three adult, prospective, randomized, controlled studies, RECESS (completed), ABLE (completed), and TRANSFUSE (completed) were designed to evaluate the morbidity and mortality in cardiovascular surgery patients (RECESS) and critically ill patients (ABLE and TRANSFUSE), 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 Operations Command (USSOCOM)), and more recently under a $3M multi-year Phase IIB bridge contract funded by NHLBI. As a result of delays caused by the COVID-19 pandemic, we expect to complete bench testing required for U.S. approval in 2021, and advance the in-line filter to human testing in the first half of 2022.

APPLICATION: Removal of anti-A and anti-B blood group antibodies from fresh whole blood and plasma

Potential Benefits: The HemoDefend-BGA blood purification technology platform is designed to reduce anti-A and anti-B antibodies in plasma and whole blood. The goal is to either enable the production of universal plasma, or enable fresh warm whole blood transfusions. 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;
- eliminate the need to blood-type plasma, improving its availability
- enable the use of low titer whole blood, ideal for trauma resuscitation; and
- easier processing of blood products.

Background and Rationale: Plasma is the straw-colored, cell-free portion of whole blood. It contains a wide range of important substances such as electrolytes, hormones, proteins such as albumin, clotting factors, and antibodies. The transfusion of plasma, or plasma-derived products, is used widely to help save the lives of trauma and bleeding victims, septic and other critically-ill patients, and patients with life-threatening blood coagulation and autoimmune disorders. In 2008, more than 4.5 million units of plasma were transfused in the United States alone. With the exception of the relatively uncommon Type AB, or "universal" plasma, most plasma contains blood-type specific antibodies and must be cross-matched with the intended recipient ahead of time or risk serious transfusion reactions. By reducing these blood-type specific antibodies, the goal is to create a cost-effective, reliable, and expanded source of "universal" plasma that can be administered immediately, without blood-typing, in a wide range of emergent and non-emergent situations.

Projected Timeline: The HemoDefend-BGA platform is a development stage product based on our advanced blood purification technology. Prototype filtration devices have been evaluated by a government agency, resulting in excellent depletion of both anti-A and anti-B antibodies. Work is continuing to advance these prototypes to commercial-ready devices. This work has received cumulatively approximately $9.6 million in Phase I and II Small Business Technology Transfer (STTR) funding by the U.S. Army Medical Research Acquisition Activity (USAMRAA), U.S. Army Medical Research and Materiel Command (USAMRMC), Defense Health Agency, and CDMRP.

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 U.S. Army and Defense Health Agency under under a Phase I and Phase II SBIR contract for a total of $1.15 million and a $3 million Rapid Innovation Fund (RIF) award from the U.S. Air Force Materiel Command. 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 Biologics Limited

In September 2013, we entered into a distribution agreement with Biocon Biologics Limited, ("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. Under the terms of the expanded partnership, the term of the distribution agreement was extended to December 2022. On May 27, 2020, Biocon announced that CytoSorb has received approval from the Drugs Controller General of India to treat COVID-19 patients in certain instances.

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, in 2019, Poland, Sweden, Denmark, and Norway were 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 underway in both countries after securing market registration clearance from the South Korean and Mexican health authorities in 2021 and 2020, respectively. These multi-year agreements include an initial stocking order and are subject to annual minimum purchases of CytoSorb to maintain exclusivity. These agreements, which commenced on January 1, 2019, have an initial term of three years and will automatically renew for an additional two years unless terminated by either party.

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 was renewed through 2023.

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. In the fourth quarter of 2020, Aferetica announced CE Mark registration of the PerLife system. At the same time, CytoSorbents announced CE Mark approval of the ECOS-300CY cartridge for the removal of inflammatory mediators during ex vivo perfusion, which has been designated, PerSorb™, a trade name exclusive to the PerLife 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, N

In August 2020, we announced an initial collaboration with Terumo to exclusively sell CytoSorb to hospitals in ten U.S. COVID-19 hotspot states including Alabama, Arizona, California, Georgia, Louisiana, Mississippi, New Mexico, Oregon, Texas, and Washington. CytoSorb previously received Emergency Use Authorization (EUA) by the U.S. Food and Drug Administration (FDA) for use in adult, critically-ill COVID-19 patients with imminent or confirmed respiratory failure. Under the initial terms of the agreement, Terumo will ensure hospitals in the defined hot-spot states have access to the CytoSorb therapy for use in critically-ill COVID-19 patients that meet strict criteria under CytoSorbents' EUA. CytoSorbents will provide all primary clinical and technical training, customer support, and product fulfillment.

B. Braun Avitum AG

In March 2021, we announced announce the launch of a global co-marketing agreement with B. Braun Avitum AG to promote the use of CytoSorb® with B. Braun's latest OMNI® continuous blood purification platform and OMNIset® Plus bloodline set (set version 3.0 or higher). The CytoSorb® adsorber is used in critical care for the extracorporeal removal of cytokines and inflammatory mediators from the bloodstream and can be operated with the B. Braun OMNI® acute dialysis machine. B. Braun will supply the market with the OMNI® and OMNIset® Plus while CytoSorbents and its network of direct sales, strategic partners, and distributors will continue to supply the market with CytoSorb®. CytoSorb® is CE Mark certified and distributed in 67 countries worldwide. This global co-marketing agreement applies to the countries where both products are registered (US market is specifically excluded). Financial terms of this agreement have not been disclosed.

B. Braun is one of the world's leading manufacturers of medical devices and pharmaceutical products and services. With 64,000 employees in 64 countries, B. Braun develops high quality product systems and services for users around the world. In 2019, the Group generated sales of €7.5 billion.

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.

Dr. John Kellum, a member of the UPMC faculty since 1994, was the Chairman of our Sepsis Advisory Board. On March 1, 2021, Dr. Kellum became the Chief Medical Officer for Toronto, Canada-based Spectral Medical, Inc. Concurrent with his appointment at Spectral, Dr. Kellum formally resigned from our Advisory Board.

Advisory Boards

From time to time our management meets with scientific advisors who sit on our Scientific Advisory Boards (“SAB”). We have 3 SABs that include a Basic Science and Technology SAB, a Critical Care Medicine SAB, and a Cardiac Surgery SAB. Each SAB comprises of approximately five scientists with deep expertise in their respective fields. We compensate all our SAB members according to fair market value and reimburse them for their travel expenses when attending meetings in person.

Royalty Agreement

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 (the “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. In February 2017, all rights, title and interest to the Royalty was assigned to The Robert Shipley Living Trust. For the year ended December 31, 2020 we have recorded royalty costs of approximately $1,172,000.

License Agreement

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, 2020 per the terms of the license agreement we have recorded royalty costs of approximately $1,954,000.

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, we have additional issued patents separate from those in this Settlement Agreement, and patents pending worldwide that may extend patent protection of our core technology. We will also continue to exclusively own any confidential and proprietary know how.

Product Payment & Reimbursement

CytoSorb

Germany

Effective January 1, 2017, we achieved a dedicated reimbursement code in Germany that provides for specific and enhanced reimbursement for our CytoSorb device. We believe in most cases that this dedicated reimbursement code provides our customers in Germany with 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

In 2019, CytoSorb was assigned two specific procedure codes from the Swiss Federal Statistical Office, a division of the Federal Department of Home Affairs in Switzerland. With cost data related to use of the CytoSorb device, a prerequisite for receiving reimbursement from the Swiss DRG system, we expect to receive a response soon regarding reimbursement levels.

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. Additional clinical data may 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. but has received FDA Emergency Use Authorization in April 2020 for use in adult critically ill COVID-19 patients with imminent or confirmed respiratory failure. There is currently no specific reimbursement for CytoSorb in the U.S. Payment for our CytoSorb device in the U.S. for this application falls 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.

In January 2021, the Centers for the Centers for Medicare & Medicaid Services (CMS) announced the Medicare Coverage of Innovative Technology pathway that will provide national Medicare coverage as early as the same day as FDA market authorization for Breakthrough medical devices, where coverage would last 4 years. This program may be applicable to CytoSorb, if it can achieve U.S. approval for the removal of ticagrelor during emergent or urgent cardiothoracic surgery, which was granted FDA Breakthrough Designation in April 2020.

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, renal disease and drug intoxication. 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® did 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.

There have been many large scale clinical trials in sepsis. The primary outcomes of these studies have generally included:

- number of days alive without CV, renal, or pulmonary organ support
- number of 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)

COVID-19 disrupted many clinical studies in 2020. 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 2019, the results of the study were published in JAMA, demonstrating no benefit in 28-day all-cause mortality. The 800 patient Phase III SCARLET-2 randomized, controlled trial, evaluating Recomodulin in patients with sepsis and coagulopathy, was scheduled to begin in July 2019, but was withdrawn to be amended following the results of the SCARLET trial. The status of the trial is unknown.

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 to the CD28 co-stimulatory receptor to attempt to restore the host's appropriate immune response to severe infections and was evaluated in the ACCUTE Trial, a Phase III randomized controlled trial in 60 investigative sites in the U.S in 290 patients with necrotizing soft tissue infections. The primary endpoint of the study was based on a modified Intent-to-treat (mITT) analysis of a primary composite endpoint that was defined as: alive at day 28, ≤ 3 debridements, no amputation beyond first operation, and day 14 mSOFA ≤ 1 with ≥ 3 point reduction (organ dysfunction resolution). A prespecified, per protocol (PP) analysis excluded 17 patients with major protocol violations before unblinding. There was no difference in 28-day mortality of 15% in each group, and the study did not reach significant improvement in the primary endpoint in the pre-defined mITT population. However, in the PP analysis that excluded 17 patients, the company claims clinical composite endpoint success of 54.3% treatment vs 40.3% control. In December 2020, Atox Bio announced that they had filed an NDA under the FDA Accelerated Approval Program with a PDUFA date of September 30, 2021.In January 2021, the company announced the termination of its Phase 3 REAKT (Reltecimod Efficacy for Acute Kidney Injury Trial) trial in patients with abdominal sepsis induced AKI due to slow enrollment.

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. Based on the 179 patients from the EUPHRATES trial, treated patients had a mortality of 38% (N=90) compared to 48% mortality in the control (N=89), but not statistically significant. The TIGRIS study will be in US sites only, randomized (2:1), open label trial, with an additional 150 new patients (100 treated, 50 control) to be added. Projected completion of trial enrollment at 10 sites is 18 months (projected June 2022).

Enlivex has developed an investigational cell-based therapy called Allocetra that is an infusion of donor mononuclear cells that have been chemically induced to be apoptotic. Once infused, the patient's macrophages and dendritic cells phagocytose these apoptotic cells which purportedly then causes them to reduce inflammatory signals that results in immune modulation. Enlivex recently reported on the use of its therapy, as a single or double dose in a single arm Phase IB study in 10 patients who presented with sepsis to the emergency room with a SOFA score > 2 above baseline. The severity of illness in this patient population was low, with a mean APACHE II score of 12.9 (range 8-21) and a predicted mortality of approximately 15%, and a mean SOFA score of 3.4 (range 2-6), with a predicted mortality of less than 10%. There were no deaths reported in the study. Results were compared with a poorly matched and significantly sicker control population who were admitted to the intensive care unit or intermediate care unit.

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 was terminated early at 501 patients due to a withdrawal of funding from the study, with results published in JAMA in February 2021. Ventilator- and vasopressor-free days showed no significant improvement with a median of 25 days (IQR, 0-29 days) in the intervention group and 26 days (IQR, 0-28 days) in the placebo group, with a median difference of −1 day (95% CI, −4 to 2 days; P = .85). Thirty-day mortality was 22% in the intervention group and 24% in the placebo group and was not statistically significant. 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 (1500 mg/d), thiamine (100 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. Results from this study were published in JAMA in August 2020. Change in the SOFA score was 4.7 in the intervention group vs 4.1 in the placebo group over 72 hours, a difference that was not statistically significant. 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. The results of the VITAMINS trial were published in JAMA in January 2020, concluding that treatment with vitamin C, hydrocortisone, and thiamine, compared with intravenous hydrocortisone alone, did not significantly improve the duration of time alive and free of vasopressor administration over 7 days, and does not lead to a more rapid resolution of septic shock compared with intravenous hydrocortisone alone. Ninety-day mortality was 28.6% in the treatment group, and 24.5% in the control group. The authors of these studies do not recommend the routine use of the combination of Vitamin C, corticosteroids, and thiamine in septic shock patients.

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 the 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. The estimated study completion date is March 2022. In 2020, oXiris received FDA Emergency Use Authorization for use in adult critically ill COVID-19 patients in imminent or confirmed respiratory failure. In October 2020, results from 4 hospitals on 37 patients from its OxirisNet Registry in the journal, Critical Care.

Mortality was 66.6% in patients receiving oXiris treatment after 14 days from admission, and a mortality of 47.4% mortality when used earlier. 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 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. In April 2018, Medtronic issued a field safety notice informing all users of CPFA that the COMPACT-2 study using CPFA in septic shock patients was terminated early due to observed higher mortality rates in septic shock patients receiving CPFA therapy compared to patients receiving standard care. The CPFA system is similar to the I.M.P.A.C.T. System that was 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. 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. The estimated study completion date is October 2020. 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 was 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., had 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 company appears to no longer be in business. 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 efficacy of bacterial removal from blood. It received EU CE-Mark approval in July 2019, and established distribution in Germany, Italy and Benelux. In addition, in 2013, it partnered with BioBridge Global to apply its technology to pathogen reduction in transfused

blood products. In 2020, Seraph received FDA Emergency Use Authorization for use in adult critically ill COVID-19 patients to reduce pathogens and inflammatory mediators from the bloodstream. 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. 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, prone ventilation, and extracorporeal membrane oxygenation ("ECMO"). Although a number of therapies have been tried such as nitric oxide, surfactant therapy, and others, only corticosteroids, such a dexamethasone or methylprednisolone, have demonstrated mortality benefit in patients with ARDS. For example, in critically ill COVID-19 patients on mechanical ventilation, the RECOVERY study demonstrated use of once daily dexamethasone led to a reduction in mortality from 41.4% control to 29.3% treatment.

See "Markets: Acute Respiratory Distress Syndrome" above for a more detailed discussion.

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 Intoxication

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 gastric 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 $beta_2$–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.

Use for Organ Transplant in *Ex Vivo* Organ Perfusion Systems or in the 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, *or in the removal of inflammatory mediators during ex vivo organ perfusion*

Removal of Anti-thrombotics such as Ticagrelor in Cardiac Patients During Surgery Requiring Cardiopulmonary Bypass

There are more than $20 billion in annual worldwide sales of anti-thrombotic drugs such as the $P2Y^{12}$ platelet inhibitors (e.g. clopidogrel, ticagrelor, prasugrel), and the Direct Oral AntiCoagulants (DOAC) comprising of direct thrombin inhibitors (dabigatran), and Factor Xa inhibitors (e.g. apixaban, rivaroxaban, edoxaban). These are generally used to reduce thromboembolic events in a wide range of applications, including dual anti-platelet therapy in percutaneous coronary intervention and stent placement, myocardial

infarction, stroke, peripheral artery disease, atrial fibrillation, deep vein thrombosis, pulmonary embolus, and others. For example, ticagrelor (Brilinta®, Astra Zeneca) is a widely-used anti-platelet agent used to decrease cardiovascular risk in patients with acute coronary syndromes or a past history of heart attack. It is also widely used during as part of the dual-anti platelet therapy regimen in patients undergoing percutaneous coronary intervention and stent placement. However, when patients on ticagrelor require emergent or urgent cardiac surgery, up to 65% of patients will have severe or massive peri-operative bleeding complications that contributes to a high risk of morbidity and death and major costs to the healthcare system.

To our knowledge, CytoSorb is the only therapy approved for the removal of ticagrelor and rivaroxaban (Xarelto®, Janssen, Bayer) in the E.U. during cardiopulmonary bypass in urgent or emergent cardiopulmonary bypass. The only recommended alternative is to wait for 3-5 days to allow natural drug elimination and washout prior to surgery.

CytoSorb has already demonstrated the ability to remove ticagrelor rapidly and efficiently from human blood *in vitro*. Meanwhile, a retrospective case series reported by clinicians at Asklepios Klinik St. Georg in Hamburg, Germany on the investigational use of CytoSorb to reverse the effects of ticagrelor and the Factor Xa inhibitor, rivaroxaban, during emergency cardiac surgery demonstrated a greatly reduced risk of bleeding complications and the need for repeat surgery to explore the source of bleeding. Extrapolations of the clinical benefits showed projected cost savings of £3,982, or approximately $5,000 USD, per patient in a U.K. based economics study. CytoSorb recently received E.U. CE Mark label expansion to remove ticagrelor and rivaroxaban during cardiac surgery involving cardiopulmonary bypass via label expansion of its CE Mark. We are currently executing the Safe and Timely Antithrombotic Removal (STAR) international registry collecting real world evidence in this application and two multicenter prospective single arm studies (TISORB in the UK and CYTATION in Germany) to obtain more country-specific data to support the use of CytoSorb for reduction of peri-operative bleeding complications in urgent or emergent cardiac surgery.

The use of platelet transfusions, Kcentra® (CSL Behring; four factor prothrombin complex concentrate; reversal for warfarin anticoagulation), Andexxa® (recombinant Factor Xa; AstraZeneca; reversal for rivaroxaban and apixaban), Praxbind® (idarucizumab, Boeringer Ingelheim; reversal agent for dabigatran) and other interventions have either not demonstrated consistent benefit, or are not used because of potential safety concerns, in the reversal of antithrombotics in the setting of cardiopulmonary bypass.

PhaseBio, a clinical-stage biopharmaceutical company, has licensed an intravenously administered monoclonal antibody fragment with high affinity for ticagrelor called bentracimab (PB2452) from Medimmune, a division of AstraZeneca. The company paid AstraZeneca $100,000 upfront, with $68 million in potential future milestones. AstraZeneca owns approximately 5% of PhaseBio's stock. PB2452 is a novel reversal agent for the antiplatelet drug ticagrelor, which was developed for the treatment of patients on ticagrelor who are experiencing a major bleeding event or those who require urgent surgery. The FDA granted Breakthrough Therapy designation for PB2452 in April 2019. PhaseBio is seeking US FDA approval of PB2452 in the United States through an accelerated approval process.

PhaseBio is currently conducting a U.S. Phase 2b clinical study evaluating the safety and efficacy of PB2452 in approximately 200 healthy volunteers aged 50-80. Patients receive loading with dual anti-platelet therapy consisting of aspirin and ticagrelor in the U.S. and will be evaluated on the ability of PB2452 to reverse platelet dysfunction. PhaseBio has also launched its REVERSE-IT (Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial) study, a Phase 3, multi-center, open-label, prospective single-arm trial designed to study reversal of the antiplatelet effects of ticagrelor with bentracimab in patients who present with uncontrolled major or life-threatening bleeding or who require urgent surgery or invasive procedure. Approximately 200 adult patients, within 72 hours of ticagrelor intake who require urgent reversal of the antiplatelet effects of ticagrelor, are being targeted to be enrolled from centers in the U.S. and worldwide. Patients with reported use of ticagrelor within the prior 3 days who require urgent ticagrelor reversal are eligible for enrollment. Patients receive an intravenous (IV) infusion comprised of an initial IV bolus of 6 grams (g) infused over 10 minutes for rapid reversal, followed immediately by a 6g IV loading infusion over 4 hours and then a 6 g IV maintenance infusion over 12 hours. In January 2021, PhaseBio expanded the study to include patients in the European Union. The primary endpoints of the study are: 1) reversal of platelet inhibition 2) Major life-threatening bleeding and 3) achievement of hemostasis in urgent surgery or invasive procedures. Bentracimab is not yet approved in any market.

Based on feedback from the FDA, PhaseBio intends to submit a Biologics License Application, or BLA, for potential accelerated approval based on an interim analysis of the first approximately 100 patients treated in their Phase 3 trial, with approximately 50 subjects from each of the major bleeding and surgical populations. To support full approval for patients with major bleeding or requiring urgent surgery, the FDA recommended enrollment of 200 total patients in the Phase 3 trial. For post-approval commitments, the FDA recommended the completion of the remaining portions of the Phase 3 trial and the establishment of post-approval registry.

Meanwhile, Andexxa is a Factor Xa analog that competes for binding to Factor Xa inhibitors. Due to the short duration of action, pro-thrombotic effect, and very high cost, it is not indicated to reduce the risk of perioperative bleeding in cardiac surgery.

CytoSorb has demonstrated very efficient removal of all the major drugs of the DOAC category in clinical use today including rivaroxaban (Xarelto®; Bayer, Janssen), apixaban (Eliquis®, Bristol-Myers Squibb), edoxaban (Savaysa®, Daiichi-Sankyo) and dabigatran (Pradaxa®, Boehringer Ingelheim).

We believe that CytoSorb represents a more cost-effective, readily available, and easy to implement solution for ticagrelor or DOAC reversal in cardiac surgery than these biologic alternatives.

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 (Haemonetics, 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.

Critical Care

In 2011, the CytoSorb adsorber 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.

In September 2019, a new publication entitled, "Hemoadsorption with CytoSorb showed a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study," in the journal Critical Care. In this study, clinical researchers at Maasstad Hospital and at Erasmus University Medical Center in Rotterdam, Netherlands conducted a retrospective evaluation of 116 patients with septic shock, who required vasopressors to increase their blood pressure, and renal replacement therapy (RRT) due to kidney failure. Of these, 49 patients received standard of care therapy, and 67 were treated with standard of care plus CytoSorb. Both groups were compared by stabilized Inverse Probability of Treatment Weights (sIPTW) to overcome baseline differences in the type of sepsis, age, comorbidities, surgery vs no surgery, Sequential Organ Failure Assessment (SOFA) score, use of the vasopressor noradrenaline, and lactate levels. Patients treated with standard of care and CytoSorb had a statistically significant reduction in 28-day all-cause mortality compared to standard of care alone (53% vs 72% control, $p<0.04$), based on the sIPTW analysis. In addition, observed 28-day all-cause mortality in the CytoSorb treatment group was significantly lower than the predicted mortality (48% observed vs 75% predicted, $p<0.001$), based on SOFA score.

In April 2020 the FDA granted Emergency Use Authorization for CytoSorb use in critically ill COVID-19 patients treated in the ICU. The company is conducting the CytoSorb Therapy in COVID-19 (CTC) Registry to systematically capture high fidelity data from U.S.institutions using CytoSorb under the EUA.

Cardiac Surgery

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 study 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 two CytoSorb devices 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 study. 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. The REFRESH I study represented the first randomized controlled study demonstrating the safety of intra-operative CytoSorb use in patients undergoing high risk cardiac operations.

Investigators of the REFRESH I study submitted an abstract with data, including free hemoglobin data, from the REFRESH I study 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 in May 2019, the manuscript of the REFRESH I study was electronically published in the journal, Seminars in Thoracic and Cardiovascular Surgery.

In December 2017, the FDA approved our IDE application for our REFRESH 2-AKI study, permitting us to conduct this pivotal study 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 study is a randomized, controlled, multi-center, clinical study designed to evaluate intraoperative use of two CytoSorb devices 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 higher mortality, and is a risk factor for developing chronic kidney disease requiring hemodialysis in the future. The study 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 study. Based on the recommendations of key clinical advisors, a protocol amendment was submitted to the FDA on July 19, 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, announced in September 2018. On November 25, 2019 the Company announced a pause in enrollment for the REFRESH 2-AKI study. The study's Data Monitoring Committee (the "DMC") recommended this pause following a blinded, interim, milestone review of clinical study data. The DMC requested that additional clinical data and data analysis, not pre-specified in the current version of the protocol, be provided by Company. In addition, the Company appointed NAMSA as the new contract research organization ("CRO") for the study to improve the monitoring of patient safety endpoints. As of November 25, 2019, the study had enrolled 153 patients at 25 initiated sites. Since then, the Company and its new CRO have completed a comprehensive program to re-monitor existing data, collect new data, and analyze the safety data from the 153 patients included in the trial to date. These data were reviewed by the DMC resulting in a favorable opinion on safety, dated July 24, 2020, and the recommendation to resume the trial with only minor modifications. The Company has been undertaking multiple activities in preparation to resume the study, which is planned in the first half of 2021, notwithstanding potential COVID-19 related delays. If the study is successful, we plan to submit a PMA application to the FDA in 2023 for U.S. regulatory approval.

In October 2019, CytoSorbents initiated TISORB (Ticagrelor CytoSorb Hemoadsorption), a Company-sponsored, multi-center single arm study in the United Kingdom to prospectively evaluate the removal of ticagrelor during cardiopulmonary bypass in patients on ticagrelor undergoing emergent cardiothoracic surgery. A protocol amendment was submitted to expand the population of eligible patients to now include patients requiring urgent cardiac surgery. These changes were approved by the UK Medicines and Healthcare products Regulatory Agency (MHRA) at the end of February 2020. In December 2020, CytoSorbents initiated CYTATION (CytoSorb Ticagrelor Hemoadsorption), a Company-sponsored multicenter study in Germany to prospectively evaluate the removal of ticagrelor during cardiopulmonary bypass in patients on ticagrelor undergoing emergent cardiothoracic surgery. Ticagrelor (Brilinta®, Astra Zeneca) is a potent platelet inhibitor and antithrombotic therapy and recognized as a standard of care to reduce the risk of heart attacks and strokes in patients with acute coronary syndromes. Unfortunately, given the absence of an approved treatment to reverse the antithrombotic effects of ticagrelor, treated patients who require urgent or emergent cardiothoracic surgery may either proceed at high risk for severe perioperative bleeding (as high as 65% higher risk due to ticagrelor) or stay waiting for days in the hospital until the ticagrelor antithrombotic effect washes out. Neither option is optimal since patients proceeding to surgery are at great risk for serious or even fatal bleeding and patients waiting for washout are at risk of a thrombotic complications such as a stroke or heart attack, while delaying surgery and increasing hospitalization costs. The benefits of CytoSorb in this setting are both clinical and economic. In the publication in 2019 by Hassan et al, outcomes of 55 patients requiring emergent cardiac surgery while on ticagrelor or rivaroxaban therapy were evaluated according to the use of CytoSorb. Antithrombotic (either ticagrelor or rivaroxaban) removal with CytoSorb was associated with significant reductions in operative time, need for red blood cell and platelet transfusions and re-operations to control bleeding and those clinical benefits resulted in shorter length of ICU stay. These significant clinical benefits are expected to also result in substantial economic benefits. This was demonstrated in the publication by Javanbakht et al. in 2019, that projected an average cost savings of £3,982 per patient (approximately $5,000 USD per patient), including the cost of the CytoSorb adsorber. The primary objective in both TISORB and CYTATION studies is the change in platelet reactivity and ticagrelor blood concentration before and after cardiopulmonary bypass for patients undergoing CytoSorb hemoadsorption removal of ticagrelor from their blood. Due to the COVID-19 pandemic, the execution of the TISORB trial has been greatly impacted and ongoing national restrictions in the UK on the conduct of non-COVID clinical studies add further uncertainty to TISORB. In Germany, however, clinical research is continuing and we therefore expect that the CYTATION study will not be equally impacted.

In January 2020, CytoSorb received European Union CE Mark label expansion to include the removal of ticagrelor during cardiopulmonary bypass in patients undergoing cardiothoracic surgery. In May 2020, CytoSorb also received European Union CE Mark label expansion to include rivaroxaban removal for the same indication. We have recently announced the Safe and Timely Antithrombotic Removal (STAR) development program that will comprise of a number of clinical projects relating to the antithrombotic removal application. The first study is the STAR Registry scheduled to commence enrollment in 2021 that will capture real world use of CytoSorb for this indication. The registry will initially launch in Europe with the intent of expanding to the United States and the rest of the territories where CytoSorb is available in the future. We anticipate that additional clinical studies, including randomized clinical trials on antithrombotic removal will be conducted as part of the STAR program.

Update on the REMOVE Investigator Initiated Study

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. An 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 study, 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." The study completed enrollment in 2020 but the COVID-19 pandemic has caused delays in data monitoring and data analysis. Topline data are expected to be reported in the first half of 2021 with full data presentation at a major international conference also in 2021.

COVID-19 Business Update

COVID-19 patients develop life-threatening complications such as ARDS, shock (i.e. a potentially fatal drop in blood pressure), kidney failure, acute cardiac injury and secondary bacterial infections. The underlying cause for these complications is often a cytokine storm that results in a massive, systemic inflammatory response, leading to the damage of vital organs such as the lungs, heart, and kidneys, and ultimately multiple organ failure and death in many cases. CytoSorb has been used in more than 121,000 treatments as an approved treatment of cytokine storm in the European Union and is distributed in 67 countries around the world, where it has helped physicians control severe inflammation while helping to reverse shock and improve lung and other organ function.

The use of CytoSorb in patients infected with COVID-19 in Italy, China, Germany and France began in March 2020. CytoSorb has now been used in approximately 5,000 COVID-19 patients to help treat cytokine storm and the related life-threatening complications in more than 30 countries. Based upon initial data and reports from physicians treating these complications, CytoSorb use has generally been associated with a marked reduction in cytokine storm and inflammation, improved lung function, weaning from mechanical ventilation, decannulation from extracorporeal membrane oxygenation (ECMO), and a reversal of shock. CytoSorb has been specifically recommended in the Italy Brescia Renal COVID Task Force Guidelines to treat patients with severe COVID-19 infection and Stage 3 renal failure on continuous renal replacement therapy. CytoSorb has also been recommended in the National Treatment Guidelines from Panama for Adult COVID-19 Patients if patients have either refractory shock, or have severe or refractory respiratory failure requiring either high ventilator support or extracorporeal membrane oxygenation. CytoSorb has now received approval from the Drugs Controller General of India to treat COVID-19 patients in certain instances. CytoSorb has also received approval to treat patients with COVID-19 from the Israel Ministry of Health (AMAR). In January 2021, Health Canada granted Medical Device Authorization for the importation, sale, and emergency use of CytoSorb in hospitalized COVID-19 patients.

The use of CytoSorb has not been approved in the U.S. by FDA. However, under certain circumstances, investigational medical devices that have not yet been FDA-approved may be made available for emergency use in the U.S. under the FDA's Expanded Access Program ("EAP"). On April 13, 2020, we announced that the FDA, in a different program than the EAP, granted Emergency Use Authorization (EUA) of CytoSorb for use in U.S. COVID-19 patients. Under the EUA, CytoSorbents can make CytoSorb available, through commercial sales, to all hospitals in the U.S. for use in patients, 18 years of age or older, with confirmed COVID-19 infection who are admitted to the intensive care unit with confirmed or imminent respiratory failure and who have early acute lung injury or ARDS, severe disease, or life-threatening illness resulting in respiratory failure, septic shock, and/or multiple organ dysfunction or failure. The CytoSorb device has been authorized by FDA under an EUA. It has neither been cleared nor approved for the indication to treat patients with COVID-19 Infection. The EUA will be effective until a declaration is made that the circumstances justifying the EUA have terminated or until revoked by the FDA.

The CTC (CytoSorb Therapy in COVID-19) Registry has been launched and is actively enrolling patients with the intent of systematically capturing usage patterns and outcomes associated with the use of CytoSorb under the EUA at U.S. institutions. The CTC Registry may be expanded to outside-U.S. territories based on the evolution of the pandemic in an effort to better characterize best practice patterns and clinical outcomes.

To meet the growing demand for CytoSorb worldwide, our manufacturing team continues to make any adjustments required to the production schedule to meet the increased sales demand.

Government Research Grants

We have historically 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 ("DARPA"), the U.S. Army, U.S. Special Operations Command ("USSOCOM"), the U.S. Air Force, Air Force Material Command ("USAF/AFMC") and others. Currently, we have ongoing projects funded, in part, by the U.S. Army Medical Research Acquisition Activity ("USAMRAA"), the NHLBI, and the USAF/AFMC.

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. We received approximately $3,825,000 in funding under this contract and no funding remains. Our performance under this contract has been completed.

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. We received approximately $1,246,000 in funding under this contract and no funding remains. Our performance under this contract has been completed.

In September 2013, the National Heart Lung and Blood Institute ("NHLBI") awarded us a Phase I Small Business Innovation Research ("SBIR") 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 and USSOCOM 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. We received approximately $1,524,000 under this contract and no funding remains. 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 Adsorption 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. Our performance under this contract has been completed.

In June 2016, we were awarded a Phase I Small Business Technology Transfer ("STTR") contract for its 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 was 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 remains under this contract. Our performance under this contract has been completed.

In July 2016, we were awarded a Phase I 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 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. Our performance under this contract has been completed.

In January 2017, we were awarded a Phase II SBIR contract to continue development of CytoSorb for fungal mycotoxin blood purification. This program focused on demonstrating the ability of CytoSorb to adsorb mycotoxins *in vivo* and improve survival in animals. This contract, W911QY-17-C-0007, provided for maximum funding of $999,996 over two years. This program was funded by the Joint Program Executive Office - Chemical and Biological Defense ("CBD") SBIR program. We received approximately $999,996 in funding under this contract and no further funding remains under this contract. Our performance under this contract has been completed.

In May 2017, we were awarded a Phase II STTR contract entitled "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 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. We received approximately $999,070 and no further funding remaining under this contract. Our performance under this contract has been completed.

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, 2020, we received approximately $659,000 and have approximately $60,000 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 approximately $999,871. As of December 31, 2020, we received approximately $999,871 and no further funding remains under this contract.

In August 2018, the Company was 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, 2020, we received approximately $1,646,000 in funding under this contract and have approximately $1,325,000 remaining under this contract. Under the terms of this contract, we must make a matching contribution equal to the funds awarded thereunder.

In September 2019, the Company was awarded a Rapid Innovation Fund contract by the USAF/AFMC to develop a simple, easy-to-use renal support system to treat severe hyperkalemia. The contract, entitled "K+ontrol Renal Support System for Reduction of Hyperkalemia" (award number FA8650-19-C-6065), provides for maximum funding of approximately $2,960,000 over a two-year period. As of December 31, 2020, we received approximately $814,000 funding under this contract and have approximately $2,146,000 remaining under this contract.

In June 2020, the Company was awarded a two-year Defense Health Agency Small Business Technology transfer (STTR) Phase III contract to advance its HemoDefend-BGA plasma and whole blood adsorber to human clinical trials. (award number *W81XWH20C0050*), provides for maximum funding of approximately $2,897,000 over a two-year period. As of December 31, 2020, we received approximately $724,000 funding under this contract and have approximately $2,173,000 remaining under this contract.

In July 2020, the Company was awarded by the Assistant Secretary of Defense for Health Affairs, endorsed by the Department of Defense office of the Congressionally Directed Medical Research Programs (CDMRP), a three-year contract as part of a Peer Reviewed Medical Research Program Technology/ Therapeutic Development Award to complete preclinical development of the HemoDefend™-BGA plasma and whole blood adsorber, (award number W81XWH2010712), provides for maximum funding of approximately $4,422,000 over a three-year period. As of December 31, 2020, we received approximately $81,000 funding under this contract and have approximately $4,341,000 remaining under this contract.

In October 2020, the Company was awarded a two-year SBIR Sequential Phase II contract by the U.S. Army Medical Research Acquisition Activity (USAMRAA), to optimize development of the HemoDefend-BGA™ adsorber. (award number W81XWH20C0087), provides for maximum funding of approximately $1,100,000 over a two-year period. As of December 31, 2020, we received approximately $133,000 funding under this contract and have approximately $967,000 remaining under this contract.

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 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.

The COVID-19 pandemic also has slowed progress on executing and invoicing for our funded grant and contract programs. This was due to social distancing and remote working requirements in our laboratories and at the facilities of our collaborators. Given the uncertain nature of COVID-19, we cannot predict the future impact of the pandemic on our research and development efforts and on our revenue recognition for total revenue.

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 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 be conducted before a device receives approval for commercial distribution.

In the EU, medical devices that we manufacture are required to comply with the Medical Devices Directive 93/42/EC (“MDD”) 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 EU-wide international symbol evidencing adherence to quality assurance standards and compliance with the MDD or other 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 conform to the MDD. As of May 27, 2021, devices that have not received CE Mark renewal under the MDD or where existing device or processes are substantially amended, certification would be required in accordance with the new European Union Medical Device Regulation (“MDR”). However, devices already certified under the MDD can continue to use the CE Mark under the MDD until the expiry of those MDD CE certificates and in August of 2019, we announced that CytoSorb received renewal of its E.U. CE Mark through May 2024.

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, which is valid through September 2022.

In the EU, as in other geographies, there are limits to the claims we are allowed to make, associated with the use of our devices. Specifically, any claims that we make should be included in our Clinical Evaluation Report, which is part of the conformity assessment process conducted by the Notified Body. If our claims exceed the assessed claims, either regarding performance or intended uses, we may be subject to regulatory actions, which could include customer notifications or even product or literature (i.e. labeling) recalls.

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 three ways. The first process requires that a pre-market notification (510(k) Submission) be made to the FDA to demonstrate that the device is as safe and effective as, or “substantially equivalent” to, a legally marketed device that is not subject to pre-market approval (“PMA”). A legally marketed device is a device that (i) was legally marketed prior to May 28,

1976, (ii) has been reclassified from Class III to Class II or I, or (iii) has been found to be substantially equivalent to another legally marketed device following a 510(k) Submission. The legally marketed device to which equivalence is drawn is known as the "predicate" device. Applicants must submit descriptive data and, when necessary, performance data to establish that the device is substantially equivalent to a predicate device. In some instances, data from human clinical studies must also be submitted in support of a 510(k) Submission. If so, these data must be collected in a manner that conforms with specific requirements in accordance with federal regulations including the Investigational Device Exemption (IDE) and human subject 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) Changes to the device 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. Should a suitable predicate device not be available, the second pathway is the de novo request pathway.

The *de novo* pathway is available for novel device technologies, including novel device changes, that have not been previously classified by FDA and for which there is no suitable predicate device. To obtain marketing authorization via the *de novo* pathway, the applicant must show that the subject device can be reclassified as Class I or Class II. The *de novo* request pathway typically requires additional testing data, which may include clinical data.

The third, 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 is the most burdensome FDA premarket submission type for devices and 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 the 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 will conduct a pre-approval inspection of the manufacturing facilities to evaluate compliance with the FDA's Quality System Regulation ("OSR"), which requires manufacturers to implement and follow design, testing, control, documentation and other quality assurance and good manufacturing practice 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 PMA) 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, complaint handling, and manufacturers' required reports of adverse events and device malfunctions 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 QSR requirements, as mentioned above. 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 work with the DOJ to assess civil or criminal penalties against our officers, employees, or us. 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.

On April 10, 2020 the FDA granted CytoSorbents Emergency Use Authorization of CytoSorb for the treatment of COVID-19. Per the FDA, "The Emergency Use Authorization (EUA) authority allows FDA to help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats by facilitating the availability and use of medical countermeasures needed during public health emergencies. Under Section 564 of the Federal Food, Drug, and Cosmetic Act (the "Act"), the FDA commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening disease or conditions caused by CBRN threat agents when there are no adequate, approved, and available alternatives."

EUA is an approval limited in scope and, subject to FDA discretion regarding duration of the approval. The FDA can at its discretion cancel the EUA approval when there is no longer a threat to public health.

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 or approval 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 under the MDR 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 other pre-market review application 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, 2020, we achieved cumulative sales of CytoSorb of approximately $111,792,000. During this time period, the CytoSorb device represented substantially all of our product sales. At the end of 2020, we had hundreds of KOLs worldwide who are either using CytoSorb or supporting its use in clinical practice and/or in clinical studies.

We are approved to sell CytoSorb in all 27 countries in the EU, including Germany, Italy, France and Spain as well as the United Kingdom, and currently have either direct sales or distributors or strategic partnerships in 67 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.

Overall, we have established either direct sales or distribution (via distributors or strategic partners) of CytoSorb in 67 countries worldwide. Registration of CytoSorb is typically required in each of these countries prior to active commercialization, in a process that can take several months to more than a year to achieve. Variability in the timing of registration affects the initiation of active commercialization in these countries, which affects the timing of expected CytoSorb sales. 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 has distribution in Turkey, India, Sri Lanka, Australia, New Zealand, Russia, Serbia, Norway, Vietnam, Malaysia, Hong Kong, Chile, Panama, Costa Rica, Colombia, Brazil, Mexico, Argentina, Perú, Guatemala, Ecuador, Bolivia, the Dominican Republic, El Salvador, Iceland, Israel, UAE, Iran, Saudi Arabia and other Middle Eastern countries, 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. For example, in December 2019, we discontinued our distributor relationship with Dr. Reddy's in South Africa due to lack of market adoption. We continuously evaluate other potential distributor and strategic partner networks in other countries that accept CE Mark approval.

In addition to our direct and distributor commercial channels, we have a number of strategic partners to market and distribute CytoSorb. These partners include Biocon Biologics Limited, Fresenius Medical Care AG, Aferetica s.r.l. and Terumo Cardiovascular Group. In March 2021, we added B. Braun Avitum AG as a global co-marketing partner. For detailed information regarding these partnerships, see the section entitled "Commercial and Research Partners" in item 1 of this report.

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.

During the years ended 2020, 2019 and 2018, no agency, distributor or direct customer represented more than 10 percent of the Company's total revenue.

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

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, 2021, our patent portfolio includes 16 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 2021 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. 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	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
CytoSorb	Use of Gastrointestinally Administered Porous Sorbent Polymers	20 Years	10/22/2035	Standard
CytoSorb	Use of Polymeric Sorbent Polymers	20 Years	8/10/2032	Standard

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®, ECOS-300CY®, VetResQ®, HemoDefend™, BetaSorb™,DrugSorb™, and K+ontrol™. 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 $324,000 for the year ended December 31, 2020.

Employees

As of March 1, 2021, we had 195 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 and we believe we have good relationships with our employees.

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, 2020, we had an accumulated deficit of approximately $196,627,000, which included net losses of approximately $7,837,000 $19,266,000, and $17,211,000 for the years ended December 31, 2020, 2019 and 2018, respectively. 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 may require additional capital in the future to fund our operations.

As of December 31, 2020, we had current assets of approximately $82,453,000, including cash on hand of approximately $71,422,000 and current liabilities of approximately $10,153,000. For year ended December 31, 2020, our cash burn, which we define as the total of cash used in operating and investing activities from our statement of cash flows, was approximately $7,290,000. Our current and historical cash burn is not necessarily indicative of our future use of cash and cash equivalents.

We are currently well-capitalized, but may 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 and costs associated 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 related to business development activities;
- 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 dated July 26, 2018 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. As of December 31, 2020, $50 million of the total shelf amount was allocated to our ATM facility, of which approximately $22 million remains available. In addition, as a result of our $57.5 million July 24, 2000 equity raise, the amount remaining on the existing shelf registration statement is approximately $42.5 million.

On July 24, 2020, the Company closed the Offering of 6,052,631 shares of its common stock at a public offering price of $9.50 per share. The Company completed the Offering pursuant to the terms of an Underwriting Agreement, dated as of July 21, 2020, by and among the Company and Cowen and Company, LLC and SVB Leerink LLC, as representatives of the several underwriters named therein. The Company received gross proceeds of approximately $57.5 million from the Offering. After deducting the underwriting discounts and commissions and fees and expenses payable by the Company in connection with the Offering, the Company received net proceeds of approximately $53.8 million.

On July 9, 2019 we entered into an Open Market Sale Agreement with Jefferies LLC and B. Riley FBR, Inc., which we amended in April 2020 (as amended the “Sale Agreement”). Pursuant to the Sale Agreement we may offer to sell, from time to time shares of our common stock, up to a maximum of $50,000,000. During the year ended December 31, 2019, the Company sold 191,244 shares pursuant to the Sale Agreement, at an average selling price of $4.11 per share, generating net proceeds of approximately $762,000. During the year ended December 31, 2020, the Company sold 4,110,625 shares pursuant to the Amended Sale Agreement, at an average selling price of $6.64 per share, generating net proceeds of approximately $26.5 million. In the aggregate, the Company has sold 4,301,869 shares pursuant to the Amended Sale Agreement, at an average selling price of $6.53 per share, generating net proceeds of approximately $27.2 million.

On July 31, 2019 (the “Settlement Date”) we entered into the First Amendment to the Amended and Restated Loan and Security Agreement (the “First Amendment”) with Bridge Bank, which amended certain provisions of the Amended and Restated Loan and Security Agreement (the “Restated Loan and Security Agreement”) and the 2018 Success Fee Letter, each previously entered into by and among us and Bridge Bank on March 28, 2018. In connection with the execution of the First Amendment, the draw period for the Term B Loan (as defined therein) was extended to August 15, 2019 and we drew down the full $5.0 million Term B Loan on the Settlement Date, bringing the total outstanding debt to $15.0 million at July 31, 2019.

On December 4, 2020, the Company closed on the Third Amendment of its Amended Loan and Security Agreement with Bridge Bank. Under the terms of the Amendment, the Company repaid the outstanding principal balance of its existing $15 million term loans and simultaneously received a commitment from Bridge Bank to provide a new term loan of $15 million, which the Company may draw down at its discretion at any time prior to December 4, 2021.

Despite the foregoing, we may 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.

A pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, may materially and adversely affect our business and operations.

The outbreak of COVID-19 originated in Wuhan, China in December 2019 and has since spread around the globe. On March 11, 2020, the World Health Organization declared the outbreak a pandemic. The COVID-19 pandemic is affecting the United States and global economies has affected and is likely to continue to affect our operations and those of third parties on which we rely, including by causing disruptions in our raw material supply, the manufacturing of our lead product, CytoSorb, the commercialization of CytoSorb, and the conduct of current and future clinical trials. In addition, the COVID-19 pandemic has affected and is likely to continue to affect the operations of the U.S. Food and Drug Administration and other health authorities, which could result in delays of reviews and approvals, including with respect to CytoSorb and our product candidates. The evolving COVID-19 pandemic has impacted and is likely to continue to directly or indirectly impact our clinical trials, including but not limited to, the anticipated completion date of these trials and the pace of enrollment in our clinical trials for at least the next several months and possibly longer as patients may avoid or may not be able to travel to healthcare facilities and physicians' offices unless due to a health emergency and clinical trial staff can no longer get to the clinic. Such facilities and offices have and may continue to be required to focus limited resources on non-clinical trial matters, including treatment of COVID-19 patients, and may not be available, in whole or in part, for clinical trial services. In particular, due to delays resulting from impacts of the COVID-19 pandemic, analysis of the study data and issuance of the study report for the 250 patient, multi-center randomized, controlled study ("REMOVE") using CytoSorb during valve replacement open heart surgery in patients with infective endocarditis is now anticipated to be completed in mid-2021(rather than by mid-2020 that we initially anticipated), with top-line data potentially this quarter, and there may be further delays in patient enrollment in the REFRESH 2, TISORB, and CYTATION clinical trials. In addition, employee disruptions and remote working environments related to the COVID-19 pandemic and the federal, state and local responses to such virus, could materially impact the efficiency and pace with which we work and develop our product candidates, our ability to execute and invoice upon government grants and contracts, and the manufacturing of CytoSorb. As of the date of this filing, our manufacturing facilities remain operational and we have resumed certain research and development activities that were temporarily suspended as a result of the COVID-19 pandemic. Further, while the potential economic impact brought on by, and the duration of, the COVID-19 pandemic is difficult to assess or predict, the impact of the COVID-19 pandemic on the global financial markets may reduce our ability to access capital, which could negatively impact our short-term and long-term liquidity. Additionally, the stock market has been unusually volatile during the COVID-19 outbreak and such volatility may continue. To date, during certain periods of the COVID-19 pandemic, our stock price fluctuated significantly, and such fluctuation will likely continue to occur. The ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, financing or clinical trial activities or on healthcare systems or the global economy as a whole. However, these effects could have a material impact on our liquidity, capital resources, operations and business and those of the third parties on which we rely. In 2020, the Company estimated that approximately $9.4 million of its product sales were related to the treatment of COVID-19 patients. Should the pandemic ease, it is uncertain whether the Company will be able to replace some or all of this revenue in 2021.

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 elsewhere, 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. Although we believe we are currently well-capitalized, we may 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 and expanding 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 generally 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 diagnosis-related group ("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 March 1, 2021, we had 195 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 President and Chief Operating Officer and Dr. Efthymios Deliargyris, our Chief Medical Officer. On July 30, 2019, we entered into amended and restated executive employment agreements with its principal executives, Dr. Phillip P. Chan, Chief Executive Officer, Vincent Capponi, President and Chief Operating Officer, and Kathleen P. Bloch, Chief Financial Officer. Each of the agreements has an initial term of three years, and was retroactively effective as of January 1, 2019. On April 12, 2020, CytoSorbents Corporation entered into an executive employment agreement with Dr. Efthymios Deliargyris, who began employment as Chief Medical Officer on May 1, 2020, with an initial term that expires on December 31, 2021. After the expiration of the initial terms, the employment agreements will automatically renew for additional terms of one year unless either party provides written notice of non-renewal at least 60 days prior to a renewal. 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 adsorber, 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 adsorber 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, our existing patents are scheduled to expire between 2021 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 previously settled "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 through 2024, after which time no royalties will be due under this settlement agreement.

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.

Our existing patents are scheduled to expire between 2021 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 or clearance 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.

If we fail to maintain the CE Mark in the European Union, we will not be able to commercially sell and market CytoSorb.

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. A re-certification audit was conducted in April 2019. The successful completion of this audit CE-certifies CytoSorb under the current Medical Device Directive (93/42/EEC) until May 2024. Prior to the expiration of such certificate, we will apply for certification under the new Medical Devices Regulation (MDR). Failure to certify CytoSorb under the Medical Devices Regulation will prevent us from using the CE mark for commercial distribution of CytoSorb in the European Union. Any new product that we submit for the CE Mark after August 2019 must be approved under the new Medical Devices Regulation.

Furthermore, if:

- we are not able to obtain re-certification for CytoSorb's current use;
- we are not able to do so in time before the existing certificate expires;
- CytoSorb does not meet the new (and more stringent) requirements under the Medical Devices Regulation; or
- any variation in the uses for which the CE Mark has been affixed CytoSorb requires us to perform further research or to modify the technical documentation required to affix the CE Mark, our revenues and operating results could be adversely affected and our reputation could be harmed.

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.

Clinical study results for our CytoSorb device may not be indicative of our future clinical study results, and we cannot assure you that any clinical study results will lead to results sufficient for necessary regulatory clearances or product sales. Additionally, clinical and pre-clinical data is susceptible to varying interpretations, which could delay, limit, reduce, or prevent additional regulatory clearances or product sales.

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 or that our current or future clinical studies will lead to results necessary to receive additional regulatory approvals in markets not covered by the CE Mark. While clinical studies conducted by us and others have produced results we believe to be encouraging, 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. CytoSorb and our other products and product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in previous studies, which could result in decreased sales of our products and product candidates and have an adverse effect on our business and results of operations. Moreover, pre-clinical and clinical data are susceptible to varying interpretations, which could delay, limit or prevent additional regulatory approvals in markets not covered by the CE Mark. 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 CytoSorb or another product under development could delay or prevent regulatory clearance of the device, resulting in delays to commercialization, and could materially harm our business and results of operations. Even though we have received approval to apply the CE Mark to our CytoSorb device as a cytokine adsorber, there can be no assurance that we will be able to receive approval under the MDR for other potential applications of CytoSorb, or that we will receive regulatory clearance from authorities in 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.

We work with many medical and clinical advisors in critical care, cardiac surgery, trauma, and other areas who are associated with healthcare institutions. 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 capabilities, we may not be able to manufacture sufficient quantities at an acceptable cost or quality, 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, and have since upgraded to 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 in the EU and around the world, as well as 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") for medical devices, as set forth in the QSR. As such, we are subject to continual review and periodic inspections to assess compliance with cGMP/QSR requirements as required by our International notified body. 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 on a timely basis, or at all.

In the second quarter of 2018 we quadrupled our manufacturing capacity upon the official completion of the expansion of our CytoSorb manufacturing facility in New Jersey. In connection with the increased demand for the CytoSorb device to treat COVID-19 patients, our commercial distribution of CytoSorb has been, and may continue to be, delayed. Supply issues remain a potential cause of delay due to impact on COVID-19 on our material and logistics suppliers. In an attempt to reduce such delays, we have scaled, and preordered materials where possible to minimize disruptions in supply and will likely need to continue to scale up and increase our manufacturing capabilities in the future. To the extent we are required to expand our manufacturing capabilities, including the use of new or additional manufacturing facilities, our production may be delayed as we seek compliance with regulatory requirments. No assurance can be given that we will be able to successfully source or leverage new manufacturing facilities or, once sourced, scale up such manufacturing facilities, and do so at an acceptable cost or quality, 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 or if it reduces the cost-competitiveness of our products. 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, often supported by clinical data. The time and cost of such an educational process, and obtaining such clinical data may be substantial. Inability to successfully carry out this education process, or obtain adequate positive clinical data, 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 or elsewhere caused by Brexit, trade conflicts, or other factors.

For the year ended December 31, 2020, 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 implications of the United Kingdom's 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.

Significant economic downturns or international trade disruptions or disputes could adversely affect our business and operating results.

Significant portions of our business are conducted in Europe, including the U.K.; Asia; and other international geographies. Interruptions in international relationships such as the recent exit by the U.K. from the EU, and trade disputes such as the current trade negotiations between the U.S. and China, could result in changes to regulations governing our products and our intellectual property, disruption of our manufacturing or commercial operations, or otherwise affect our ability to do business. Additionally, global events such as the current COVID-19 coronavirus pandemic, that slow worldwide economies, disrupt travel and trade, and destabilize financial markets, may interfere with our ability to raise capital, sell and market our products, obtain reimbursement and payment of our products, or reduce the ability of our customers to pay for our product. Although these global problems transcend our company and afflict companies across industries and borders, these and similar events could adversely affect us, or our business partners or customers.

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 by other companies 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, as well as employee personal data. The secure storage, maintenance, and transmission of and access to this information is important to our operations our day-to-day business and our reputation. Security breaches have become more common across industries. 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, as well as our intellectual property and business data. 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. Further, while many of our employees and certain suppliers with whom we do business operate in a remote working environment during the COVID-19 pandemic, the risk of cybersecurity attacks, particularly through phishing, are increased. We have recently experienced multiple attempts by third parties to penetrate our computer systems. While we have certain safeguards in place to reduce the risk of and detect cyber-attacks, as well as limit the potential exposure of proprietary and confidential information, including multi-layer security protections, our information technology networks and infrastructure may be vulnerable to unpermitted access by hackers or other breaches powered by new and sophisticated technologies, or employee error or malfeasance. Further, we may not be immediately aware of any unpermitted access by hacker or other breaches and we may be unable to quickly and effectively remediate any such breaches. 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.

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 went 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.

Our common stock closed as high as $11.55 and as low as $3.77 per share between January 1, 2020 December 31 2020 on Nasdaq. On March 5, 2021, the closing price of our common stock, as reported on Nasdaq, was $8.58. 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, 2020, two shareholders hold 11.5% of our shares and our directors and officers hold 4.9% 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 June 12, 2019, authorizes the issuance of up to 100,000,000 shares of common stock, of which approximately 56,778,000 shares remain available for issuance as of December 31, 2020 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. 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.

On July 9, 2019 we entered into an Open Market Sale Agreement with Jefferies LLC and B. Riley FBR, Inc., which we amended in April 2020 (as amended the "Sale Agreement"). Pursuant to the Sale Agreement we may offer to sell, from time to time shares of our common stock through "at-the-market" offerings, up to a maximum of $50,000,000. 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 20,820 sq. ft., housing research laboratories, manufacturing operations and clinical and administrative offices, under a lease agreement which expires in May 2021, and contains a provision allowing us to renew the lease for another year. We expect to secure new, expanded facilities in the future. 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 2021 is approximately $33,600 and additionally we reimburse the landlord for monthly operating expenses of approximately $29,700.

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 approximately $9,000 per month. In January 2021, we entered to a lease for additional warehouse space in Germany. The lease commences on April 1, 2021, requires monthly payments of base rent of approximately $7,900 and has a term of five years. The lease also has an option to extend the lease term for an additional five years.

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.

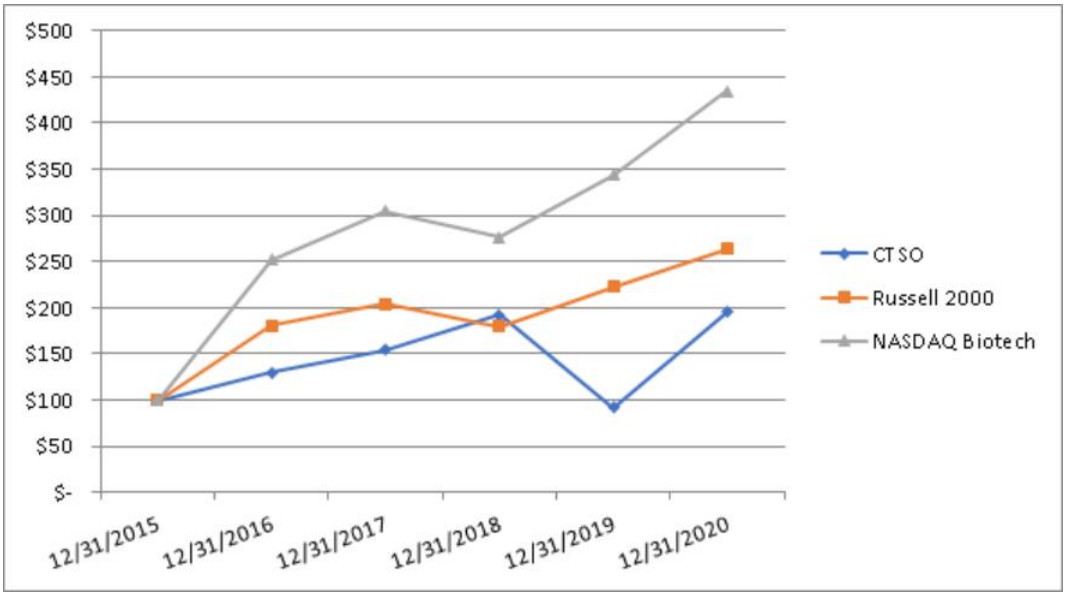
Approximate Number of Equity Security Holders

As of February 15, 2021, there were approximately 12,300 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, 2015 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 31st 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, 2015



Issuer Purchases of Securities

There were no repurchases of the Company's securities during the year ended December 31, 2020.

Recent Sales of Unregistered Securities

We had no sales of unregistered securities in 2020 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.

	2020	2019	2018	2017	2016
Revenue:					
Sales	$ 39,452,502	$ 22,765,854	$ 20,252,383	$ 13,381,853	$ 8,206,036
Grant income	1,552,099	2,183,619	2,251,525	1,768,901	1,321,807
Other revenue	—	—	—	—	—
Total revenue	41,004,601	24,949,473	22,503,908	15,150,754	9,527,843
Cost of revenue	11,052,409	7,363,919	7,489,400	5,518,360	3,953,725
Gross margin	29,952,192	17,585,554	15,014,508	9,632,394	5,574,118
Operating expenses:					
Research and development	8,810,561	12,091,797	7,723,028	3,221,233	4,073,093
Legal, financial and other consulting	3,048,242	2,462,151	2,002,032	1,339,493	1,184,788
Selling general and administrative	28,463,723	22,005,670	20,874,376	14,914,266	11,808,362
Total operating expenses	40,322,526	36,559,618	30,599,436	19,474,992	17,066,243
Loss from operations	(10,370,334)	(18,974,064)	(15,584,928)	(9,842,598)	(11,492,125)
Other income (expense):					
Interest expense, net	(1,201,067)	(1,033,661)	(1,461,045)	(749,076)	(231,804)
Foreign currency transaction gain (loss)	2,607,139	(350,365)	(784,752)	1,454,136	(358,077)
Total other income (expense), net	1,406,072	(1,384,026)	(2,245,797)	705,060	(589,881)
Loss before benefit from income taxes	(8,964,262)	(20,358,090)	(17,830,725)	(9,137,538)	(12,082,006)
Benefit from income taxes	1,127,074	1,092,446	619,546	676,739	318,550
Net loss	(7,837,188)	(19,265,644)	(17,211,179)	(8,460,799)	(11,763,456)
Dividends	—	—	—	335,731	—
Net loss available to common stockholders, basic and diluted	$ (7,837,188)	$ (19,265,644)	$ (17,211,179)	$ (8,796,530)	$ (11,763,456)
Weighted average common shares outstanding, basic and diluted	38,818,990	32,255,253	30,719,176	27,613,911	25,433,719
Net loss per share, basic and diluted	$ (0.20)	$ (0.60)	$ (0.56)	$ (0.32)	$ (0.46)

	As of December 31,				
	2020	2019	2018	2017	2016
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 71,421,601	$ 12,232,418	$ 22,368,837	$ 17,321,862	$ 5,245,178
Working capital	72,299,881	10,965,262	21,725,888	12,891,009	3,550,353
Total assets	89,950,471	27,382,510	34,196,763	24,103,307	9,693,844
Preferred stock	—	—	—	—	—
Accumulated deficit	(196,626,647)	(188,789,459)	(169,523,815)	(152,312,636)	(143,516,106)
Total stockholders' equity	79,215,579	3,418,042	16,934,600	10,262,835	1,337,459

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, 2020, 2019 and 2018 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 16 issued U.S. patents, multiple issued foreign patents and multiple applications pending both in the U.S. and internationally. Our intellectual property consists of composition of matter, materials, methods of production, systems incorporating the technology and multiple medical uses with expiration dates ranging from one to 15 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 expansion increasing treatment time from six hours to 24 hours. In May 2018, we received a label expansion for CytoSorb covering use of the device for the removal of bilirubin and myoglobin in the treatment of liver disease and trauma, respectively. In January 2020, we received CE-Mark label expansion for CytoSorb covering the use of the device for the removal of the anti-platelet agent, ticagrelor, in patients undergoing surgery requiring cardiopulmonary bypass. In April 2020, the United States Food and Drug Administration (the "FDA") granted Breakthrough Designation to CytoSorb for the removal of ticagrelor in a cardiopulmonary bypass circuit during emergent and urgent cardiothoracic surgery. In April 2020, we announced that the FDA has granted Emergency Use Authorization ("EUA") of CytoSorb for use in patients with COVID-19 infection. In May 2020, we received CE-Mark label expansion for CytoSorb for the removal of rivaroxaban during cardiothoracic surgery requiring cardiopulmonary bypass.

Our CE Mark enables CytoSorb to be sold throughout all 27 countries of the EU and the United Kingdom. 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 predominantly 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 from 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 13485:20016 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 specific reimbursement for CytoSorb in Germany. We have also been assigned two specific procedure codes for our CytoSorb device in Switzerland that are 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.

In the third quarter of 2019, we established CytoSorbents UK Limited, a wholly-owned subsidiary of CytoSorbents Medical, Inc., to manage our clinical trial activities in the United Kingdom.

In January 2020, we received CE-Mark label expansion approving the use of CytoSorb to remove the anti-platelet agent, ticagrelor, in cardiac patients during surgery requiring cardiopulmonary bypass.

In April 2020, the Company announced that the United States Food and Drug Administration (the “FDA”) granted Emergency Use Authorization (“EUA”) of CytoSorb for use in critically-ill patients infected with COVID-19. Under the EUA, the Company can make CytoSorb available, through commercial sales, to all hospitals in the United States for use in patients, 18 years of age or older, with confirmed COVID-19 infection who are admitted to the intensive care unit (ICU) with confirmed or imminent respiratory failure who have early acute lung injury or acute respiratory distress syndrome (ARDS), severe disease, or life-threatening illness resulting in respiratory failure, septic shock, and/or multiple organ dysfunction or failure. The CytoSorb device has neither been cleared nor approved for the indication to treat patients with COVID-19 infection. The EUA will be effective until a declaration is made that the circumstances justifying the EUA have terminated or until revoked by the FDA.

In April 2020, the Company also announced that the FDA had granted Breakthrough Designation to CytoSorb for the removal of ticagrelor in a cardiopulmonary bypass circuit during emergent and urgent cardiothoracic surgery. The Breakthrough Devices Program provides for more effective treatment of life-threatening or irreversibly debilitating disease or conditions, in this case the need to reverse the effects of ticagrelor in emergent or urgent cardiac surgery that can otherwise cause a high risk of serious or life-threatening bleeding. Through Breakthrough Designation, the FDA intends to work with CytoSorbents to expedite the development, assessment, and regulatory review of CytoSorb for the removal of ticagrelor, while maintaining statutory standards of regulatory approval (e.g., 510(k), *de novo* 510(k) or premarket approval) consistent with the FDA’s mission to protect and promote public health.

In May 2020, we received CE-Mark label expansion approving the use of CytoSorb for the removal of rivaroxaban, a widely-used Factor Xa inhibitor and novel oral anticoagulant, during cardiothoracic surgery requiring cardiopulmonary bypass. With this announcement, and the E.U. approval earlier this year to remove ticagrelor, for the same indication, CytoSorb is providing cardiac surgeons and perfusionists an easy-to-use and rapid new treatment option to help reduce the risk of serious and potentially fatal perioperative bleeding complications caused by these two drugs, in separate categories of blood thinners.

At the end of 2020, we had hundreds of KOLs in our commercialized territories worldwide in critical care, cardiac surgery, and blood purification who were either using CytoSorb or supporting its use in clinical practice or clinical trials.

As of March 1, 2021, our European commercialization team includes 95 people.

Overall, we have established either direct sales or distribution (via distributors or strategic partners) of CytoSorb in 67 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 has distribution in Turkey, India, Sri Lanka, Australia, New

Zealand, Russia, Serbia, Norway, Vietnam, Malaysia, Hong Kong, Chile, Panama, Costa Rica, Colombia, Brazil, Mexico, Argentina, Perú, Guatemala, Ecuador, Bolivia, the Dominican Republic, El Salvador, Iceland, Israel, UAE, Iran, Saudi Arabia and other Middle Eastern countries, 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. For example, in December 2019, we discontinued our distributor relationship with Dr. Reddy's in South Africa due to lack of market adoption. We continuously evaluate other potential distributor and strategic partner networks in other countries that accept CE Mark approval.

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 Biologics Limited, 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 were 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 South Korea and Mexico. Commercial sales of CytoSorb are underway in both countries after securing market registration clearance from Korean and Mexican health authorities in 2020. 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 August 2020, we announced an initial collaboration with Terumo to exclusively sell CytoSorb to hospitals in ten U.S. COVID-19 hotspot states including Alabama, Arizona, California, Georgia, Louisiana, Mississippi, New Mexico, Oregon, Texas, and Washington. CytoSorb previously received Emergency Use Authorization (EUA) by the U.S. Food and Drug Administration (FDA) for use in adult, critically-ill COVID-19 patients with imminent or confirmed respiratory failure. Under the initial terms of the agreement, Terumo will ensure hospitals in the defined hot-spot states have access to the CytoSorb therapy for use in critically-ill COVID-19

patients that meet strict criteria under CytoSorbents' EUA. CytoSorbents will provide all primary clinical and technical training, customer support, and product fulfillment.

In March 2017, we announced a partnership with Dr. Reddy's Laboratories to exclusively distribute CytoSorb in South Africa for multiple applications. In December 2019, we discontinued this partnership.

In March 2021, we announced a strategic partnership with B. Braun Avitum AG, and the launch of a global co-marketing agreement to promote the use of CytoSorb with B Braun's latest OMNI® continuous blood purification platform and OMNIset® Plus bloodline set (set version 3.0 or higher).

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 supporting the safety and efficacy of CytoSorb when used 24 hours per day for seven days, each day with a new device.

In addition, we now have more than 50 investigator-initiated studies planned, enrolling or completed in many countries such as Germany, Austria, Switzerland, the Netherlands, Hungary, the United Kingdom, India, and the U.S. These trials, which are funded and supported by well-known university hospitals and KOLs, are post-market clinical studies. They have provided and are expected to continue to provide invaluable information regarding the success of the device in the treatment of sepsis, cardiac surgery, liver failure, 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 study 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 study. 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. The REFRESH I study represented the first randomized controlled study demonstrating the safety of intra-operative CytoSorb use in patients undergoing high risk cardiac operations.

Investigators of the REFRESH I study submitted an abstract with data, including free hemoglobin data, from the REFRESH I study 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 in May 2019, the manuscript of the REFRESH I study was electronically published in the journal, Seminars in Thoracic and Cardiovascular Surgery.

In December 2017, the FDA approved our IDE application for our REFRESH 2-AKI study, permitting us to conduct this pivotal study 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 study is a randomized,

controlled, multi-center, clinical study designed to evaluate intraoperative use of two CytoSorb devices 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 higher mortality, and is a risk factor for developing chronic kidney disease requiring hemodialysis in the future. The study 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 study. Based on the recommendations of key clinical advisors, a protocol amendment was submitted to the FDA on July 19, 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, announced in September 2018. On November 25, 2019 the Company announced a pause in enrollment for the REFRESH 2-AKI study. The study's Data Monitoring Committee (the "DMC") recommended this pause following a blinded, interim, milestone review of clinical study data. The DMC requested that additional clinical data and data analysis, not pre-specified in the current version of the protocol, be provided by Company. In addition, the Company appointed NAMSA as the new contract research organization ("CRO") for the study to improve the monitoring of patient safety endpoints. As of November 25, 2019, the study had enrolled 153 patients at 25 initiated sites. Since then, the Company and its new CRO have completed a comprehensive program to re-monitor existing data, collect new data, and analyze the safety data from the 153 patients included in the trial to date. These data were reviewed by the DMC resulting in a favorable opinion on safety, dated July 24, 2020, and the recommendation to resume the trial with only minor modifications. The Company has been undertaking multiple activities in preparation to resume the study, which is estimated to take place in the first half of 2021. If the study is successful, we plan to submit a PMA application to the FDA in 2023 for U.S. regulatory approval.

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. An 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 study, 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." The study completed enrollment in 2020 but the COVID-19 pandemic has caused delays in data monitoring and data analysis. Topline data are expected to be reported in the first half of 2021 with full data presentation at a major international conference also in 2021.

In September 2019, a new publication entitled, "Hemoadsorption with CytoSorb showed a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study," in the journal Critical Care. In this study, clinical researchers at Maasstad Hospital and at Erasmus University Medical Center in Rotterdam, Netherlands conducted a retrospective evaluation of 116 patients with septic shock, who required vasopressors to increase their blood pressure, and renal replacement therapy (RRT) due to kidney failure. Of these, 49 patients received standard of care therapy, and 67 were treated with standard of care plus CytoSorb. Both groups were compared by stabilized Inverse Probability of Treatment Weights (sIPTW) to overcome baseline differences in the type of sepsis, age, comorbidities, surgery vs no surgery, Sequential Organ Failure Assessment (SOFA) score, use of the vasopressor noradrenaline, and lactate levels. Patients treated with standard of care and CytoSorb had a statistically significant reduction in 28-day all-cause mortality compared to standard of care alone (53% vs 72% control, $p<0.04$), based on the sIPTW analysis. In addition, observed 28-day all-cause mortality in the CytoSorb treatment group was significantly lower than the predicted mortality (48% observed vs 75% predicted, $p<0.001$), based on SOFA score.

In October 2019, CytoSorbents initiated TISORB (Ticagrelor CytoSorb Hemoadsorption), a Company-sponsored, multicenter study in the United Kingdom to prospectively evaluate the removal of ticagrelor during cardiopulmonary bypass in patients on ticagrelor undergoing emergent cardiothoracic surgery. A protocol amendment was submitted to expand the population of eligible patients to now include patients requiring urgent cardiac surgery. These changes were approved by the UK Medicines and Healthcare products Regulatory Agency (MHRA) at the end of February 2020. In December 2020, CytoSorbents initiated CYTATION (CytoSorb Ticagrelor Hemoadsorption), a Company-sponsored multicenter study in Germany to prospectively evaluate the removal of ticagrelor during cardiopulmonary bypass in patients on ticagrelor undergoing emergent cardiothoracic surgery. Ticagrelor (Brilinta®, Astra Zeneca) is a potent platelet inhibitor and antithrombotic therapy and recognized as a standard of care to reduce the risk of heart attacks and strokes in patients with acute coronary syndromes. Unfortunately, given the absence of an approved treatment to reverse the antithrombotic effects of ticagrelor, treated patients who require urgent or emergent cardiothoracic surgery may either proceed at high risk for severe perioperative bleeding (as high as 65% higher risk due to ticagrelor) or stay waiting for days in the hospital until the ticagrelor antithrombotic effect washes out. Neither option is optimal since patients proceeding to surgery are at great risk for serious or even fatal

bleeding and patients waiting for washout are at risk of a thrombotic complications such as a stroke or heart attack, while delaying surgery and increasing hospitalization costs. The benefits of CytoSorb in this setting are both clinical and economic. In the publication in 2019 by Hassan et al, outcomes of 55 patients requiring emergent cardiac surgery while on ticagrelor or rivaroxaban therapy were evaluated according to the use of CytoSorb. Antithrombotic (either ticagrelor or rivaroxaban) removal with CytoSorb was associated with significant reductions in operative time, need for red blood cell and platelet transfusions and re-operations to control bleeding and those clinical benefits resulted in shorter length of ICU stay. These significant clinical benefits are expected to also result in substantial economic benefits. This was demonstrated in the publication by Javanbakht et al. in 2019, that projected an average cost savings of £3,982 per patient (approximately $5,000 USD per patient), including the cost of the CytoSorb adsorber. The primary objective in both TISORB and CYTATION studies is the change in platelet reactivity and ticagrelor blood concentration before and after cardiopulmonary bypass for patients undergoing CytoSorb hemoadsorption removal of ticagrelor from their blood. Due to the COVID-19 pandemic, the execution of the TISORB trial has been greatly impacted and ongoing national restrictions in the U.K. on the conduct of non-COVID clinical studies add further uncertainty to TISORB. In Germany, however, clinical research is continuing and we therefore expect that the CYTATION study will not be equally impacted.

In January 2020, CytoSorb received European Union CE Mark label expansion to include the removal of ticagrelor during cardiopulmonary bypass in patients undergoing cardiothoracic surgery. In May 2020, CytoSorb also received European Union CE Mark label expansion to include rivaroxaban removal for the same indication. We have recently announced the Safe and Timely Antithrombotic Removal (STAR) development program that will comprise of a number of clinical projects relating to the antithrombotic removal application. The first study is the STAR Registry scheduled to commence enrollment in 2021 that will capture real world use of CytoSorb for this indication. The registry will initially launch in Europe with the intent of expanding to the United States and the rest of the territories where CytoSorb is available in the future. We anticipate that additional clinical studies on antithrombotic removal will be conducted as part of the STAR program.

The market focus of 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 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, liver disease, 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 polymer technologies form the basis of a broad technology portfolio. Some of our products and product candidates include:

- CytoSorb - an extracorporeal hemoperfusion cartridge approved in the EU for cytokine removal, with the goal of reducing SIRS and sepsis and preventing or treating organ failure.
- ECOS-300CY - an adsorption cartridge for use with *ex vivo* organ perfusion systems to remove cytokines and other inflammatory mediators in the organ perfusate, with the goal of improving solid organ support or rehabilitation.
- 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 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-RBC—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.
- HemoDefend-BGA—a development-stage purification technology that can remove anti-A and anti-B antibodies from plasma and whole blood, to enable "universal plasma," and safer whole blood transfusions, respectively.
- K^+ontrol—a development-stage blood purification technology designed to reduce excessive levels of potassium in the blood that can be fatal in severe hyperkalemia.
- ContrastSorb—a development-stage extracorporeal hemoperfusion cartridge designed to remove IV contrast from the blood of high risk patients undergoing radiological imaging with contrast, or interventional radiology procedures such as cardiac catheterization and angioplasty. 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

Comparison of the year ended December 31, 2020 and 2019

Revenues:

For the year ended December 31, 2020, we generated total revenue, which includes product revenue and grant income, of approximately $41,005,000 as compared to revenues of approximately $24,949,000 for the year ended December 31, 2019, an increase of approximately $16,056,000, or 64%. Revenue from product sales was approximately $39,453,000 for the year ended December 31, 2020, as compared to approximately $22,766,000 in the year ended December 31, 2019, an increase of approximately $16,787,000 or 73%. This increase was driven by an increase in direct sales of approximately $8,917,000 resulting from sales to both new customers and repeat orders from existing customers and an increase in distributor sales of approximately $7,769,000. Sales to hospitals in the United States under the EUA granted by the FDA amounted to approximately $1,341,000 for the year ended December 31, 2020. Though difficult to quantitate, we estimate that approximately $9.4 million of total product sales during the year ended December 31, 2020 was due to the demand for CytoSorb to treat COVID-19 patients. In addition, as a result of the increase in the average exchange rate of the Euro to the U.S. dollar, sales were positively impacted by approximately $693,000. For the year ended December 31, 2020, the average exchange rate of the Euro to the U.S. dollar was $1.14 as compared to an average exchange rate of $1.12 for the year ended December 31, 2019.

Cost of Revenue:

For the years ended December 31, 2020 and 2019, cost of revenue was approximately $11,052,000 and $7,364,000, respectively, an increase of approximately $3,688,000. Product cost of revenues increased approximately $4,180,000 during the year ended December 31, 2020 as compared to the year ended December 31, 2019 as a result of the increase in product sales. Product gross margins were approximately 76% for the year ended December 31, 2020 and approximately 77% for the year ended December 31, 2019. The decrease in gross margin was due to an increase in percent contribution of lower margin distributor sales as well as certain costs associated with the rapid ramp-up of production during the year ended December 31, 2020.

Gross Profit:

Gross profit was approximately $29,952,000 for the year ended December 31, 2020, an increase of approximately $12,366,000 or 70%, over gross profit of $17,586,000 in 2019. This increase is attributed to an increase in CytoSorb product sales during 2020.

Research and Development Expenses:

Our research and development costs were approximately $8,811,000 and $12,092,000 for the years ended December 31, 2020 and 2019, respectively, a decrease of approximately $3,281,000, or 27%. This decrease was due to a decrease in clinical trial and related costs of approximately $3,769,000, due primarily to the pause in our Company-sponsored clinical trials as a result of hospital restrictions due to the COVID-19 pandemic, and a decrease in our non-grant related research and development costs of approximately $393,000.

These decreases were offset by an increase in non-clinical research and development salary related costs of approximately $160,000 due primarily to COVID-19 related incentive pay, decreases in direct labor and other costs being deployed toward grant-funded activities of approximately $675,000, which had the effect of increasing the amount of our non-reimbursable research and development costs and an increase in new product development costs of approximately $46,000.

Legal, Financial and Other Consulting Expenses:

Our legal, financial and other consulting costs were approximately $3,048,000 and $2,462,000 for the years ended December 31, 2020 and 2019, respectively, an increase of approximately $586,000, or 24%. This increase was due to an increase in employment agency fees of approximately $395,000 related to the hiring of senior level personnel, an increase in consulting fees of approximately $219,000 primarily related to certain financial advisory fees and an increase in accounting and auditing fees of approximately $40,000. These increases were offset by a decrease in legal fees of approximately $70,000.

Selling, General and Administrative Expenses:

Our selling, general and administrative expenses were approximately $28,464,000 and $22,006,000 for the years ended December 31, 2020 and 2019, respectively, an increase of approximately $6,458,000, or 29%. This increase was due to an increase in salaries, commissions and related costs of approximately $4,849,000 due primarily to headcount additions and increased commissions due to increase sales, an increase in royalty expenses of approximately $1,327,000 due to the increase in product sales, and an increase in non-cash stock option expense of approximately $1,879,000. These increases were offset by reductions in sales and marketing costs, which include advertising and conference attendance of approximately $824,000 and travel and entertainment and other general and administrative expenses of approximately $773,000. These reductions were due primarily to travel restrictions related to the COVID-19 pandemic.

Interest Expense, Net:

For the year ended December 31, 2020, interest expense, net was approximately $1,201,000, as compared to interest expense, net of approximately $1,034,000 for the year ended December 31, 2019. This increase in net interest expense of approximately $167,000 is related to the final fee that was due upon repayment of our term loans in conjunction with the Third Amendment to the Amended Loan and Security Agreement with Bridge Bank that closed on December 4, 2020.

Gain (Loss) on Foreign Currency Transactions:

For the year ended December 31, 2020, the gain on foreign currency transactions was approximately $2,607,000, as compared to a loss on foreign currency transactions of approximately $350,000 for the year ended December 31, 2019. The 2020 gain is directly related to the increase of the exchange rate of the Euro at December 31, 2020 as compared to December 31, 2019. The exchange rate of the Euro to the U.S. dollar was $1.22 per Euro at December 31, 2020 as compared to $1.12 per Euro at December 31, 2019. The 2019 loss is directly related to the decrease in the exchange rate of the Euro at December 31, 2019, as compared to December 31, 2018. The exchange rate of the Euro to the U.S. dollar was $1.12 per Euro at December 31, 2019 as compared to $1.15 per Euro at December 31, 2018.

Benefit from Income Taxes:

Our benefit from income taxes was approximately $1,127,000 and $1,092,000 for the years ended December 31, 2020 and 2019, 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, 2019 and 2018

Revenues:

For the year ended December 31, 2019, we generated total revenue, which includes product revenue and grant income, of approximately $24,949,000 as compared to revenues of approximately $22,504,000 for the year ended December 31, 2018, an increase of approximately $2,445,000, or 11%. Revenue from product sales was approximately $22,766,000 for the year ended December 31, 2019, as compared to approximately $20,252,000 in the year ended December 31, 2018, an increase of approximately $2,514,000 or 12%. This increase was primarily driven by an increase in direct sales of approximately $3,194,000 resulting from both new customers and repeat orders from existing customers. This increase was offset by a decrease in distributor sales of approximately $680,000. In addition, sales were negatively impacted by approximately $1,201,000 as a result of the decrease in the average exchange rate of the Euro to the U.S. dollar. For the year ended December 31, 2019, the average exchange rate of the Euro to the U.S. dollar was $1.12 as compared to an average exchange rate of $1.18 for the year ended December 31, 2018.

Cost of Revenue:

For the years ended December 31, 2019 and 2018, cost of revenue was approximately $7,364,000 and $7,489,000, respectively, a decrease of approximately $125,000. Product cost of revenues decreased approximately $63,000 during the year ended December 31, 2019 as compared to the year ended December 31, 2018 as a result of achieved production efficiencies. Product gross margins were approximately 77% for the year ended December 31, 2019 and approximately 74% for the year ended December 31, 2018.

Gross Profit:

Gross profit was approximately $17,586,000 for the year ended December 31, 2019, an increase of approximately $2,571,000 or 17%, over gross profit of $15,015,000 in 2018. This increase is attributed to an increase in CytoSorb product sales during 2019 as well as achieved production efficiencies.

Research and Development Expenses:

Our research and development costs were approximately $12,092,000 and $7,723,000 for the years ended December 31, 2019 and 2018, respectively, an increase of approximately $4,369,000, or 57%. This increase was due to an increase in clinical trial and related costs of approximately$3,890,000, which include expenditures related to our REFRESH 2-AKI study and our TISORB study, an increase in non-clinical research and development salary related costs of approximately $223,000, decreases in direct labor and other costs being deployed toward grant-funded activities of approximately $62,000, which had the effect of increasing the amount of our non-reimbursable research and development costs and an increase in our non-grant related research and development costs of approximately $194,000.

Legal, Financial and Other Consulting Expenses:

Our legal, financial and other consulting costs were approximately $2,462,000 and $2,002,000 for the years ended December 31, 2019 and 2018, respectively, an increase of approximately $460,000, or 23%. This increase was due to an increase in legal fees of approximately $334,000 related to patent matters and certain corporate initiatives, an increase in employment agency fees of approximately $88,000 related to the hiring of senior level personnel, an increase in accounting and auditing fees of approximately $24,000 and an increase in consulting fees of approximately $14,000.

Selling, General and Administrative Expenses:

Our selling, general and administrative expenses were approximately $22,006,000 and $20,874,000 for the years ended December 31, 2019 and 2018, respectively, an increase of approximately $1,132,000, or 5%. This increase was due to an increase in salaries, commissions and related costs of approximately $2,323,000, additional sales and marketing costs, which include advertising and conference attendance of approximately $863,000, an increase in royalty expenses of approximately $198,000 due to the increase in product sales, and an increase in restricted stock expense of approximately $226,000 related to restricted stock units granted to the Company’s executive officers, an increase in public relations cost of approximately $78,000 and increase in other general and administrative costs of approximately $215,000. These increases were offset by a decrease in non-cash stock compensation expense of approximately $2,771,000.

Interest Expense, Net:

For the year ended December 31, 2019, interest expense, net was approximately $1,034,000, as compared to interest expense, net of approximately $1,461,000 for the year ended December 31, 2018. This decrease in net interest expense of approximately $427,000 is 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, offset by an increase in interest due to the draw down of the $5,000,000 Term B Loan with Bridge Bank on July 31, 2019.

Gain (Loss) on Foreign Currency Transactions:

For the year ended December 31, 2019, the loss on foreign currency transactions was approximately $350,000, as compared to a loss on foreign currency transactions of approximately $785,000 for the year ended December 31, 2018. The 2019 loss is directly related to the decrease in the exchange rate of the Euro at December 31, 2019, as compared to December 31, 2018. The exchange rate of the Euro to the U.S. dollar was $1.12 per Euro at December 31, 2019 as compared to $1.15 per Euro at December 31, 2018. 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.

Benefit from Income Taxes:

Our benefit from income taxes was approximately $1,092,000 and $620,000 for the years ended December 31, 2019 and 2018, 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, 2020, we had an accumulated deficit of approximately $196,627,000, which included losses of approximately $7,837,000, $19,266,000 and $17,211,000 for years ended December 31, 2020, 2019 and 2018, 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 $40,323,000, $36,560,000 and $30,599,000 for the years ended December 31, 2020, 2019 and 2018, 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, 2020, we had current assets of approximately $82,453,000 including cash on hand of approximately $71,422,000 and had current liabilities of approximately $10,153,000. During the period from January 1, 2020 through July 15, 2020, we raised approximately $26,427,000 by utilizing our ATM facility with co-agents Jefferies LLC and B. Riley FBR. In addition, we received net proceeds of approximately $53,800,000 from our underwritten public offering that closed on July 24, 2020. Also, we expect to receive approximately $1,127,000 in cash from the approved sale of our net operating losses and research and development credits from the State of New Jersey in the first quarter of 2021.

We believe that we have sufficient cash to fund our operations and clinical trial activities well into the future.

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 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”). On July 31, 2019, the Borrower entered into the First Amendment to the Amended and Restated Loan and Security Agreement (the “First Amendment”) with the Bank, which amended certain provisions of the Amended and Restated Loan and

Security Agreement and the 2018 Success Fee Letter (the "2018 Letter"). In connection with the execution of the First Amendment, the draw period for the Term B Loan was extended to August 15, 2019 and the Company drew down the full $5.0 million Term B Loan on the Settlement Date, bringing the total outstanding debt to $15,000,000 at July 31, 2019. The proceeds of Term Loans were used for general business requirements in accordance with the Amended and Restated Loan and Security Agreement. On December 4, 2020 (the "Closing Date"), the Company closed on the Third Amendment (the "Third Amendment") of its Amended Loan and Security Agreement with Bridge Bank. Under the terms of the Amendment, the Company repaid the outstanding principal balance of its existing $15 million term loans and simultaneously received a commitment from Bridge Bank to provide a new term loan of $15 million (the "New Term Loan"), which can be drawn down at the Company's discretion at any time prior to December 4, 2021.

The New Term Loan, if drawn, shall bear interest at the Index Rate (defined in the Third Amendment as the greater of 3.25% or the Prime Rate as published by the Wall Street Journal on the last business date of the month the immediately preceding the month in which the interest will accrue) plus 1.25%. In addition, the Company would be required to make payments of interest-only commencing on the first day of the month after the New Term Loan was made until January 2023. The interest-only period may be further extended through July 2023 if the Company maintains compliance certain conditions as outlined in the Amendment. Following the interest-only period, the Company will be required to make equal monthly payments of principal and interest until maturity of the New Term Loan. The maturity date of the New Term Loan is December 1, 2024.

On the Closing Date, the Company was required to pay a non-refundable closing fee of $75,000. As of the Closing Date, the total unamortized loan costs related to the Term Loans amounted to approximately $45,000. These costs were written off on the closing date as a charge to interest expense. For the years ended December 31, 2020, 2019, and 2018, the Company recorded interest expense amounting to $76,718, $33,175, and $31,946, respectively related to these costs. 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. On the Closing Date, the Company paid a final fee of $325,000. For the years ended December 31, 2020, 2019 and 2018 the Company recorded interest expense of $246,095, $82,031 and $65,104, respectively, related to accrual and payment of the final fee.

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).

2018 Success Fee Letter:

Pursuant to the amended 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 (as defined in the Restated Loan and Security Agreement) (the "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 the Nasdaq Capital Market 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 average price of Company's common stock for the 365 day period ending on the date of the funding of the Term B Loan. This obligation shall terminate on the fifth anniversary of the funding of the Term B Loan and shall survive the termination of the loan agreement and the prepayment of the Term B Loan.

Critical Accounting Policies and Estimates

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 and estimates 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, other agreements provide for reimbursement of costs and an overhead margin and certain agreements are performance based, where revenue is earned based upon the achievement of milestones outlined in the contract. 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

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

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

Lease Commitments

We currently operate a facility near Princeton, New Jersey with approximately 20,821 sq. ft., housing research laboratories, clinical manufacturing operations and administrative offices, under a lease agreement which expires in May 2021. The lease includes a one year option to renew. We expect to secure additional square footage to support increased manufacturing capacity in the future. Our monthly base rent is approximately $33,600 and, additionally, we reimburse the landlord for monthly operating expenses of approximately $29,700.

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. In January 2021, we entered to a lease for additional warehouse space in Germany. The lease commences on April 1, 2021, requires monthly payments of base rent and other costs of approximately $7,900 and has a term of five years. The lease also has an option to extend the lease term for an additional five years.

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, 2020, 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, 2020. 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, 2020 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

2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 2021 annual meeting of stockholders scheduled to be held on June 1, 2021, 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 consolidated 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	Second Amended and Restated Certificate of Incorporation, dated June 12, 2019 (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on June 13, 2019).
3.2	Amended and Restated Bylaws of CytoSorbents Corporation (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on January 2, 2020).
4.1*	Description of Capital Stock of CytoSorbents Corporation(incorporated by reference to Exhibit 4.1 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2019 filed on March 5, 2020.
10.1.+	Amended and Restated Employment Agreement, dated as of July 30, 2019, by and between CytoSorbents Medical, Inc. and Phillip P. Chan (incorporated by reference to Exhibit 10.1 of the Registrant's current report on Form 8-K filed on August 5, 2019).
10.2.+	Amended and Restated Employment Agreement, dated as of July 30 2019, by and between CytoSorbents Medical, Inc. and Vincent Capponi (incorporated by reference to Exhibit 10.2 of the Registrant's current report on Form 8-K filed on August 5, 2019).
10.3+	Amended and Restated Employment Agreement, dated as of July 30, 2019, by and between CytoSorbents Medical, Inc. and Kathleen P. Bloch (incorporated by reference to Exhibit 10.3 of the Registrant's current report on Form 8-K filed on August 5, 2019).
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+	Separation Agreement and Release, dated December 9, 2019, by and between CytoSorbents Corporation and Dr. Eric Mortensen incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on December 12, 2019).
10.6+	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).
10.7	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).
10.8	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).
10.9	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).
10.10	Eighteenth Amendment to Lease Agreement by and between the Registrant and Princeton Corporate Plaza, LLC, dated January 4, 2019 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on August 6, 2019).
10.11	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).
10.12	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).

10.13†	Distribution Agreement between Biocon Biologics 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).
10.14†	First Amendment to the Distribution Agreement between Biocon Biologics 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).
10.15+	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).
10.16+	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+	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).
10.18	Amended and Restated CytoSorbents Corporation 2014 Long-Term Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-8, filed with the SEC on August 26, 2019).
10.19	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).
10.20	First Amendment to Amended and Restated Loan and Security Agreement, dated as of July 30, 2019, by and among CytoSorbents Corporation, CytoSorbents Medical, Inc. and Western Alliance Bank (incorporated by reference to Exhibit 10.1 of the Registrant's current report on Form 8-K filed on August 5, 2019).
10.21	Third Amendment to Amended and Restated Loan and Security Agreement, dated as of December 4, 2020, 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 December 10, 2020).
10.22	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).
10.23*†	Exclusive Distribution Agreement, dated as of September 26, 2014, by and between CytoSorbents Europe GmbH and Aferetica s.r.l. (incorporated by reference to Exhibit 10.23 of Registrant's Annual Report on Form 10-K filed on March 7, 2019).
10.24*†	Amendment to Exclusive Distribution Agreement, dated December 15, 2014, by and between CytoSorbents Europe GmbH and Aferetica s.r.l (incorporated by reference to Exhibit 10.24 of Registrant's Annual Report on Form 10-K filed on March 7, 2019).
10.25	Open Market Sale Agreement℠, dated as of July 9, 2019, by and among CytoSorbents Corporation, Jefferies LLC and B. Riley FBR, Inc. (incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K, filed with the SEC on July 9, 2019).
10.26	Amendment No. 1 to Open Market Sale Agreement℠, dated as of April 20, 2020, by and among CytoSorbents Corporation, Jefferies LLC and B. Riley FBR, Inc. (incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K, filed with the SEC on April 20, 2020).
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, 2020, formatted in Extensible Business Reporting Language (XBRL): (1) Consolidated Balance Sheets at December 31, 2020 and December 31, 2019, (iii) Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2020, 2019 and 2018, (iii) Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity/(Deficit) for the years ended December 31, 2020, 2019 and 2018, (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2020, 2019 and 2018, and (v) Notes to the Consolidated Financial Statements.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* 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 9th day of March, 2021.

CYTOSORBENTS CORPORATION

By: */s/ Dr. Phillip P. Chan*
Dr. Phillip P. Chan
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	Chief Executive Officer (Principal Executive Officer) and Director	March 9, 2021
/s/ Kathleen P. Bloch Kathleen P. Bloch	Chief Financial Officer (Principal Financial and Accounting Officer)	March 9, 2021
/s/ Al Kraus Al Kraus	Chairman of the Board	March 9, 2021
/s/ Alan D. Sobel Alan D. Sobel	Director	March 9, 2021
/s/ Edward R. Jones Edward R. Jones	Director	March 9, 2021
/s/Michael G. Bator Michael G. Bator	Director	March 9, 2021

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, 2020.

WithumSmith+Brown, PC, the independent registered public accounting firm that audited the Company's consolidated financial statements included in this Annual Report on Form 10-K, was engaged to audit our Internal Controls. Their report appears on page F-3.

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

March 9, 2021

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, 2020 and 2019, 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, 2020, 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, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, 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, 2020, based on criteria established in *Internal Control-Integrated Framework* (2013) issued by the COSO.

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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which they relate.

Stock Based Compensation

Description of the Matter

As discussed in Notes 2 and 11 of the consolidated financial statements, the Company grants stock-based awards including stock options, restricted stock units and performance-based stock awards to their employees as compensation for their service. The Company recorded approximately $3,500,000 of stock-based compensation expense during the year ended December 31, 2020. Certain awards include performance conditions that only vest if those conditions are met, and the quantity of awards received can range based on the level performance achieved. In 2020, the Company had 1,114,325 of such awards outstanding, and recorded stock-based compensation expense related to these performance awards of approximately $914,000.

Auditing the Company's accounting for stock-based compensation required complex auditor judgment due to the number and the variety of the types of equity awards, the subjectivity of assumptions used to value stock-based awards and the frequent use of performance-based vesting conditions. In particular, judgment was required to evaluate the nature of the annual performance conditions, as well as to assess the satisfaction of the performance targets.

How we Addressed the Matter in our Audit

Addressing the matter involved obtaining an understanding, evaluating the design and testing the operating effectiveness of controls over the Company’s process for determining stock-based compensation expense, including testing management’s review controls over the underlying calculations, the significant assumptions used in valuing certain awards, identification of the terms of the performance conditions and the key inputs used in determining the outcome of each performance condition. We assessed the appropriateness of judgments made by management in determining key assumptions related to the awards, such as service inception date based on the annual performance conditions. We tested the accuracy of the data used in measuring the awards by agreeing the underlying inputs, such as grant date, grant price, performance targets and vesting terms, among others, back to source documents, such as compensation meeting minutes or award letters. Additionally we tested the related valuation report on volatility prepared by its specialists by involving our internal valuation specialists to assess the valuation methodologies and assumptions used. We determined whether performance targets were satisfied in accordance with the contractual conditions, and recalculated grant date fair value by multiplying the awarded quantity of awards by the grant price. We also evaluated the adequacy of the Company’s stock-based compensation disclosures included in Notes 2 and 11 in relation to these matters.

/s/ WithumSmith+Brown, PC

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

East Brunswick, New Jersey
March 9, 2021

CYTOSORBENTS CORPORATION
CONSOLIDATED BALANCE SHEETS

December 31,	2020	2019
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 71,421,601	$ 12,232,418
Grants and accounts receivable, net of allowance for doubtful accounts of $46,851 and $145,313 at December 31, 2020 and 2019, respectively	5,159,275	4,467,087
Inventories	2,673,799	2,113,897
Prepaid expenses and other current assets	3,198,460	2,088,127
Total current assets	82,453,135	20,901,529
Property and equipment - net	2,119,927	1,925,325
Right of use asset	1,029,123	1,070,762
Other assets	4,348,286	3,484,894
Total Assets	$ 89,950,471	$ 27,382,510
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 1,835,082	$ 2,039,222
Accrued expenses and other current liabilities	7,870,687	5,802,296
Current maturities of long-term debt	—	1,666,666
Lease liability – current portion	447,485	428,083
Total current liabilities	10,153,254	9,936,267
Lease liability, net of current portion	581,638	642,679
Long-term debt, net of current maturities and debt issuance costs	—	13,385,522
Total liabilities	10,734,892	23,964,468
Commitments and contingencies (Note 10)		
Stockholders' Equity:		
Preferred Stock, Par Value $0.001, 5,000,000 shares authorized; - 0 - shares issued and outstanding at December 31, 2020 and 2019	—	—
Common Stock, Par Value $0.001, 100,000,000 shares authorized; 43,221,999 and 32,616,107 shares issued and outstanding at December 31, 2020 and 2019, respectively	43,222	32,616
Additional paid-in capital	277,533,082	191,648,907
Accumulated other comprehensive income (loss)	(1,734,078)	525,978
Accumulated deficit	(196,626,647)	(188,789,459)
Total stockholders' equity	79,215,579	3,418,042
Total Liabilities and Stockholders' Equity	$ 89,950,471	$ 27,382,510

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, 2020	Year ended December 31, 2019	Year ended December 31, 2018
Revenue:			
CytoSorb sales	$ 39,342,102	$ 22,545,754	$ 20,143,354
Other sales	110,400	220,100	109,029
Total product sales	39,452,502	22,765,854	20,252,383
Grant income	1,552,099	2,183,619	2,251,525
Total revenue	41,004,601	24,949,473	22,503,908
Cost of revenue	11,052,409	7,363,919	7,489,400
Gross profit	29,952,192	17,585,554	15,014,508
Operating expenses:			
Research and development	8,810,561	12,091,797	7,723,028
Legal, financial and other consulting	3,048,242	2,462,151	2,002,032
Selling, general and administrative	28,463,723	22,005,670	20,874,376
Total operating expenses	40,322,526	36,559,618	30,599,436
Loss from operations	(10,370,334)	(18,974,064)	(15,584,928)
Other income (expense):			
Interest expense, net	(1,201,067)	(1,033,661)	(1,461,045)
Gain/(loss) on foreign currency transactions	2,607,139	(350,365)	(784,752)
Total other income (expense), net	1,406,072	(1,384,026)	(2,245,797)
Loss before benefit from income taxes	(8,964,262)	(20,358,090)	(17,830,725)
Benefit from income taxes	1,127,074	1,092,446	619,546
Net loss attributable to common shareholders	$ (7,837,188)	$ (19,265,644)	$ (17,211,179)
Basic and diluted net loss per common share	$ (0.20)	$ (0.60)	$ (0.56)
Weighted average number of shares of common stock outstanding	38,818,990	32,255,253	30,719,176
Comprehensive loss:			
Net loss	$ (7,837,188)	$ (19,265,644)	$ (17,211,179)
Other comprehensive income (loss):			
Currency translation adjustment	(2,260,056)	237,803	649,160
Comprehensive loss	$ (10,097,244)	$ (19,027,841)	$ (16,562,019)

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, 2020, 2019 and 2018

	Common Stock		Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Stockholders' Equity (Deficit)
	Shares	Par value				
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
Stock based compensation - employees, consultants and directors	—	—	1,666,024	—	—	1,666,024
Issuance of common stock - offerings, net of fees incurred	191,244	192	673,461	—	—	673,653
Issuance of restricted stock options	84,249	84	663,284	—	—	663,368
Proceeds from exercise of warrants	360,358	361	1,768,130	—	—	1,768,491
Cashless exercise of warrants	9,029	9	(9)	—	—	—
Proceeds from exercise of stock options	173,734	174	739,573	—	—	739,747
Cashless exercise of stock options	23,354	22	(22)	—	—	—
Other comprehensive income, foreign translation adjustment	—	—	—	237,803	—	237,803
Net loss	—	—	—	—	(19,265,644)	(19,265,644)
Balance at December 31, 2019	32,616,107	32,616	191,648,907	525,978	(188,789,459)	3,418,042
Stock based compensation - employees, consultants and directors	—	—	3,513,671	—	—	3,513,671
Issuance of common stock - offerings, net of fees incurred	10,163,256	10,162	80,203,846	—	—	80,214,008
Issuance of restricted stock options	87,728	88	657,692	—	—	657,780
Proceeds from exercise of stock options	341,507	342	1,508,980	—	—	1,509,322
Cashless exercise of stock options	13,401	14	(14)	—	—	—
Other comprehensive loss, foreign translation adjustment	—	—	—	(2,260,056)	—	(2,260,056)
Net loss	—	—	—	—	(7,837,188)	(7,837,188)
Balance at December 31, 2020	43,221,999	$ 43,222	$ 277,533,082	$ (1,734,078)	$ (196,626,647)	$ 79,215,579

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

CYTOSORBENTS CORPORATION
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31, 2020	Year ended December 31, 2019	Year ended December 31, 2018
Cash flows from operating activities:			
Net loss	$ (7,837,188)	$ (19,265,644)	$ (17,211,179)
Adjustments to reconcile net loss to net cash used by operating activities:			
Non-cash interest expense	—	—	637,000
Non-cash compensation	1,193,949	1,173,743	947,910
Depreciation and amortization	660,788	581,532	390,551
Bad debt expense (recovery)	(102,310)	72,429	14,762
Foreign currency transaction (gains) losses	(2,607,139)	350,365	784,752
Stock-based compensation	3,513,671	1,666,024	4,437,250
Amortization of loan acquisition costs	322,812	115,206	97,041
Changes in operating assets and liabilities:			
Grants and accounts receivable	(326,860)	(642,171)	(1,847,848)
Inventories	(461,512)	(1,284,848)	(56,751)
Prepaid expenses and other current assets	(1,076,849)	(953,888)	(731,672)
Other assets	—	4,030	(6,345)
Accounts payable and accrued expenses	1,107,352	1,424,440	1,704,845
Net cash used by operating activities	(5,613,286)	(16,758,782)	(10,839,684)
Cash flows from investing activities:			
Purchases of property and equipment	(708,395)	(698,165)	(671,970)
Patent costs	(967,823)	(821,952)	(848,294)
Net cash used by investing activities	(1,676,218)	(1,520,117)	(1,520,264)
Cash flows from financing activities:			
Proceeds from long-term debt	1,410,900	5,000,000	666,667
Repayment of long-term debt	(16,410,900)	—	(666,667)
Final fee on long-term debt	(375,000)	—	—
Payment of loan acquisition costs	—	(4,212)	(147,988)
Equity contributions - net of fees incurred	80,214,008	673,653	14,126,525
Proceeds from exercise of stock options	1,509,322	739,747	2,206,860
Proceeds from exercise of warrants	—	1,768,491	1,280,456
Net cash provided by financing activities	66,348,330	8,177,679	17,465,853
Effect of exchange rates on cash	130,357	(35,199)	(58,930)
Net change in cash and cash equivalents	59,189,183	(10,136,419)	5,046,975
Cash and cash equivalents at beginning of year	12,232,418	22,368,837	17,321,862
Cash and cash equivalents at end of year	$ 71,421,601	$ 12,232,418	$ 22,368,837
Supplemental disclosure of cash flow information:			
Cash paid during the year for interest	$ 1,127,647	$ 1,059,541	$ 891,386
Supplemental disclosure of non-cash financing activities:			
Settlement of accrued bonuses with restricted stock units	$ 657,780	$ 425,639	$ 545,693

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 consolidated financial statements include CytoSorbents Switzerland GmbH and CytoSorbents Poland Sp. z.o.o., wholly owned subsidiaries of CytoSorbents Europe GmbH, and CytoSorbents UK Limited, a wholly-owned subsidiary of CytoSorbents Medical, Inc. These entities are collectively referred to as "the Company".

In years prior to December 31, 2020, the Company's consolidated financial statements were prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. On July 24, 2020, the Company closed an underwritten public offering of 6,052,631 shares of its common stock at a public offering price of $9.50 per share (the "Offering"). Gross proceeds from the Offering amounted to approximately $57.5 million and, after deducting the underwriting discounts and commissions and expenses related to the Offering, the Company received total net proceeds of approximately $53.8 million. See Note 11. As of December 31, 2020, the Company's cash balance was approximately $71.4 million, which the Company expects will fund the Company's operations well beyond the next twelve months. As a result, the Company has determined that the going concern risk has been substantially mitigated.

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. In the third quarter of 2019, the Company formed CytoSorbents UK Limited, a wholly-owned subsidiary of CytoSorbents Medical, Inc. which is responsible for the management of our clinical trial activities in the United Kingdom.

CytoSorb, the Company's flagship product, was approved in the European Union (“EU”) in March 2011, and is currently being marketed and distributed in sixty-seven 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. In January 2020, CytoSorb received European Union CE Mark label expansion to include the removal of ticagrelor during cardiopulmonary bypass in patients undergoing cardiothoracic surgery. In May 2020, CytoSorb also received European Union CE Mark label expansion to include rivaroxaban removal for the same indication.

In April 2020, the Company announced that the United States Food and Drug Administration (the “FDA”) granted Emergency Use Authorization (“EUA”) of CytoSorb for use in critically-ill patients infected with COVID-19. Under the EUA, the Company can make CytoSorb available, through commercial sales, to all hospitals in the United States for use in patients, 18 years of age or older, with confirmed COVID-19 infection who are admitted to the intensive care unit (ICU) with confirmed or imminent respiratory failure who have early acute lung injury or acute respiratory distress syndrome (ARDS), severe disease, or life-threatening illness resulting in respiratory failure, septic shock, and/or multiple organ dysfunction or failure. The CytoSorb device has neither been cleared nor approved for the indication to treat patients with COVID-19 infection. The EUA will be effective until a declaration is made that the circumstances justifying the EUA have terminated or until revoked by the FDA.

In April 2020, the Company also announced that the FDA had granted Breakthrough Designation to CytoSorb for the removal of ticagrelor in a cardiopulmonary bypass circuit during emergent and urgent cardiothoracic surgery. The Breakthrough Devices Program provides for more effective treatment of life-threatening or irreversibly debilitating disease or conditions, in this case the need to reverse the effects of ticagrelor in emergent or urgent cardiac surgery that can otherwise cause a high risk of serious or life-threatening bleeding. Through Breakthrough Designation, the FDA intends to work with CytoSorbents to expedite the development, assessment, and regulatory review of CytoSorb for the removal of ticagrelor, while maintaining statutory standards of regulatory approval (e.g., 510(k), *de novo* 510(k) or premarket approval) consistent with the FDA’s mission to protect and promote public health.

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 adsorption. The Company has numerous products under development based upon this unique blood purification technology, which is protected by 16 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 2021 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 CytoSorbents Corporation and its wholly-owned subsidiaries, CytoSorbents Medical, Inc. and CytoSorbents Europe GmbH. In addition, the consolidated financial statements include CytoSorbents Switzerland GmbH and CytoSorbents Poland Sp. z.o.o., wholly owned subsidiaries of CytoSorbents Europe GmbH, and CytoSorbents UK Limited, a wholly-owned subsidiary of CytoSorbents Medical, Inc. 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 $2,607,000, $(350,000) and $(785,000) for the years ended December 31, 2020, 2019 and 2018, 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 reserved for to the allowance for doubtful accounts.

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, 2020 and 2019, the Company's inventory was comprised of finished goods, which amounted to $1,164,635 and $305,452, respectively, work in process which amounted to $1,222,062 and $1,523,923, respectively and raw materials which amounted to $287,102 and $284,522, 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, other agreements provide for reimbursement of costs and an overhead margin and certain agreements are performance based, where revenue is earned based upon the achievement of milestones outlined in the contract. Revenues are recognized when the associated performance obligation is fulfilled. Costs are recorded as incurred. Amounts invoiced in excess of costs actually incurred on fixed price contracts are classified as deferred revenue. 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 $285,000, $314,000 and $212,000 in 2020, 2019 and 2018, respectively, and is included in selling, general, and administrative expenses on the consolidated statements of operations and comprehensive loss.

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 reduced the U.S. federal corporate tax rate from 35% to 21%. See Note 9 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, 2020 or 2019. 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 and Research and Development credits to an industrial company.

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

Use of Estimates

The preparation of consolidated 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. The valuation of options granted is a significant estimate in these consolidated financial statements.

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, 2020 and 2019, no agency, distributor/strategic partners or direct customer represented more than 10%of outstanding grants and accounts receivables. For the years ended December 31, 2020, 2019 and 2018 no agency, distributor/strategic partners or direct customer represented more than 10% of the Company’s total revenue.

Financial Instruments

The carrying values of cash and cash equivalents, accounts receivable, accounts payable and accrued expenses and other current liabilities 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 12).

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 non-employees for acquiring, or in conjunction with selling, goods or services for equity instruments issued to consultants.

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 $560,000, $476,000 and $424,000 for the years ended December 31, 2020, 2019 and 2018, respectively.

3. Revenue

The following table disaggregates the Company's revenue by customer type and geographic area for the year ended December 31, 2020:

	Direct	Distributors/ Strategic Partners	United States Government Agencies	Total
Product sales:				
United States	$ 1,148,300	$ 192,900	$ —	$ 1,341,200
Germany	20,257,410	–	—	20,257,410
All other countries	5,275,619	12,578,273	—	17,853,892
Total product	26,681,329	12,771,173	—	39,452,502
Grant and other income:				
United States	—	—	1,552,099	1,552,099
Total revenue	$ 26,681,329	$ 12,771,173	$ 1,552,099	$ 41,004,601

The following table disaggregates the Company's revenue by customer type and geographic area for the year ended December 31, 2019:

	Direct	Distributors/ Strategic Partners	United States Government Agencies	Total
Product sales:				
United States	$ 220,100	$ —	$ —	$ 220,100
Germany	14,396,418	—	—	14,396,418
All other countries	3,147,529	5,001,807	—	8,149,336
Total product	17,764,047	5,001,807	—	22,765,854
Grant and other income:				
United States	—	—	2,183,619	2,183,619
Total revenue	$ 17,764,047	$ 5,001,807	$ 2,183,619	$ 24,949,473

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	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 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. The majority of sales of the device are outside the United States, as CytoSorb is not yet approved for commercial sale in the United States. However, in April 2020, the Company was granted Emergency Use Authorization ("EUA") of CytoSorb for use in critically-ill patients infected with COVID-19 by the United States Food and Drug Administration (the "FDA"). Direct sales outside the United States relate to sales to hospitals located in Germany, Switzerland, Austria, Belgium, Luxembourg, Poland, the Netherlands, Sweden, Denmark and Norway. Direct sales are fulfilled from the Company's office in Berlin, Germany. 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 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. In addition, certain distributors are eligible for volume discount pricing if their unit sales are in excess of the base amount in the contract.

Most distributor's/strategic partner's contracts have 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.

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. If billings on fixed price contracts exceed the costs incurred, revenue will be deferred to the extent of the excess billings.

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.

4. Performance based - the Company submits invoices only upon the achievement of the milestones listed in the contract. The amount to be invoiced for each milestone is documented 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, 2020	December 31, 2019
Contract receivables, which are included in accounts receivable	$ 2,996,679	$ 2,246,821
Contract liabilities, which are included in expenses and other current liabilities	$ 1,014,652	$ 171,842

Contract receivables represent balances due from sales to distributors and amounts invoiced on grant contracts.

Contract liabilities represent the value of free of charge goods and credit rebates earned in accordance with the terms of certain direct customer agreements and deferred grant revenue related to the billing on fixed price contracts in excess of costs incurred as of December 31, 2020 and 2019.

4. PROPERTY AND EQUIPMENT, NET:

Property and equipment - net, consists of the following:

December 31,	2020	2019	Depreciation/ Amortization Period
Furniture and fixtures	$ 1,081,366	$ 795,167	7 years
Equipment and computers	4,318,323	3,861,912	3 to 7 years
Leasehold improvements	971,247	927,894	Lesser of term of lease or estimated useful life
	6,370,936	5,584,973	
Less accumulated depreciation and amortization	4,251,009	3,659,648	
Property and Equipment, Net	$ 2,119,927	$ 1,925,325	

Depreciation expense for the years ended December 31, 2020, 2019 and 2018 amounted to $553,946, $495,728 and $329,469 respectively.

5. OTHER ASSETS:

Other assets consist of the following:

December 31,	2020	2019
Patent applications pending	$ 2,970,354	$ 2,308,780
Patents issued	1,748,938	1,442,688
Less accumulated amortization of patents issued	(496,898)	(390,056)
Patents, net	4,222,394	3,361,412
Security deposits	125,892	123,482
Total	$ 4,348,286	$ 3,484,894

Amortization expense amounted to $106,842, $85,804 and $61,082 for the years ended December 31, 2020, 2019 and 2018, respectively.

Amortization expense for the next five years will be approximately $116,200 for the year ended December 31, 2021; approximately $113,000 for the year ended December 31, 2022; approximately $109,600 for the year ended December 31, 2023; approximately $109,600 for the year ended December 31, 2024; and approximately $109,600 for the year ended December 31, 2025.

6. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES:

Accrued expenses and other current liabilities consist of the following:

December 31,	2020	2019
Accrued salaries and commissions	$ 3,165,635	$ 1,926,167
Accrued royalties	916,695	525,004
Sales, payroll and income taxes payable	901,900	402,816
Clinical studies	781,041	1,384,564
Deferred revenue	728,351	—
Accrued accounts payable	631,642	629,186
Professional fees	317,575	394,088
Customer rebates	305,852	157,656
Board of Director fees	62,140	59,750
Congresses	35,589	—
Travel and entertainment	24,267	214,436
Interest	—	108,629
	$ 7,870,687	$ 5,802,296

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 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”). On July 31, 2019, the Borrower entered into the First Amendment to the Amended and Restated Loan and Security Agreement (the "First Amendment") with the Bank, which amended certain provisions of the Amended and Restated Loan and Security Agreement and the 2018 Success Fee Letter (the "2018 Letter"). In connection with the execution of the First Amendment, the draw period for the Term B Loan was extended to August 15, 2019 and the Company drew down the full $5.0 million Term B Loan on the Settlement Date, bringing the total outstanding debt to $15 million at July 31, 2019. The proceeds of Term Loans were used for general business requirements in accordance with the Amended and Restated Loan and Security Agreement. On December 4, 2020 (the “Closing Date”), the Company closed on the Third Amendment (the “Third Amendment”) of its Amended Loan and Security Agreement with Bridge Bank. Under the terms of the Amendment, the Company repaid the outstanding principal balance of its existing $15 million term loans and simultaneously received a commitment from Bridge Bank to provide a new term loan of $15 million (the “New Term Loan”), if needed.

Under the terms of the Third Amendment, the Company may, at its sole discretion, draw down the New Term Loan at any time over the next twelve months. The New Term Loan, if drawn, shall bear interest at the Index Rate (defined in the Amendment as the greater of 3.25% or the Prime Rate as published by the Wall Street Journal on the last business date of the month the immediately preceding the month in which the interest will accrue) plus 1.25%. In addition, the Company would be required to make payments of interest-only commencing on the first day of the month after the New Term Loan was made until January 2023. The interest-only period may be further extended through July 2023 if the Company maintains compliance certain conditions as outlined in the Amendment. Following the interest-only period, the Company will be required to make equal monthly payments of principal and interest until maturity of the New Term Loan. The maturity date of the New Term Loan is December 1, 2024.

On the Closing Date, the Company was required to pay a non-refundable closing fee of $75,000. As of the Closing Date, the total unamortized loan costs related to the Term Loans amounted to approximately $45,000. These costs were written off on the Closing Date as a charge to interest expense. For the years ended December 31, 2020, 2019, and 2018, the Company recorded interest expense amounting to $76,718, $33,175, and $31,946, respectively related to these costs. 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. On the Closing Date, the Company paid a final fee of $375,000. For the years ended December 31, 2020, 2019 and 2018 the Company recorded interest expense of $246,095, $82,031 and $65,104, respectively, related to accrual and payment of the final fee.

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).

2018 Success Fee Letter:

Pursuant to the amended 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 (as defined in the Restated Loan and Security Agreement) (the "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 the Nasdaq Capital Market 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 average price of Company's common stock for the 365 day period ending on the date of the funding of the Term B Loan. This obligation shall terminate on the fifth anniversary of the funding of the Term B Loan and shall survive the termination of the loan agreement and the prepayment of the Term B Loan.

Long-term debt consists of the following at December 31, 2020 and 2019 as follows:

	December 31,	
	2020	2019
Principal amount	$ —	$ 15,000,000
Less unamortized debt acquisition costs	—	(76,718)
Plus accrued final fee	—	128,906
Subtotal	—	15,052,188
Less current maturities	—	1,666,666
Long-term debt net of current maturities	$ —	$ 13,385,522

Payroll Protection Program:

On April 13, 2020, the Company received approximately $1,411,000 in loan proceeds from the Payroll Protection Program (the "PPP") administered by the Small Business Administration (the "SBA") of the United States government. This program was established under the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act"). On April 29, 2020, following a reassessment of the Company's financial and operating position, including cash on hand and access to public capital markets, the Company repaid the PPP loan.

8. LEASES:

Effective January 1, 2019, the Company adopted the provisions of Accounting Standards Update ("ASU") 2016-02, Leases (Topic 842). The provisions of this ASU require the Company to record a right-of-use asset and related lease liability related to their leases.

The Company leases its operating facilities in both the United States and Germany under operating lease agreements. In the United States, in May 2020, the Company entered into a Nineteenth Amendment to Lease with the landlord which became effective May 1, 2020. This amendment expands the Company's space to 20,821 square feet and extends the term of the lease to May 31, 2021. The Company's base rent is approximately $34,000 per month. In addition, the Company is obligated to pay monthly operating expenses of approximately $30,000 per month. The amendment also includes a one year renewal option. The base rent for the renewal term will increase by the greater of five percent or the increase in the Consumer Price Index. There were no lease incentives and no initial direct costs were incurred related to this lease amendment.

In Germany, the Company leases its operating facility under two operating lease agreements. These leases require combined base rent payments amounting to approximately $9,000 per month. The initial lease term of both leases ends August 31, 2021. In addition, the Company is obligated to monthly operating expenses of approximately $2,900 per month. Both leases have a five year option to renew that would extend the lease term to August 31, 2026. There are no provisions in the leases to increase the base rent during the renewal period. There were no lease incentives and no initial direct costs were incurred related to these leases.

Right-Of-Use Asset and Lease Liability:

The Company's consolidated balance sheets reflect the value of the right-of-use asset and related lease liability. This value was calculated based on the present value of the remaining base rent lease payments. The remaining lease payments include the renewal periods for both facilities as the Company has determined that it is probable that the renewal options will be exercised under each of the lease agreements. The discount rate used was the Company's incremental borrowing rate, which is 9.16%, as the Company could not determine the rate implicit in the lease. As a result, the value of the right-of-use asset and related lease liability is as follows:

	December 31,	
	2020	2019
Right-of-use asset	$ 1,029,123	$ 1,070,762
Total lease liability	$ 1,029,123	$ 1,070,762
Less current portion	(447,485)	(428,083)
Lease liability, net of current portion	$ 581,638	$ 642,679

The maturities of the lease liabilities are as follows as of December 31, 2020:

2021	$ 447,485
2022	246,251
2023	80,642
2024	88,347
2025	96,788
Thereafter	69,610
Total	$ 1,029,123

For the years ended December 31, 2020, 2019 and 2018, operating cash flows paid in connection with operating leases amounted to approximately $937,000, $906,000 and $805,000, respectively.

As of December 31, 2020 and 2019 the weighted average remaining lease term was 4.0 years, respectively.

9. 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, 2020, 2019 and 2018 is as follows:

	Year Ended December 31,		
	2020	2019	2018
Domestic	$ (5,682,628)	$ (11,921,799)	$ (14,105,664)
Foreign	(3,281,636)	(8,436,291)	(3,725,061)
Total	$ (8,964,262)	$ (20,358,090)	$ (17,830,725)

The benefit from income taxes consists of the following:

	Year Ended December 31,		
	2020	2019	2018
State Tax, including sale of New Jersey losses & credits	$ 1,127,074	$ 1,092,446	$ 619,546
Foreign tax provision	—	—	—
	$ 1,127,074	$ 1,092,446	$ 619,546

As of December 31, 2020, the Company had federal net operating loss ("NOL") carry forwards of approximately $72.8 million, state NOL carry forwards of approximately $5.0 million, and foreign NOL carry forwards of approximately $22.2 million, which may be available to offset future taxable income, if any. The federal NOL carryforwards of $47.8 million, if not utilized, will expire between 2021 and 2037. The federal NOL carryforwards of $25.0 million generated since 2018 are subject to an 80% limitation on taxable income, do not expire and will carry forward indefinitely. The state NOL carryforwards of $5.0 million, if not utilized, will begin to expire in 2039. As of December 31, 2020, the Company had Federal and state research and development tax credit carryforwards of approximately $2.2 million and $151,000, 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 expected 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, is 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 2019 and as such there was no impact from GILTI included in its 2019 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.

The Company will receive a net cash amount of approximately $1,127,000 from the approved sale of the 2019 state NOL and research and development credits in the first quarter of 2021.

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

	Year Ended December 31,		
	2020	2019	2018
Deferred tax assets:			
Net operating loss carry forward	$ 22,301,154	$ 20,843,902	$ 16,722,801
Stock options	305,982	329,726	349,810
Research and development credit carryforward	2,194,211	1,720,558	1,210,153
Accruals and others	135,330	56,461	(27,098)
Lease liability	289,287	300,991	—
Gross deferred tax assets	25,225,964	23,251,638	18,255,666
Less valuation allowance	(24,794,474)	(22,857,741)	(18,233,810)
	431,490	393,897	21,856
Deferred tax liability:			
Fixed assets	(431,490)	(393,897)	(21,856)
Net deferred tax assets	$ —	$ —	$ —

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

The increases in valuation allowance for the years ended December 31, 2020, 2019 and 2018 were $1,936,733, $4,623,931 and 4,806,456, 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,		
	2020	2019	2018
Federal statutory rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	(9.5)	(4.4)	(2.2)
Foreign rate differential	3.3	3.7	1.9
Permanent items	(2.0)	(2.0)	(2.9)
Rate change and true-up	17.0	8.0	7.6
Change in valuation allowance	(21.6)	(22.7)	(22.9)
R&D credit	4.4	1.8	0.7
Effective income tax rate	12.6 %	5.4 %	3.2 %

10. COMMITMENTS AND CONTINGENCIES:

Customs Examination

In October 2020, the Company received a notice from the German Customs Authorities that they would be conducting an audit of the Company's import transactions for the years 2018 through 2020 in order to determine if any import taxes would be due. The audit commenced in early December 2020. The primary import activity of the Company is the importation of CytoSorb devices from the United States. The German Customs Authorities are challenging the Harmonized Code that the Company utilizes to import the CytoSorb devices into Germany. The code that has been utilized by the Company has zero import taxes associated with it. The German Customs Authorities have indicated that the Company's device might be better classified under a different code which has a 1.7% tax attached to it. As part of the audit process, the Company has provided the German Customs Authorities with extensive information about the CytoSorb device, including data regarding the uses of the device, as well as the instructions for use. In addition, employees of the Company gave the auditors a technical presentation of the scientific properties of the device, focusing on it as an adsorber, as opposed to a filter. The German Customs Authority's technical staff is currently reviewing this information. The audit process is on-going and the authorities have indicated it is expected to be completed by approximately March 31, 2021. The Company's maximum potential exposure arising to the audit is approximately $732,000. Based on a thorough review of the facts, management believes that it is not probable that this contingency is likely to occur. Accordingly, no expense or related liability has been recorded in the Company's December 31, 2020 consolidated financial statements related to this contingency.

Employment Agreements

On July 30, 2019, CytoSorbents Corporation entered into amended and restated executive employment agreements with its principal executives, Dr. Phillip P. Chan, Chief Executive Officer, Vincent Capponi, President and Chief Operating Officer, and Kathleen P. Bloch, Chief Financial Officer. Each of the agreements has an initial term of three years, and was retroactively effective as of January 1, 2019. On April 12, 2020, CytoSorbents Corporation entered into an executive employment agreement with Dr. Efthymios Deliargyris, who began employment as Chief Medical Officer on May 1, 2020, with an initial term that expires on December 31, 2021. After the expiration of the initial terms, the employment agreements will automatically renew for additional terms of one year unless either party provides written notice of non-renewal at least 60 days prior to a renewal. The foregoing 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 of 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 Agreement

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, 2020, 2019 and 2018, the Company recorded royalty expenses of approximately $1,172,000, $675,000, and $600,000, respectively. These expenses are included in selling, general and administrative expenses in the consolidated statements of operations and comprehensive loss.

License Agreement

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, 2020, 2019 and 2018 per the terms of the license agreement, the Company recorded licensing expenses of approximately $1,954,000 $1,125,000 and $1,002,000, respectively. These expenses are included in selling, general and administrative expenses in the consolidated statements of operations and comprehensive loss.

11. STOCKHOLDERS' EQUITY:

Preferred Stock

In June 2019, the Company amended and restated its certificate of incorporation. The amended and restated certificate of incorporation 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.

Common Stock

In June 2019, the Company amended and restated its certificate of incorporation. The amended and restated certificate of incorporation increased the number of shares of common stock authorized for issuance from 50,000,000 shares to 100,000,000 shares.

July 24, 2020 Offering

On July 24, 2020, the Company closed an underwritten public offering of 6,052,631 shares of its common stock at a public offering price of $9.50 per share (the "Offering"). The Company completed the Offering pursuant to the terms of an Underwriting Agreement, dated as of July 21, 2020, by and among the Company and Cowen and Company, LLC and SVB Leerink LLC, as representatives of the several underwriters named therein. The Company received gross proceeds of approximately $57.5 million from the Offering and after deducting the underwriting discounts and commissions and fees and expenses payable by the Company in connection with the Offering, the Company received net proceeds of approximately $53.8 million.

Shelf Registration

On July 26, 2018, the Company filed a 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.

Termination of Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co.

On May 31, 2019, the Company delivered to Cantor Fitzgerald & Co. ("Cantor") written notice of termination (the "Termination Notice") of the Controlled Equity Offering Sales Agreement, dated November 4, 2015, by and between the Company and Cantor, as amended by Amendment No. 1 to Sales Agreement, dated July 26, 2018 (collectively, the "Sales Agreement"). In accordance with Section 13(b) thereof, the Sales Agreement terminated on June 10, 2019, ten (10) days after the delivery of the Termination Notice. As provided in the Sales Agreement, the Sales Agreement terminated without liability of any party to any other party, except that certain provisions of the Sales Agreement identified therein shall remain in full force and effect notwithstanding the termination. Pursuant to the Sales Agreement, the Company offered and sold, from time to time through Cantor, shares of the Company's common stock. In the aggregate, the Company sold 2,094,140 shares pursuant to the Sales Agreement, at an average selling price of $8.72 per share, generating net proceeds of approximately $17.7 million from November 4, 2015 through December 31, 2018. There were no sales during the year ended December 31, 2019.

Open Market Sale Agreement with Jefferies LLC and B. Riley FBR, Inc.

On July 9, 2019, the Company entered into an Open Market Sale Agreement (the "New Sale Agreement") with Jefferies LLC and B. Riley FBR, Inc. (each an "Agent" and, together, the "Agents"), pursuant to which the Company may sell, from time to time, at its option, shares of the Company's common stock having an aggregate offering price of up to $25 million through the Agents, as the Company's sales agents. All shares of the Company's common stock offered and sold, or to be offered and sold under the New Sale Agreement were or will be issued and sold pursuant to the Company's 2018 Shelf by methods deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, in block transactions or if specified by the Company, in privately negotiated transactions.

On April 20, 2020, the Company and the Agents entered into an amendment to the New Sale Agreement (the "Amendment") to provide for an increase in the aggregate offering amount under the New Sales Agreement, such that as of April 20, 2020, the Company may offer and sell Shares having an additional aggregate offering price of up to $50 million under the New Sale Agreement, as amended by the Amendment (the "Amended Sale Agreement").

Subject to the terms of the Amended Sales Agreement, the Agents are required to use their commercially reasonable efforts consistent with their normal sales and trading practices to sell the shares of the Company's common stock from time to time, based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company is required to pay the Agents a commission of up to 3.0% of the gross proceeds from the sale of the shares of the Company's common stock sold thereunder, if any. The Company has also agreed to provide the Agents with customary indemnification rights. The offering of the shares of the Company's common stock under the Amended Sales Agreement will terminate upon the earliest of (a) the sale of the maximum number or amount of the shares of the Company's stock permitted to be sold under the Amended Sale Agreement and (b) the termination of the Amended Sale Agreement by the parties thereto. During the year ended December 31, 2019, the Company sold 191,244 shares pursuant to the Amended Sale Agreement, at an average selling price of $4.11 per share, generating net proceeds of approximately $762,000. During the year ended December 31, 2020, the Company sold 4,110,625 shares pursuant to the Amended Sale Agreement, at an average selling price of $6.64 per share, generating net proceeds of approximately $26.5 million. In the aggregate, the Company has sold 4,301,869 shares pursuant to the Amended Sale Agreement, at an average selling price of $6.53 per share, generating net proceeds of approximately $27.2 million. In addition, during the year ended December 31, 2020, the Company paid approximately $49,000 in expenses related to the Amended Sale Agreement.

Stock Option Plans

As of December 31, 2020, 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 13,400,000 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, 2020, there were shares remaining to purchase approximately 8,216,000 and 236,000 units 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, 2020, 2019 and 2018 amounted to approximately $3,514,000, $1,666,000 and $4,437,000, respectively. These amounts are included in selling, general, and administrative expenses on the consolidated statements of operations and comprehensive loss.

The summary of the stock option activity for the years ended December 31, 2020, 2019 and 2018 is as follows:

	Shares	Weighted Average Exercise per Share	Weighted Average Remaining Contractual Life (Years)
Outstanding January 1, 2018	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
Granted	1,557,300	$ 7.19	9.5
Forfeited	(747,671)	$ 7.39	
Expired	(16,320)	$ 4.16	—
Exercised	(233,582)	$ 4.09	—
Outstanding, December 31, 2019	4,218,189	$ 6.16	7.0
Granted	1,579,106	$ 6.37	9.0
Forfeited	(34,644)	$ 7.50	—
Expired	(226,440)	$ 5.60	—
Exercised	(371,007)	$ 4.46	—
Outstanding, December 31, 2020	5,165,204	$ 6.36	7.26

The fair value of each stock option was estimated using the Black Scholes pricing model which takes into account as of the grant date the exercise price (ranging from $5.00 - $10.58 per share in 2020) and expected life of the stock option (10 years in 2020), the current price of the underlying stock and its expected volatility (ranging from 61.7 to 69.8 percent in 2020), expected dividends (-0- percent) on the stock and the risk free interest rate (0.28 to 0.96 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, 2020 of $7.97 and the exercise price of the shares.

Options Exercisable			
Number Exercisable at December 31, 2020	Weighted Average Exercise Price	Aggregate Intrinsic Value	
3,167,087	$ 6.18	$ 6,002,524	

Options Outstanding				
Range of Exercise Price	Number Outstanding at December 31, 2020	Weighted Average Exercise Price	Weighted Average Remaining Life (Years)	Aggregate Intrinsic Value
$5.68 - $10.58	5,165,204	$ 6.36	7.26	$ 8,786,197

The summary of the status of the Company's non-vested options for the year ended December 31, 2020 is as follows:

	Shares	Weighted Average Grant Date Fair Value
Non-vested, January 1, 2020	1,183,790	$ 4.49
Granted	1,579,106	3.88
Forfeited	(34,644)	4.74
Vested	(730,135)	4.15
Non-vested, December 31, 2020	1,998,117	$ 4.12

As of December 31, 2020, the Company had approximately $2,898,000 of total unrecognized compensation cost related to stock options which will, on average, be amortized over 27 months.

In 2021, 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 2021 operations. Since these options relate exclusively to the achievement of 2021 milestones, no charge for these options has been recorded in the consolidated statements of operations for the year ended December 31, 2020. The Company will assess the likelihood of meeting these milestones throughout 2021 and will record stock option expense as appropriate.

Awards of Stock Options:

On February 28, 2020, the Board of Directors granted options to purchase 1,114,325 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 2020 operations. Once awarded, these options will vest in four equal tranches, the first tranche vesting on the date of the award. The grant date fair value of these unvested options amounted to approximately $3,883,000. Based upon an assessment by management, which was reviewed with the Board of Directors, as of December 31, 2020, the Company met approximately 88% of these milestones, and accordingly we have recorded $914,000 in stock option expense related to these options for the year ended December 31, 2020.

On July 22, 2019, the Board of Directors granted options to purchase 926,800 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. The grant date fair value of these unvested options amounted to approximately $4,294,000. On February 18, 2020, Board of Directors determined that the Company has met 35% of these milestones, and accordingly we have recorded approximately $735,000 and $315,000 of stock option expense related to these options for the years ended December 31, 2020 and 2019, respectively.

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, based upon the finalization of its review of the Company's progress to meeting the predetermined milestones for 2018, the Board of Directors determined that 726,920 of these options would immediately vest. Accordingly, a charge of approximately $3,381,000 related to these options has been recorded in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2018.

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, 2018	277,200	724,500	1,002,300	2,004,000	
Granted 2019	—	—	264,500	264,500	
Forfeited 2019	—	(120,000)	(61,750)	(181,750)	
December 31, 2019	277,200	604,500	1,205,050	2,086,750	$ 8,033,988
Granted 2020	—	120,000	265,700	385,700	
Forfeited 2020	—	—	(25,250)	(25,250)	
December 31, 2020	277,200	724,500	1,445,500	2,447,200	$ 19,504,184

Due to the uncertainty over whether these restricted stock units will vest, which will only happen upon a Change in Control, no charge for these restricted stock units has been recorded in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2020.

Performance-Based Awards of Restricted Stock Units:

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, 2020, 2019 and 2018, the Company recorded an expense/(recovery) of approximately $(23,000), $150,000, and $329,000, 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 2018, on March 4, 2019 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 date of the grant, and one third on the second anniversary of the date of the grant. For the years ended December 31, 2020, and 2019, the Company recorded a charge of approximately $33,000 and $39,000, 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 2019, on July 22, 2019 the Board of Directors granted 180,300 restricted stock units to certain senior managers of the Company. These awards were valued at approximately $1,300,000 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 date of the grant, and one third on the second anniversary of the date of the grant. For the years ended December 31, 2020, and 2019, the Company recorded a charge of approximately $564,000 and $621,000, 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 2019, on February 28, 2020, the Board of Directors granted 168,100 restricted stock units to certain senior managers of the Company in order to settle bonuses accrued as of December 31, 2020. These awards were valued at approximately $1,014,000 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 date of the grant, and one third on the second anniversary of the date of the grant. For the years ended December 31, 2020, the Company recorded a charge of approximately $619,000 related to these restricted stock unit awards.

The following table outlines the restricted stock unit activity for the year ended December 31, 2020:

	Shares	Weighted Average Grant Date Fair Value
Non-vested, January 1, 2020	167,872	$ 7.52
Granted	168,100	$ 6.03
Vested	(162,000)	$ 7.05
Non-vested, December 31, 2020	173,972	$ 6.52

Warrants:

As of December 31, 2020, the Company had no warrants outstanding.

12. NET LOSS PER SHARE

Basic earnings per share and diluted earnings per share for the years ended December 31, 2020, 2019 and 2018 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 7,786,000, 6,503,000, and 6,232,000 incremental shares at December 31, 2020, 2019 and 2018, respectively, have been excluded from the computation of diluted loss per share as they are anti-dilutive.

13. 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 five percent of compensation. Effective January 1, 2021, the Company changed its matching contribution to 100% of the participants contribution up to three percent of compensation plus 50% of the participants contribution over three percent of compensation up to a maximum of five percent of compensation. Matching contributions amounted to approximately $59,200, $43,800 and $43,600 for the years ended December 31, 2020, 2019 and 2018, respectively.

14. SUBSEQUENT EVENT

In January 2021, CytoSorbents Europe GmbH entered into a lease for additional warehouse space. The lease commences on April 1, 2021, requires monthly payments of base rent and other costs of approximately $7,900 and has a term of five years. The lease also has an option to extend the lease term for an additional five years.

15. QUARTERLY FINANCIAL RESULTS (UNAUDITED)

Summarized quarterly data for 2020, 2019 and 2018 are as follows:

	For the Quarters Ended			
	March 31	June 30	September 30	December 31
2020:				
Total revenue	$ 8,707,310	$ 9,794,903	$ 10,546,612	$ 11,955,776
Gross margin	6,322,468	6,545,136	7,656,230	9,428,358
Loss from operations	(2,478,754)	(3,297,667)	(1,959,652)	(2,634,264)
Net loss attributable to common stockholders	(3,452,779)	(2,866,956)	(839,729)	(677,724)
Net loss per share, basic and diluted	(0.10)	(0.08)	(0.02)	0.00
2019				
Total revenue	$ 5,191,629	$ 6,232,526	$ 6,095,007	$ 7,430,311
Gross margin	3,453,040	4,398,160	4,398,733	5,335,621
Loss from operations	(4,285,193)	(3,629,997)	(5,627,546)	(5,431,328)
Net loss attributable to common stockholders	(4,883,827)	(3,547,405)	(6,885,061)	(3,949,351)
Net loss per share, basic and diluted	(0.15)	(0.11)	(0.21)	(0.13)
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)

Exhibit 21.1

CytoSorbents Corporation

List of Subsidiaries

Name	Jurisdiction
CytoSorbents Medical Inc.*	Delaware
CytoSorbents Europe GmbH*	Germany
CytoSorbents Switzerland**	Switzerland
CytoSorbents Poland Sp. z.o.o.**	Poland
CytoSorbents UK Limited***	United Kingdom

*Wholly-owned subsidiary of CytoSorbents Corporation

**Wholly-owned subsidiary of CytoSorbents Europe GmbH

***Wholly-owend subsidiary of CytoSorbents Medical Inc.

Exhibit 23.1

CONSENT OF REGISTERED INDEPENDENT PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference of our reports dated March 9, 2021 relating to the consolidated financial statements of CytoSorbents Corporation (the "Company") as of December 31, 2020 and 2019 and for each of the three years in the period ended December 31, 2020 and the effectiveness of the Company's internal control over financial reporting which appears in this annual report on Form 10-K into the Company's previously filed Registration Statements on Forms S-3 (Registration Nos. 333-226372, 333-194394, 333-193053, and 333-205806) and Forms S-8 (Registration Nos. 333-233459, 333-220630, 333-199852, and 333-203244) and to the reference to our Firm under the caption "Experts".

/s/ WithumSmith+Brown, PC

East Brunswick, New Jersey
March 9, 2021

Exhibit 31.1

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

I, Phillip Chan, certify that:

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

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

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

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

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

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

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

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

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

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

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

Dated: March 9, 2021

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

Exhibit 31.2

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

I, Kathleen P. Bloch, certify that:

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

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

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

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

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

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

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

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

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

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

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

Dated: March 9, 2021

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

Exhibit 32.1

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

In connection with the Annual Report of CytoSorbents Corporation (the "Company") on Form 10-K for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Dr. Phillip Chan, President and Chief Executive Officer of the Company, certifies, pursuant to 18 U.S.C. section 1350 of the Sarbanes-Oxley Act of 2002, that:

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

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

Dated: March 9, 2021

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

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

Exhibit 32.2

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

In connection with the Annual Report of CytoSorbents Corporation (the "Company") on Form 10-K for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Kathleen P. Bloch, Chief Financial Officer of the Company, certifies, pursuant to 18 U.S.C. section 1350 of the Sarbanes-Oxley Act of 2002, that:

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

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

Dated: March 9, 2021

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

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