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, 2022

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.)

305 College Road East, Princeton, New Jersey 08540
(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. ☑

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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 December 31, 2022 was approximately $61,461,000 based upon the closing price reported for such date on the Nasdaq Capital Market. As of March 7, 2023, there were outstanding 43,663,009 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," "CytoSorb XL," "ECOS-300CY," "BetaSorb," "ContrastSorb," "DrugSorb," "HemoDefend-RBC," "HemoDefend-BGA, "K+ontrol" and "VetResQ," which are protected under applicable intellectual property laws and are the property of CytoSorbents Corporation and its subsidiaries. This Report also contains the trademarks, trade names and service marks of other companies, which are the property of their respective owners. Solely for convenience, trademarks, trade names and service marks referred to in this Report may appear without the ™, ®, or ^{SM} symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, trade names and service marks. We do not intend our use or display of other parties' trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

PART I

Item 1. Business.

Overview

We are a leader in the treatment of life-threatening conditions in the intensive care ("ICU") and cardiac surgery using blood purification via our proprietary polymer adsorption technology. We have a number of products commercialized and in development based on this technology platform. Our flagship product, CytoSorb®, is already commercialized, and is being used to reduce deadly uncontrolled inflammation and dangerous substances in hospitalized patients around the world, with the goal of preventing or treating multiple organ failure, bleeding, and other potentially fatal complications. Organ failure is the cause of nearly half of all deaths in the ICU, with little to improve clinical outcome. CytoSorb, is approved in the European Union ("EU") as an effective extracorporeal cytokine absorber, designed to reduce the "cytokine storm" or "cytokine release syndrome" that could otherwise cause massive inflammation, organ failure and death in common critical illnesses such as sepsis, burn injury, trauma, lung injury, cytokine release syndrome due to cancer immunotherapy, and pancreatitis. These are conditions where the mortality is extremely high, yet few to 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 Device 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 U.S. FDA has granted U.S. Emergency Use Authorization ("EUA") of CytoSorb for use in critically ill patients with COVID-19 infection and respiratory failure. In May 2020, we received a CE-Mark label expansion for CytoSorb for the removal of rivaroxaban during cardiothoracic surgery requiring cardiopulmonary bypass. In August 2021, the Company announced that it was granted a second Breakthrough Device Designation for its DrugSorb-ATR Antithrombotic Removal System by the FDA to remove the direct oral anticoagulants, rivaroxaban and apixaban. The Company has initiated two U.S. clinical trials evaluating the use of DrugSorb-ATR during cardiothoracic surgery to remove ticagrelor, apixaban and rivaroxaban to prevent or reduce perioperative bleeding complications in pursuit of U.S. FDA marketing approval. The first clinical trial, STAR-T, is underway and currently enrolling patients. We currently anticipate that the second clinical trial, STAR-D, which was previously postponed, will resume patient enrollment once the STAR-T trial is completed. We believe CytoSorb has the potential to be used in many other inflammatory conditions, including the treatment of autoimmune disease flares, and other applications in cancer, such as cancer cachexia. More than 195,000 cumulative CytoSorb devices have been utilized globally as of December 31, 2022 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 18 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 CytoSorb XL, HemoDefend, ContrastSorb, DrugSorb, DrugSorb-ATR and others.

In March 2011, CytoSorb was "CE Marked" in the EU as an extracorporeal cytokine adsorber 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 adsorber 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. In the past, we manufactured CytoSorb at our older manufacturing facilities in New Jersey for commercial sales abroad and for additional clinical studies. Upon expanding our facility in June 2018, 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. 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.

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. In 2021, the Company expanded direct sales to include all indications in 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 Device 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 the Company's proprietary polymer adsorption technology 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 July 2021, the Company received full approval of its Investigational Device Exemption ("IDE") by the FDA to conduct the pivotal STAR-T (Safe and Timely Antithrombotic Removal – Ticagrelor) double-blind, randomized control trial ("RCT") for up to 120 patients in the United States to support FDA marketing approval of DrugSorb-ATR, which is based on the same proprietary polymer technology as CytoSorb.

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 in January 2020 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 October 2020, we announced the E.U. approval of the ECOS-300CY cartridge for the removal of inflammatory mediators during *ex vivo* organ perfusion under CE Mark designation, with the goal of helping to preserve or improve the health and quality of solid organs to be transplanted. CytoSorbents also 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. In 2021, commercialization of PerSorb™ and Aferetica's PerLife™ *ex vivo* organ perfusion system commenced in Italy.

In June 2021, we began construction on the Company's new global headquarters and state-of-the-art manufacturing facility following the lease of a 48,500 square foot mixed-use facility in Princeton, New Jersey. The new production facility was designed to support annual sales of up to $400 million while improving product gross margins and allowing space for future product line expansions. The new production facility successfully passed its E.U. notified body audit in early 2022, and received ISO 13485 certification from its E.U. notified body in September 2022, clearing the way for full manufacturing of CytoSorb, DrugSorb-ATR, ECOS-300CY from this site.

In August 2021, the Company announced that it was granted a second Breakthrough Device designation for its DrugSorb-ATR Antithrombotic Removal System by the U.S. Food and Drug Administration (FDA). This Breakthrough Device designation covers the removal of the Direct Oral Anticoagulants (DOACs) apixaban and rivaroxaban in a cardiopulmonary bypass circuit to reduce the likelihood of serious perioperative bleeding during urgent cardiothoracic surgery. In October 2021, the Company also received full FDA approval of an IDE application to conduct a double-blind, randomized, controlled clinical study for up to 120 patients entitled, "Safe and Timely Antithrombotic Removal – Direct Oral Anticoagulants (STAR-D)," in the United States to support FDA marketing approval. This trial is currently paused until the anticipated completion of the STAR-T trial.

If FDA marketing approval is obtained for either the removal of ticagrelor or direct oral anticoagulants indications, the device would be marketed as DrugSorb-ATR in the United States. The DrugSorb-ATR Antithrombotic Removal System is based on the same polymer technology as CytoSorb.

In May 2022, the Company announced that it entered into a 3-year preferred supplier agreement with the private German hospital network, Asklepios, making CytoSorb available without restrictions to all of the approximate 170 healthcare facilities across 14 states throughout Germany at which Asklepios operates. This includes Asklepios Klinik St. Georg in Hamburg, Germany, which pioneered the use of CytoSorb to remove antithrombotic drugs during cardiothoracic surgery and is well-known for their seminal publication on CytoSorb use for this application during emergency cardiac surgery in patients at high risk of bleeding.

In June 2022, the Company announced that, following a successful pilot program in three countries, the Company signed an expanded non-exclusive agreement with Nikkiso Europe GmbH ("Nikkiso") to distribute Nikkiso's PureADJUST stand-alone hemoperfusion pump and accessories in a total of 14 countries. In addition to securing the rights to sell Nikkiso's stand-alone pump and accessories in Germany, Austria, and Luxembourg, the Company entered into an expanded multi-country reseller agreement with Nikkiso covering the following countries: Belgium, Bosnia and Herzegovina, Croatia, Finland, France, Iceland, Lichtenstein, Poland, Serbia, Slovenia and Switzerland. The Company will provide field support services in these countries.

In August 2022, the Company entered into a Marketing Agreement (the "Marketing Agreement") with Fresenius Medical Care Deutschland GmbH ("Fresenius"), which expands the Company's strategic partnership with Fresenius by establishing a multi-stage global collaboration to combat life-threatening diseases in critical care. The Marketing Agreement provides for the combined marketing and promotion of CytoSorb with Fresenius' critical care products by Fresenius' marketing organization worldwide, excluding the United States. The Marketing Agreement has an initial term of three years, with an automatic renewal for an additional two years at the end of such initial term, subject to earlier termination by either of the parties (the "Term"). Compared to the prior co-marketing agreement between the parties, the Marketing Agreement intends to increase the commitments from both parties and to ensure an ongoing and consistent level of marketing and promotional activity specifically focused around CytoSorb, where Fresenius will actively market and promote CytoSorb as the featured blood purification therapy for removal of cytokines, bilirubin, and myoglobin on its critical care platforms. Specifically, the Marketing Agreement provides that various Fresenius-led in-person, virtual, social media, and web-based marketing programs and events will feature the CytoSorb therapy and highlight the cooperation between the two companies in the field of critical care during the Term. To help support the increased marketing and promotional efforts of the expanded collaboration, CytoSorbents has agreed to subsidize a portion of the marketing costs through a royalty payment to Fresenius Medical Care based on CytoSorb sales in the intensive care unit on Fresenius Medical Care platforms, excluding the United States. In addition to strengthening and expanding the global marketing of CytoSorb, the Company and Fresenius also plan to work together to bring new innovative solutions to the market. The Marketing Agreement also includes the certification of compatibility of CytoSorb for usage on Fresenius' current critical care platforms. Certain initial activities have been completed with the formal of this program expected to occur sometime in 2023.

In addition, there are many investigator-initiated and additional Company sponsored trials that are currently planned, enrolling, or completed in Europe and in other countries abroad, using our blood purification technology that may provide valuable information regarding the use of the device in the treatment of different conditions such as sepsis, cardio-pulmonary bypass surgery, liver failure, COVID-19, organ transplant and many others. If successful, these studies may help to drive additional usage and adoption of our blood purification technologies.

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.

Overall, we have established either direct sales or distribution (via distributors or strategic partners) of CytoSorb in more than 75 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. Outside of the EU, CytoSorb has distribution in Turkey, India, Sri Lanka, Australia, New Zealand, Russia, Serbia, 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. 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 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/or 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 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 mediators, such as cytokines, activated complement, and toxic plasma free hemoglobin released by hemolysis. 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. A more recent application is the use of CytoSorb during cardiothoracic surgery to prevent or reduce perioperative bleeding by removing the blood thinners, ticagrelor and rivaroxaban.

The Company is currently conducting the following clinical trials:

Country	Trial Name	Indication	Status
United States	STAR-T	Ticagrelor Removal During Cardiac Surgery	Enrolling
United States	STAR-D	Direct Anticoagulants Removal During Cardiac Surgery	Temporarily paused
United States	CTC Registry	CytoSorb in COVID-19 patients on ECMO under EUA	Completed
Germany	PROCYSS	Refractory Septic Shock Patients	Enrolling
International	STAR Registry	Real world outcomes in antithrombotic removal	Enrolling
International	COSMOS Registry	Real world outcomes in multiple critical care applications	Enrolling

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.

We have been successful in obtaining technology development contracts from multiple U.S. 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, the U.S. Air Force, Special Operations Command, and Joint Program Executive Office (JPEO). See the section entitled "Government Research Grants" of this Item 1 of this Report for information regarding the specific grants.

In 2023, our goal is to successfully complete the STAR-T trial, finalize our data analysis, and file for U.S. FDA and Health Canada regulatory approvals. We are preparing for commercialization of DrugSorb-ATR in the U.S. In addition, we are seeing improvements in market conditions, and we are focused on a return to sales growth in our existing markets.

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. Separately, Gilder Enterprises, Inc., was incorporated in Nevada on April 25, 2002, 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, Gilder Enterprises, Inc disposed of its 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 its 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. CytoSorbents Corporation uplisted to, and began trading on, the NASDAQ Capital Markets on December 23, 2014.

Our executive offices are located at 305 College Road East, Princeton, New Jersey 08540, 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 and product commercialization and have raised approximately $215 million from investors as of December 31, 2022. These proceeds have been used to fund the development of multiple product applications, to conduct clinical studies, to establish in-house manufacturing capacity to meet commercial and clinical testing needs, expand our intellectual property through additional patents, to develop extensive proprietary know-how with regard to our products and to commercialize our products internationally.

We have raised funds through various means including convertible note offerings, equity transactions, and term loans. Our most recent 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 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 14, 2021, the Company filed a registration statement on Form S-3 with the SEC, which was amended on July 20, 2021 and declared effective by the SEC on July 27, 2021 (as amended, the "2021 Shelf"). The 2021 Shelf 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

On December 30, 2021, the Company entered into an Open Market Sale Agreement (the "Sale Agreement") with Jefferies LLC (the "Agent"), pursuant to which the Company could 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 Agent, as the Company's sales agent. All shares of the Company's common stock offered and sold, or to be offered and sold under the Sale Agreement would have been issued and sold pursuant to the Company's 2021 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.

Subject to the terms of the Sales Agreement, the Agent is 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 Agent 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. There were no sales pursuant to the Sale Agreement during the years ended December 31, 2022 and 2021.

Research and Development

We have been engaged in research and development since inception. Since 2012, we have been awarded an aggregate of approximately $40.3 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), 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, $1.5M Sequential Phase II), Universal Plasma ($150K Phase I and 1.0M Phase II STTR; $2.9M US Army and CDMRP Rapid Innovation Fund; $4.4M CDMRP; $1.1M US Army Sequential Phase II; $2M DMRDP; and $4.3M JWMRP), Lipopolysaccharide Adsorption In Sepsis (National Institution of General Medical Sciences $282K), the U.S. Air Force program ($75K), New Jersey Technology Business Tax Certificate Program for research related expenses ($6.7M), 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 many different substances from whole blood and physiologic fluids, including for example, drugs, bioactive lipids, inflammatory mediators such as cytokines, free hemoglobin, and bacterial toxins, immunoglobulin, bilirubin, and myoglobin, depending on the polymer construct. The technology has been used in a wide variety of acute healthcare applications 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, liver failure, and pancreatitis; the prevention of post-operative complications of cardiopulmonary bypass surgery; 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 removal of non-infectious contaminants in transfused blood products; the treatment of drug overdose, and the removal of antithrombotic drugs during cardiothoracic surgery that could otherwise cause severe perioperative bleeding. These applications vary by cause and complexity as well as by severity but share a common characteristic, i.e., high concentrations of inflammatory mediators,toxins, or drugs in the circulating blood.

Our flagship product, CytoSorb, animal-targeted VetResQ, DrugSorb-ATR, 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 extracorporeal 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 extracorporeal 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

CytoSorb, through its ability to bind mediators that regulate inflammation, is a critical care-focused immunotherapy. 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, extracorporeal liver support, 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 adsorber 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. CytoSorb is also used intra-operatively to remove blood thinners to prevent or reduce bleeding and associated complications during cardiothoracic surgery. 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 $30 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, knees and heart valves 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. 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, selective cytapheresis from CytoPheryx, and others.

For more information regarding our competitors, see the section entitled "Competition" in Item 1 of this report.

Severe sepsis and septic shock patients are among the most difficult and 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, the United Kingdom and the Netherlands with our own direct sales force. In December 2016, we announced the achievement of a 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 distribution of CytoSorb for critical care applications in France, Finland, the Czech Republic, Colombia, Ecuador, Mexico, and Korea, and Terumo Cardiovascular, the largest cardiac surgery disposables company, for exclusive distribution of the CytoSorb Cardiopulmonary Bypass Kit in France. 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 approximately 75 countries worldwide.

We estimate that the market potential in Europe for CytoSorb is larger than that in the U.S. For example, in the U.S. there are an estimated 1.6 million cases of sepsis each year, 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 effect. 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®, Brilique®) 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®) and rivaroxaban (Janssen and Bayer - Xarelto®) are estimated to reach 40 billion USD in sales by 2026.

There is a clear and large unmet medical need 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 U.S. alone there are approximately 1.1 million ACS hospital admissions annually. CytoSorb is able to very efficiently remove ticagrelor and DOACs from blood and is approved in the EU for the removal of both ticagrelor and rivaroxaban during cardiothoracic surgery requiring cardiopulmonary bypass. The use of CytoSorb during emergency coronary artery bypass surgery (CABG) in patients on ticagrelor or rivaroxaban significantly reduced perioperative bleeding complications in a landmark observational study and had projected cost savings of approximately $5,000 per patient, including the cost of the device. In the U.S. and Canada, the Company is currently conducting the pivotal, randomized, controlled STAR-T trial to evaluate the potential ability of the DrugSorb-ATR antithrombotic removal system, which uses an equivalent polymer technology to CytoSorb, to reduce perioperative bleeding risk in patients undergoing cardiothoracic surgery in the presence of ticagrelor. The Company expects to resume the STAR-D trial, targeting a reduction in perioperative bleeding risk in cardiothoracic surgery through the removal of the direct oral anticoagulants, apixaban and rivaroxaban, upon completion of the STAR-T trial. The STAR-T trial and STAR-D trial (if resumed), if successful, are each intended to independently support U.S. FDA marketing approval for DrugSorb-ATR for this indication., or the direct oral anticoagulants, apixaban and rivaroxaban, respectively. The Company expects to resume the STAR-D trial upon completion of the STAR-T trial. The STAR-T trial and STAR-D trial (if resumed), are each intended to independently support U.S. FDA marketing approval for DrugSorb-ATR for this indication. The initial annual addressable market in the U.S. to remove these drugs during cardiothoracic surgery is estimated between $500 million to $750 million.

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 contributed or were responsible for more than 900,000 deaths in the U.S. alone. Patients with ALI and ARDS typically require mechanical ventilation, and sometimes extracorporeal membrane oxygenation (ECMO) therapy if the lungs become so diseased that mechanical ventilation fails, 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 and ECMO 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. Published results from our U.S. CytoSorb Therapy in COVID-19 (CTC) registry in the medical journal, Frontiers in Medicine, in December 2021, demonstrated that in 52 consecutive patients from 5 U.S. ECMO centers, 90-day survival was 73% in critically ill COVID-19 patients who failed mechanical ventilation and were treated with ECMO and CytoSorb under FDA Emergency Use Authorization. The CTC Registry completed enrollment at 100 patients, confirming 90-day survival of 74%. For context, 90-day survival was 53% (as of December 2022) among more than 7,300 adult patients in the North American cohort of the Extracorporeal Life Support Organization (ELSO) COVID-19 ECMO Registry. 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. In general, patients studied in the RECOVERY study were not as severely ill as those treated for refractory respiratory failure with CytoSorb and ECMO in the CTC Registry. Techniques to improve ventilation and reduce ongoing lung injury are also 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 theEU 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 to bed more than $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 more than 41,000 organ transplants in 2020, with approximately 106,000 patients on the waiting list. This represents a U.S. and European total addressable market for the ECOS-300CY device of approximately $400 million to $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 westernized 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 contrast -induced nephropathy ("CIN"). CIN 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 is intended 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 adsorber 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 Princeton, 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 the largest market 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 195,000 devices utilized as of December 31, 2022.

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.

Projected Timeline: In 2011, the CytoSorb adsorber received EU regulatory approval under the CE Mark as an extracorporeal cytokine adsorber to be used in clinical situations where cytokines are elevated. Our U.S. 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, Finland, Sweden, Denmark, the United Kingdom 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 more than 75 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, 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.

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 adsorber 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 many 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 hemoadsorption 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 perioperative 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 antithrombotic drugs such as ticagrelor and rivaroxaban during cardiopulmonary bypass in patients requiring urgent or emergent surgery. The primary goals for these applications 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 perioperative bleeding complications such as need for blood and platelet transfusions, re-thoracotomy, 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. Intraoperative use of CytoSorb on high-risk cardiac surgery patients, such as those with infective endocarditis, aortic dissection, or heart or lung transplantation, where the risk of post-operative complications is the highest, is one of our main markets. The use of CytoSorb in the post-operative period to treat postoperative SIRS is another application of the technology.

In 2020, CytoSorb was 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.

CytoSorb was also approved for the removal of rivaroxaban, a widely used Factor Xa inhibitor and novel oral anticoagulant, during cardiothoracic surgery requiring cardiopulmonary bypass via label expansion of its CE Mark. This 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 chronic, often lifelong protection. The two leaders in the category are apixaban (Bristol Myers Squibb - Eliquis®) and rivaroxaban (Janssen and Bayer - Xarelto®).

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 50,000 treatments in cardiac surgery patients. This application is also the focus of number of planned and enrolling company-sponsored and investigator-initiated studies of DrugSorb-ATR in the United States and CytoSorb in Europe.

In July 2021, we received full FDA approval of an Investigational Device Exemption (IDE) application to conduct a double-blind, randomized, controlled clinical study in 120 patients entitled, "**S**afe and **T**imely **A**ntithrombotic **R**emoval – **T**icagrelor (**STAR-T**)," in the United States to support FDA marketing approval. This was done under the previously announced FDA Breakthrough Device Designation granted for the removal of ticagrelor in a cardiopulmonary bypass circuit to reduce the likelihood of serious perioperative bleeding during urgent cardiac surgery. In October 2021, the first patient was enrolled and the STAR-T study is now actively recruiting at multiple U.S. sites. In November 2022, the first milestone was completed with the first one-third of patients enrolled, triggering the first Data Safety Monitoring Board (DSMB) meeting. The DSMB recommended to continue the study as planned without any modifications. In 2022, we also received FDA approval to expand the study to Canada and subsequently received Health Canada approval allowing inclusion of Canadian sites into the STAR-T trial in January 2023. Enrollment is expected to be complete during summer of 2023.

In October 2021, we also received full FDA approval of an Investigational Device Exemption (IDE) application to conduct a double-blind, randomized, controlled clinical study for up to 120 patients entitled, "**S**afe and **T**imely **A**ntithrombotic **R**emoval – **D**irect Oral Anticoagulants (**STAR-D**)," in the United States to support FDA marketing approval. This was done under the previously announced 2nd FDA Breakthrough Device Designation granted for our DrugSorb-ATR Antithrombotic Removal System. This Breakthrough Device designation covers the removal of the Direct Oral Anticoagulants (DOACs) apixaban and rivaroxaban in a cardiopulmonary bypass circuit to reduce the likelihood of serious perioperative bleeding during urgent cardiac surgery. The study was placed on temporary enrollment hold in November of 2022 for business reasons and is scheduled to resume enrollment upon completion of the STAR-T trial.

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 more than 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. In 2021, commercialization of PerSorb™ and Aferetica's PerLife™ *ex vivo* organ perfusion system commenced in Italy.

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 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, heat stroke 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 to 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 such as free hemoglobin, bioactive lipids, potassium, and others during blood storage that can lead to transfusion reactions. Three adult, prospective, randomized, controlled studies 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) 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, particularly in patients who receive massive transfusions defined as more than 10 pRBC units in 24 hours, those patients who receive blood chronically, and pediatric patients, 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, potassium, 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 $1.5 million Phase II SBIR contract (funded by NHLBI and U.S. Special Operations Command (USSOCOM)), and more recently under a $3 million multi-year Phase IIB bridge contract funded by NHLBI. Barring additional delays due to the COVID-19 pandemic, including nationwide blood shortages, we expect to advance the in-line filter to human testing in the next 12 - 18 months.

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. Approximately 4.0 million units of plasma are transfused annually 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 clinical study-ready devices. This work has received cumulative funding of approximately $15.9 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, CDMRP, DMRDP, and JWMRP.

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 a Phase I and Phase II SBIR contract for a total of $1.5 million and a $3 million Rapid Innovation Fund (RIF) award from the U.S. Air Force Materiel Command. We are currently discussing the potential clinical development plan of K^+ontrol with the FDA.

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 could 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 would 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 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. We are currently negotiating an additional extension to this agreement. 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, while guaranteed minimum quarterly purchases and payments requirements were removed. In January 2022, we converted the agreement with Fresenius in France, Finland, and the Czech Republic to be non-exclusive.

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. Registration clearance was obtained 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 automatically renew for an additional two years unless terminated by either party.

In 2020, we entered into agreements to expand the partnership with Fresenius into Colombia and Ecuador.

In August 2022, the Company entered into a Marketing Agreement (the "Marketing Agreement") with Fresenius, which expanded the Company's current strategic partnership with Fresenius by establishing a multi-stage global collaboration to combat life-threatening diseases in critical care. The Marketing Agreement provides for the combined marketing and promotion of CytoSorb with Fresenius' critical care products by Fresenius' marketing organization worldwide, excluding the United States. The Marketing Agreement has an initial term of three years, with an automatic renewal for an additional two years at the end of such initial term, subject to earlier termination by either of the parties (the "Term"). Compared to the prior co-marketing agreement between the parties, the Marketing Agreement intends to increase the commitments from both parties and to ensure an ongoing and consistent level of marketing and promotional activity specifically focused around CytoSorb, where Fresenius will actively market and promote CytoSorb as the featured blood purification therapy for removal of cytokines, bilirubin, and myoglobin on its critical care platforms. Specifically, the Marketing Agreement provides that various Fresenius-led in-person, virtual, social media, and web-based marketing programs and events will feature the CytoSorb therapy and highlight the cooperation between the two companies in the field of critical care during the Term. To help support the increased marketing and promotional efforts of the expanded collaboration, CytoSorbents has agreed to subsidize a portion of the marketing costs through a royalty payment to Fresenius Medical Care based on CytoSorb sales in the intensive care unit on Fresenius Medical Care platforms, excluding the United States. In addition to strengthening and expanding the global marketing of CytoSorb, the Company and Fresenius also plan to work together to bring new innovative solutions to the market. The Marketing Agreement also includes the certification of compatibility of CytoSorb for usage on Fresenius' current critical care platforms. Certain initial activities have been completed with the formal launch of this program expected to occur sometime in 2023.

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. In August 2021, we announced that commercialization of PerSorb(TM) and Aferetica's PerLife(TM) *ex vivo* organ perfusion system commenced in various European countries.

Terumo Cardiovascular Group

In September 2016, we entered into a multi-country strategic partnership with Terumo Cardiovascular Group ("Terumo") to commercialize CytoSorb for cardiac surgery applications. Under the terms of the agreement, Terumo has exclusive rights to distribute the CytoSorb CPB procedure pack for intra-operative use during cardiac surgery in France, Sweden, Denmark, Norway, Finland and Iceland. Terumo launched CytoSorb in its six exclusive countries in December 2016. In 2021, the agreement was revised to a non-exclusive collaboration agreement in Sweden, Denmark, Norway and Iceland. This agreement allows the Company to sell directly to customers in these countries for the cardiac surgery application. supported by marketing and promotional activities with Terumo. Financial terms of this agreement have not been disclosed. This agreement expired on March 31, 2022.

On January 1, 2023, we amended and restated the original distribution agreement from October 2016. Under the terms of the amended and restated agreement, Terumo will have non-exclusive distribution rights in France to promote and sell the CytoSorb CPB procedure pack for intra-operative use during cardiac surgery at specifically named hospitals in France. The amended and restated agreement allows the Company to sell directly to other hospital customers in France for the cardiac surgery application. Financial terms of this agreement have not been disclosed. The agreement terminates on December 31, 2023.

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.

B. Braun Avitum AG

In March 2021, we announced announce the launch of a global co-marketing agreement with B. Braun Avitum AG, one of the world's leading manufacturers of medical devices and pharmaceutical products and services, 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®. This global co-marketing agreement applies to the countries where both products are registered (U.S. market is specifically excluded). Financial terms of this agreement have not been disclosed.

Nikkiso Europe GmbH

In June 2022, the Company announced that, following a successful pilot program in three countries, the Company signed an expanded non-exclusive agreement with Nikkiso Europe GmbH ("Nikkiso") to distribute Nikkiso's PureADJUST stand-alone hemoperfusion pump and accessories in a total of 14 countries. In addition to securing the rights to sell Nikkiso's stand-alone pump and accessories in Germany, Austria, and Luxembourg, the Company entered into an expanded multi-country reseller agreement with Nikkiso covering the following countries: Belgium, Bosnia and Herzegovina, Croatia, Finland, France, Iceland, Lichtenstein, Poland, Serbia, Slovenia and Switzerland. The Company will also be able to provide field support services in these countries.

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 our 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 to obtain expert opinions on basic science, critical care medicine and cardiac surgery.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. In November 2022, all rights, title and interest to the Royalty was assigned to ROKK, LLC. For the year ended December 31, 2022 we have recorded royalty costs of approximately $849,000.

On August 1, 2022, the Company entered into the Marketing Agreement with Fresenius, which expands the Company's strategic partnership with Fresenius by establishing a multi-stage global collaboration to combat life-threatening diseases in critical care. The Marketing Agreement has an initial term of three years, with an automatic renewal for an additional two years at the end of such initial term, subject to earlier termination by either of the parties (the "Term") To help support the increased marketing and promotional efforts of the expanded collaboration, the Company has agreed to subsidize a portion of the marketing costs through royalty payments to Fresenius. Initially, the Marketing Agreement provides for royalty payments equal to 0.9% of the Company's net sales of CytoSorb products made during the Term (excluding net sales in the United States). This initial royalty rate was determined based on certain assumptions regarding the percentage of the Company's sale of CytoSorb products that are used with the Fresenius critical care platforms in the intensive care unit outside of the United States but is subject to adjustment if the Company determines that the underlying assumptions have changed significantly. For the year ended December 31, 2022, the Company did not record any expense related to this agreement as Fresenius did not commence any marketing activities as defined by the agreement.

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, 2022 per the terms of the license agreement we have recorded royalty costs of approximately $1,416,000.

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 a procedure code from the Swiss Federal Statistical Office, a division of the Federal Department of Home Affairs in Switzerland under the category "Adsorption of Cytokines and Interleukin". During 2020, this code category was replaced by a new category entitled "Extracorporeal Adsorption of Specific Substances". Use of this code gives Swiss hospitals the ability to collect cost data related to CytoSorb treatments. In 2021, SwissDRG performed the first cost analysis of CytoSorb. This analysis showed that there were no additional treatment costs associated with use of CytoSorb against the relevant DRGs, suggesting CytoSorb may be cost neutral or even cost-saving across all indications. The Company is working with these Swiss hospitals to publish the analysis.

Europe (excluding Germany and Switzerland)

Payment for our CytoSorb device in patients with life-threatening illnesses is country dependent in Europe. Most European markets issue reimbursement for standard therapies only, i.e. those recommended in relevant treatment guidelines. The Company is currently conducting randomized controlled trials (RCTs) to achieve this in all major indications. In the meantime, we are leveraging health economics, local data generation and KOL management in all major territories, with our partners and local sales teams, such as France, England, Italy, Spain, Russia, Belgium, Netherlands, Luxembourg, Poland, Sweden, Norway, Denmark and Finland.

In the United Kingdom, market access and reimbursement of drugs, medical devices and diagnostics is heavily dependent on the guidance published by the National Institute for Health and Care Excellence (NICE). In 2021, NICE published its report on CytoSorb for the removal of ticagrelor in urgent and emergent cardiac surgery patients in a MedTech Innovation Briefing (MIB) called "CytoSorb for reducing risk of bleeding during cardiac surgery". The MIB highlights the safety and efficacy of CytoSorb in this indication, as well its innovative nature and the substantial cost savings CytoSorb generates and has aided adoption in the UK.

Other Markets

CytoSorb is currently marketed and distributed in more than 75 countries around the world. It is generally paid for through the standard DRG (diagnosis related group) payment, dedicated reimbursement codes, tender orders, private insurance, and/or self-pay. We are actively pursuing generation of new procedure codes in many countries we are currently serving. Across all countries, we are mitigating financial barriers though use of health economics, local data generation and targeted KOL management.

In August 2022, we disclosed that the Israeli Ministry of Health (MoH) had approved national reimbursement for CytoSorb in certain cardiac surgery indications, including the intraoperative treatment for urgent or emergency cardiac surgery in patients treated with ticagrelor or rivaroxaban, the intraoperative treatment during cardiac surgery in patients with acute infective endocarditis, and the intraoperative treatment during surgery for correction of aortic dissection. In the same month, we announced that the Turkish Ministry of Health had approved national reimbursement for CytoSorb, which is now a reimbursed catalog product in the State Supply Office of Turkey (DMO) portal and can be purchased directly by hospitals and physicians without restrictions.

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., that was increased for COVID-19 applications as part of the CARES Act. 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 (MCIT) pathway that will provide national Medicare coverage as early as the same day as FDA market authorization for Breakthrough Designated medical devices, where coverage would last 4 years. Although this program was rescinded by CMS in November 2021, a legislative version of the program is currently contained within the CARES 2.0 bill, though not yet approved. In addition, CMS has announced a new initiative called "Transitional Coverage for Emerging Technologies" (TCET) as a potential replacement for MCIT, with more detail planned for April 2023. If passed, either of these programs may be applicable to DrugSorb-ATR, if it can achieve U.S. approval for the removal of ticagrelor and Direct Oral Anticoagulants (DOACs) apixaban and rivaroxaban during emergent or urgent cardiothoracic surgery. These indications were granted FDA Breakthrough Designation in April 2020 and August 2021, respectively.

Competition

General

Our core adsorbent porous polymer bead technology is used in our marketed products, such as the CytoSorb, ECOS-300CY, and VetResQ cartridges, and other products under advanced development, such as CytoSorb XL and DrugSorb-ATR. We believe these 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) and poorly dialyzable drugs 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. For example, researchers have explored the potential of using standard 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.

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 was controversial and 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.

COVID-19 disrupted many clinical studies in 2020 and 2021. 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.

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. To date, no publicly available update has been provided.

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 of 450 patients 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. 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. As of January 12, 2023, 50 patients of the targeted 150 patients have been enrolled, with an expansion of trial sites to a total of 25, with 15 currently active.

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. In September 2021, Enlivex announced the start of a Phase IIb study using Allocetra in severe and critical COVID-19 patients with acute respiratory distress syndrome (ARDS). In November 2021, Enlivex reported that Allocetra is being evaluated in a randomized, controlled, Phase II multi-center trial in patients with pneumonia-associated sepsis. It is expected to enroll 120-160 patients across 4 cohorts of varying doses of Allocetra or placebo. The primary endpoints of the trial are safety and change in SOFA score from baseline at 28 days. As of February 2023, enrollment has not been disclosed.

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. Also, multiple large scale randomized controlled trials have since failed to demonstrate clinical or mortality benefit including VICTAS, VITAMINS, ACTS, and others. 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. 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. 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 2008 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. As of February 2022, clinicaltrials.gov currently lists 12 small studies recruiting, evaluating oXiris in the fields of sepsis and cardiac surgery. 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 outside the U.S. to improve the efficiency of hemodialysis, claiming improved mid-molecular weight substance removal. Neither oXiris nor Theranova are approved in the U.S. for treatment of sepsis or respiratory failure.

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. As noted above, Baxter acquired Gambro in 2013. 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. 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. 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. 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. According to clinicaltrials.gov, there are 5 investigator-initiated studies evaluating Jafron's technology in sepsis, cardiac and respiratory failure and liver disease. 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 status of the trial has not been updated since February 2019. Another investigator-initiated RCT evaluating the HA-330 device in 200 patients with norepinephrine-resistant septic shock (CLEANSE) began in Thailand in November 2021 and is still enrolling. 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. 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 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. In 2021 and 2022, Exthera expanded distribution to market Seraph in select European countries and Mexico with Fresenius to remove certain bacterial and viral pathogens during dialysis. 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, ventilation and prone positioning, and extracorporeal membrane oxygenation ("ECMO"). Although a number of pharmacologic 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

Previously, leukocyte reduction filters sold by Pall Corporation, Terumo Medical Corporation and others were used in the cardiopulmonary bypass circuit to reduce cytokine-producing white blood cells from blood. They did not remove cytokines, free hemoglobin, or activated complement directly and were 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. CytoSorb has been used 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 therapeutic plasma exchange, 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, and mid to high molecular weight cutoff filters by Baxter, 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 those mentioned above and 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 Antithrombotics such as Ticagrelor and Direct Oral Anticoagulants 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 to 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. In 2020, CytoSorb 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. In 2021, we also began enrolling the STAR (Safe and Timely Antithrombotic Removal) international registry collecting real world evidence in this application.

In the U.S., we are currently executing the U.S. STAR-T (Safe and Timely Antithrombotic Removal of Ticagrelor,) pivotal randomized, controlled clinical trials designed to support U.S. FDA Marketing approval of the DrugSorb-ATR antithrombotic removal system, which uses an equivalent polymer technology to CytoSorb.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. We anticipate resuming the STAR-D (Safe and Timely Antithrombotic Removal of DOACs) trial upon completion of the STAR-T trial.

PhaseBio, a now defunct clinical-stage biopharmaceutical company, had licensed an intravenously administered monoclonal antibody fragment with high affinity reversal agent for ticagrelor called bentracimab (PB2452) from Medimmune, a division of AstraZeneca. PhaseBio paid AstraZeneca $100,000 upfront, with $68 million in potential future milestones. AstraZeneca owned approximately 5% of PhaseBio's stock. The FDA granted Breakthrough Therapy designation for PB2452 in April 2019. PhaseBio was conducting its U.S. REVERSE-IT (Rapid and SustainEd ReVERSal of TicagrElor – Intervention Trial) study, a Phase 3, prospective, multi-center, open-label, single-arm trial designed to study reversal of the antiplatelet effects of ticagrelor with bentracimab to treat patients who present with uncontrolled major or life-threatening bleeding or when used prophylactically in patients who require urgent surgery or an invasive procedure to prevent bleeding. In November 2021, PhaseBio presented top-line data from an interim analysis of the study, having enrolled 142 patients who required urgent surgery or an invasive procedure and 8 patients with an uncontrolled major or life-threatening bleed. For the end-point analysis, 129 patients had analyzable platelet data, 122 had data on adjudicated hemostasis. Investigators reported a rapid reversal of anti-platelet activity in both subgroups. Among surgical patients, 66.4% had mild GUSTO (Global Use of Strategies to Open Occluded Coronary Arteries bleeding scale) bleeding, and 33.6% had moderate GUSTO bleeding perioperatively. Treatment-emergent adverse events (i.e. adverse events that were not present prior to treatment initiation or an event already present that worsens in either intensity or frequency following exposure to the treatment) were reported by 92.7% of enrolled patients. Four patients died (2.8%): two with septic shock, and two with cardiogenic shock. Of 150 patients, eight patients (5.3%) had thrombotic events, including two ischemic strokes, one transient ischemic attack, three myocardial infarctions, and two with arterial thromboembolisms in the right lower extremity. The FDA had recommended an interim analysis of approximately 100 patients, comprising approximately 50 patients in each arm, in order to support the submission of a Biologics License Application (BLA) for accelerated approval of bentracimab. In November 2021, PhaseBio announced that it continues to enroll more patients into the uncontrolled major or life-threatening bleeding arm of the study and intends to submit a BLA for both subgroups by Summer 2022. However, in October 2022, PhaseBio filed for Chapter 11 bankruptcy. The bentracimab asset was transferred to PhaseBio's creditor, SFJ Pharmaceuticals in December 2022, that expects to file the BLA in mid-2023.

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, interference with heparin anticoagulation, 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 and DrugSorb-ATR, if it receives FDA marketing approval in the United States, would represent 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

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

Critical Care

In 2011, CytoSorb received EU regulatory approval under the CE Mark as an extracorporeal cytokine adsorber 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 well-tolerated and safe 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.

In April 2020, we received U.S. FDA Emergency Use Authorization for the treatment of adult critically ill COVID-19 patients with confirmed or imminent respiratory failure. The U.S. **C**ytoSorb **T**herapy in **C**OVID-19 (**CTC**) **Registry** was launched to capture outcomes and device utilization patterns from multiple U.S. participating centers. Initial results on critically ill COVID-19 patients on extracorporeal membrane oxygenation (ECMO) treated with CytoSorb at participating U.S. centers showed high survival rates (73%) compared with the international benchmark Extracorporeal Life Support Organization (ELSO) Registry. The initial CTC results on the first 52 critically ill patients from five U.S. ECMO centers were presented at the International Symposium of Intensive Care Medicine conference in August 2021 in Brussels, Belgium, and published in the peer reviewed journal Frontiers in Medicine. The CTC registry completed enrollment with 100 patients from five centers, and the final results mirror the high survival (74%) seen in the previous analysis, and have been submitted for publication.

The German **PROCYSS** multicenter, randomized controlled trial evaluating the ability of CytoSorb to restore hemodynamic stability in patients with refractory septic shock is now actively enrolling. The speed of enrollment remains uncertain due to COVID-19 related institutional research staff shortages, however we anticipate conditions to improve in the second half of 2023 which should help recruitment toward the next milestone of the interim analysis after 50% enrollment.

The international **COSMOS Registry** was designed to capture real world outcomes and device utilization patterns across multiple critical care indications including but not limited to sepsis, acute respiratory failure, postoperative vasoplegia, acute liver failure, and acute pancreatitis. The Registry is actively enrolling in Spain and Germany with plans to expand in more countries in 2023. The intent of the Registry is to report outcomes at international conferences and submit the results for publication on a rolling basis as enrollment progresses.

Cardiac Surgery

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. The international **S**afe and **T**imely **A**ntithrombotic **R**emoval (**STAR**) **Registry** is designed to capture real world clinical and health economic outcomes with intraoperative antithrombotic drug removal. The Registry is actively recruiting in the U.K., Germany, Austria and Sweden and is planned to expand to additional countries in 2023. The intent of the Registry is to report outcomes at international conferences and submit the results for publication on a rolling basis as enrollment progresses with estimated first data readouts in 2023.

In July 2021, we received full FDA approval of an Investigational Device Exemption (IDE) application to conduct a double-blind, randomized, controlled clinical study in 120 patients entitled, "**S**afe and **T**imely **A**ntithrombotic **R**emoval – **T**icagrelor (**STAR-T**)," in the United States to support FDA marketing approval. This was done under the previously announced FDA Breakthrough Device Designation granted for the removal of ticagrelor in a cardiopulmonary bypass circuit to reduce the likelihood of serious perioperative bleeding during urgent cardiac surgery. In October 2021, the first patient was enrolled, and the STAR-T study is now actively recruiting at multiple U.S. sites. In November 2022, the first milestone was completed with the first one-third of patients enrolled, triggering the first Data Safety Monitoring Board (DSMB) meeting. The DSMB recommended to continue the study as planned without any modifications. In 2022, we also received FDA approval to expand the study to Canada and subsequently received Health Canada approval allowing inclusion of Canadian sites into the STAR-T trial in January 2023. In early 2023, the study exceeded 50% enrollment and is expected to reach the 2nd milestone of 67% enrollment in the spring of 2023 triggering another DSMB safety review. The study is expected to reach 100% enrollment sometime in the summer of 2023. Based on the accelerated enrollment rate and expected evaluation period associated with an interim analysis, we are considering foregoing the interim analysis and proceeding to study completion and final analysis. Should we choose to forego the interim analysis, we would be required to notify the FDA.

In October 2021, we also received full FDA approval of an Investigational Device Exemption (IDE) application to conduct a double-blind, randomized, controlled clinical study for up to 120 patients entitled, "**S**afe and **T**imely **A**ntithrombotic **R**emoval – **D**irect Oral Anticoagulants (**STAR-D**)," in the United States to support FDA marketing approval. This was done under the previously announced 2nd FDA Breakthrough Device Designation granted for our DrugSorb-ATR Antithrombotic Removal System. This Breakthrough Device designation covers the removal of the Direct Oral Anticoagulants (DOACs) apixaban and rivaroxaban in a cardiopulmonary bypass circuit to reduce the likelihood of serious perioperative bleeding during urgent cardiac surgery. Study enrollment was paused in November of 2022 for business reasons and is scheduled to resume after completion of the STAR-T trial.

COVID-19 Business Update

COVID-19 patients develop life-threatening complications such as acute respiratory distress syndrome (ARDS), shock (i.e., a potentially fatal drop in blood pressure), kidney failure, acute cardiac injury, thromboses and emboli, and secondary bacterial infections. The underlying cause for these complications is often 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. Hypercoagulability, thought triggered by inflammation, and resulting thromboembolic events such as pulmonary emboli and thrombotic microangiopathy, play another critical role in the pathophysiology of COVID-19 infection and severity of illness.

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 to treat dangerous inflammation and related life-threatening complications in more than 7,650 COVID-19 patients in more than 30 countries as of December 31, 2022. 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 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 the 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 U.S. Emergency Use Authorization (EUA) of CytoSorb for use in adult critically ill 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 U.S. CTC (CytoSorb Therapy in COVID-19) Registry was launched to capture outcomes and device utilization patterns from multiple U.S. participating centers. Primary results on observed ICU mortality of COVID-19 patients with acute respiratory distress syndrome (ARDS) requiring extracorporeal membrane oxygenation (ECMO) and treated with CytoSorb according to FDA EUA criteria were presented at the International Symposium of Intensive Care Medicine conference in September 2021 in Brussels, Belgium. In December 2021, we announced the publication of these results in the peer-reviewed journal *Frontiers in Medicine*. The CTC Registry has completed enrollment and the final results confirming high survival (74%) were presented at the European Society of Intensive Care Medicine conference in October 2022 and also have been submitted for publication.

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 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 $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, 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, 2022, we received $719,000 and have no further funding remaining under this contract.

In September 2017, the Company was awarded a Phase II SBIR contract for its development program entitled "Investigation of a sorbent-based potassium adsorber for the treatment of hyperkalemia induced by traumatic injury and acute kidney injury". The purpose of this contract is to continue development of two novel and distinct treatment options for life-threatening hyperkalemia. This work is being funded by the USAMRAA under contract W81XWH-17-C-0142 and provides for maximum funding of $999,871. As of December 31, 2022, we received $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, 2022, we received approximately $2,386,000 in funding under this contract and have approximately $585,000 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, 2022, we received approximately $2,396,000 funding under this contract and have approximately $564,000 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, 2022, we received approximately $2,472,000 funding under this contract and have approximately $425,000 remaining under this contract.

In July 2020, the Company was a three-year contract 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), 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). This award provides for maximum funding of approximately $4,422,000 over a three-year period. As of December 31, 2022, we received approximately $1,825,000 funding under this contract and have approximately $2,596,000 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). This award provides for maximum funding of approximately $1,100,000 over a two-year period. As of December 31, 2022, we received approximately $840,000 funding under this contract and have approximately $260,000 remaining under this contract.

On April 19, 2021, the Company received notification that it received a U.S. Army Medical Research Acquisition Activity Award (the "USAMRAAA") entitled "Investigation of a potassium adsorber for the treatment of hyperkalemia induced by traumatic injury and acute kidney injury in austere medicine." The USAMRAAA Phase II Sequential Award, for up to $1,499,987, was granted to the Company to continue development of two novel and distinct treatment options for life-threatening hyperkalemia. This award is being funded by the USAMRAAA under Contract No. W81XWH21C0045. As of December 31, 2022, we have received $871,000 funding under the contract and have approximately $629,000 remaining under the contract.

On May 9, 2022, the Company received a U.S. Army Medical Research Acquisition Activity Award (the "USAMRAAA") entitled "Demonstration of the Safety and Efficacy of Field-Ready Blood Group Antibody (BGA) Adsorber in the Porcine Universal Transfusion Model." The Department of Defense (DoD) Defense Medical Research and Development Program (DMRDP) Joint Program Committee 6 (JPC-6) Combat Casualty Care Research Program (CCCRP) Battlefield Resuscitation for the Immediate Stabilization of Combat Casualties Award, for up to $1,977,024, was granted to the Company to validate the safety and efficacy of the BGA device in a preclinical study in pigs. This award is being funded by the USAMRAAA under Contract No. W81XWH-22-1-0235. As of December 31, 2022, we have received $124,000 funding under the contract and have approximately $1,853,000 remaining under the contract.

On August 22, 2022, the Company received a U.S. Army Medical Research Acquisition Activity Award (the "USAMRAAA") entitled "Integrating Isoagglutinin Reduction for a Universal Dried Plasma Product for Battlefield and First Responder Use." This three-year Phase III contract, which is valued at $4,292,641, is to be used to customize the design of the HemoDefend-BGA™ filter for sterile integration into collections systems for freeze-dried plasma processing to generate freeze-dried universal plasma. Without the need for blood typing, widespread availability of universal plasma could help save lives via faster emergency treatment in both civilian and military settings. This award is being funded by the USAMRAAA under Contract No. W81XWH-22-C0046. As of December 31, 2022, we have received $35,000 funding under the contract and have approximately $4,257,000 remaining under the contract.

On August 29. 2022, the Company was granted a Phase I Small Business Innovation Research (SBIR) award entitled "Novel Extracorporeal Therapy for the Reversal of Septic Shock and Restoring Hemodynamic Stability" by the National Institute of General Medical Sciences (NIGMS), a division of the U.S. National Institutes of Health. This eight-month award, which is valued at $281,835, will allow CytoSorbents to test the ability of its novel and existing polymers to remove cytokines and lipopolysaccharide (LPS) endotoxin, a well-known potent and deadly trigger of sepsis and septic shock, from septic porcine plasma. As of December 31, 2022, we have received $29,000 funding under the contract and have approximately $253,000 remaining under the contract.

On December 1, 2022, the Company was granted a Phase I Small Business Innovation Research (SBIR) award by AFWERX, a United States Air Force program with the goal of fostering a culture of innovation within the service. This three-month award, which is valued at $74,955, will allow CytoSorbents to perform customer discovery within the Department of the Air Force (DAF) and to better understand DAF end-user needs and help define product requirements for our solution to prevent and treat certain infectious diseases that threaten warfighters. As of December 31, 2022, we have received $18,000 funding under the contract and have approximately $57,000 remaining under the 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 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 of grant 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 require 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 EU 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 adsorber. 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, however, Canada has replaced this earlier program with the Medical Device Single Audit Program ("MDSAP") and the Company is now evaluating the requirements for this certification.

Since 2011, CytoSorbents has maintained a valid ISO13485 certificate. In July 2018, we successfully completed an audit upgrade from an ISO 13485:2003 certification to an ISO 13485:2016 certification, valid through 2019. Subsequent surveillance and recertification audits have been successfully completed to maintain the certification. In April 2022, we successfully completed an annual ISO 13485:2016 surveillance audit that encompassed both the Deer Park manufacturing site and the new manufacturing facility at 305 College Road East, Princeton, NJ. In September 2022, we received ISO 13485 Certification of this new facility, clearing the way for full manufacturing of CytoSorb, DrugSorb-ATR, and ECOS-300C from this site.

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, claims that are made are required to 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, 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 510(k) De Novo request. The *de novo* pathway is available for medium risk 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 includes 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 rigorous 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.

Regardless of the path to FDA clearance or approval, 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 to treat patients 18 years of age or older, with confirmed COVID-19 admitted to the ICU with confirmed or imminent respiratory failure. Per the FDA, "The Emergency Use Authorization (EUA) authority allows the 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 authorization limited in scope and, subject to FDA discretion regarding EUA duration. Devices with EUA are neither formally cleared nor approved for the indication to treat patients with COVID-19 infection. Such devices are authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the device under Section 564(b)(l) of the Act, 21 U.S.C § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner. The FDA can at its discretion cancel the EUA approval when there is no longer a threat to public health.

The placement 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 pre-clinical, 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 adsorption 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 some post-marketing reporting. FDA does have regulatory oversight over veterinary devices and can take appropriate regulatory action. 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. In 2021, we expanded direct sales to include all applications in Sweden, Denmark and Norway. As part of this effort, the Company established CytoSorbents Poland Sp. z.o.o. and in 2022 we established CytoSorbents France SAS as wholly-owned subsidiaries of CytoSorbents Europe GmbH. From the beginning of the controlled market release in the fourth quarter of 2011 through December 31, 2022, we achieved cumulative sales of CytoSorb of approximately $181.7 million. During this time period, the CytoSorb device represented substantially all of our product sales.

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 more than 75 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. Outside of the EU, CytoSorb has distribution in Turkey, India, Sri Lanka, Australia, New Zealand, Russia, Serbia, Vietnam, Malaysia, Hong Kong, Chile, Panama, Costa Rica, Colombia, Brazil, Mexico, Argentina, Perú, Peru, 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. 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, B. Braun Avitum AG, Aferetica s.r.l. and Terumo Cardiovascular Group. In August 2022, we expanded our partnership with Fresenius Medical Care to a global marketing collaboration. 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 government agencies in the United States.

During the years ended 2022, 2021 and 2020, 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 March 9, 2023, our patent portfolio includes 18 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 2023 and 2038 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	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	3/31/2031	Standard
CytoSorb	Method of Treating Inflammation	20 Years	4/1/2031	Standard
CytoSorb	Method of Treating Inflammation	20 Years	4/1/2031	Standard
CytoSorb	Method of Treating Inflammation	20 Years	4/1/2031	Standard
CytoSorb	Method of Treating Inflammation	20 Years	4/30/2031	Standard
CytoSorb	Polymer Modification	20 Years	12/31/2031	Standard
CytoSorb	Method of Removal of Impurities from Whole Blood	20 Years	1/6/2032	Standard
CytoSorb	Use of Polymeric Sorbent Polymers	20 Years	8/10/2032	Standard
CytoSorb	Hemocompatible Modifiers	20 Years	3/31/2034	Standard
CytoSorb	Method of Treating Acute Radiation Syndrome	20 Years	10/22/2035	Standard
CytoSorb	Use of Gastrointestinally Administered Porous Sorbent Polymers	20 Years	10/22/2035	Standard
CytoSorb	Hemocompatible Porous Beads	20 Years	10/21/2036	Standard
CytoSorb	Removal of Endotoxemia	20 Years	5/17/2037	Standard
CytoSorb	Method of Removing Toxins From Blood	20 Years	7/30/2038	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 $384,000 for the year ended December 31, 2022.

Employees

As of March 7, 2023, we had 198 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.

We have experienced substantial operating losses since inception. As of December 31, 2022, we had an accumulated deficit of approximately $253,998,000, which included net losses of approximately $32,813,000, $24,559,000 and $7,837,000 for the years ended December 31, 2022, 2021 and 2020, 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, 2022, we had current assets of approximately $33.8 million, including cash, cash equivalents and restricted cash on hand of approximately $23.8 million and current liabilities of approximately $9.7 million. For year ended December 31, 2022, 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 $35 million, which included approximately $6.3 million of capital spending and improvements related to our new manufacturing facility and corporate headquarters. Our current and historical cash burn is not necessarily indicative of our future use of cash and cash equivalents.

We are currently adequately capitalized but will require additional financing in the future in order to complete additional clinical studies and to support the commercialization of our proposed products. There can be no assurance that we will be successful in our capital raising efforts. The amount of long-term capital needed is expected to depend on many factors, including but not limited to:

- 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 14, 2021 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. All of this amount is available as we have not utilized the existing shelf. All of the $25 million of our total shelf amount allocated to our ATM facility was available as of December 31, 2022.

On July 24, 2020, the Company closed on 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 December 30, 2021, we entered into an Open Market Sale Agreement with Jefferies LLC (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 $25,000,000. There were no sales pursuant to the Sale Agreement during the year ended December 31, 2022.

On January 19, 2022 (the "Fourth Amendment Closing Date"), the Company closed on the Fourth Amendment (the "Fourth Amendment") of its Amended Loan and Security Agreement with Bridge Bank. Under the terms of the Amendment, the Company received a commitment from Bridge Bank to provide a new term loan of up to $15 million, if needed until December 31, 2022. On December 27, 2022, the Company drew down the first $5 million tranche of the Term C loans available under the terms of the Fourth Amendment.

On December 28, 2022 (the "Fifth Amendment Date"), the Company entered into the Fifth Amendment of its Amended Loan and Security Agreement with Bridge Bank. The Fifth Amendment extends the draw period under the Fourth Amendment to the earlier of (i) March 1, 2023 and (ii) the occurrence of an Event of Default. On March 9, 2023, the Company entered into the Sixth Amendment of its Amended Loan and Security Agreement. The Sixth Amendment further extends the draw period to March 24, 2023.

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

In addition, in the event that additional funds are obtained through arrangements with collaborative partners or other non-dilutive sources, we may have to relinquish economic and/or proprietary rights to some of our technologies or products under development that we would otherwise seek to develop or commercialize by ourselves. Such events may have a material adverse effect on our business, operating results, financial condition and prospects.

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 and is likely to continue to affect our operations and those of third parties on which we rely, including by causing disruptions in our global supply chain, our ability to obtain raw materials, the manufacturing of and short-term demand for our lead product, CytoSorb, the commercialization of CytoSorb, our research and development activities, 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 DrugSorb-ATR 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. There may be new or further delays in patient enrollment in the PROCYSS and the STAR clinical trials. For example, in April 2021 we stopped the TISORB single arm study due to continued delays and poor enrollment caused by the COVID-19 pandemic in the U.K., in favor of redirecting those resources to the U.S. STAR-T randomized, controlled trial and in November 2022, we temporarily paused the STAR-D trial for business reasons. 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 research and development activities that were temporarily suspended as a result of the COVID-19 pandemic, however we have experienced, and may continue to experience, challenges in hiring necessary staff members to conduct our research and development activities, including technical staff. 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 and following the COVID-19 outbreak and such volatility may continue. Macro factors have impacted, and may continue to negatively impact, our critical care and cardiac surgery markets, including in certain geographies such as Germany. For example, widespread staffing shortages, decreased availability of hospital beds, fewer patients, increased hospital restrictions resulting in decreased access of our sales representatives to hospitals and fewer sales meetings with physicians resulted in lower-than-expected sales of CytoSorb during the years ended December 31, 2022 and 2021, respectively, and may contribute to lower-than-expected sales of CytoSorb in the future. 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. The Company estimated that approximately $0.3 million and $6.3 million of its 2022 and 2021 product sales, respectively, were related to the treatment of COVID-19 patients. As the pandemic continues to ease and the amount of our revenues attributable to the treatment of COVID-19 is reduced, it is uncertain whether the Company will be able to replace some or all of this revenue in the future.

Our operating results are subject to seasonal fluctuation.

Our total revenue and product sales are subject to seasonal fluctuation. Our sales seasonality is affected by a number of factors, including but not limited to, hospital budgets and buying patterns, customer, employee and healthcare worker vacation schedules, religious, national, and state holidays, scientific and medical conference schedules, seasonal illnesses such as influenza, seasonal or weather-related differences in hospital admissions and the timing of insurance benefits, among others. Our normal seasonality cycle has also been impacted by the COVID-19 pandemic and related events, making it more difficult to predict and determine a more consistent seasonality trend. See "A pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, may materially and adversely affect our business and operations." As a result, seasonality has had, and we expect it to continue to have, an impact on our results of operations.

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, product labeling, 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 adequately capitalized, we will 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. 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 7, 2023, we had 198 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 had an initial term of three years and were 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 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 employment agreements for the Named Executive Officers above have automatically renewed for another year term. On September 30, 2022, Ms. Bloch notified the Company of her intention to retire effective March 31, 2023. A search has been initiated for Ms. Bloch's replacement. Ms. Bloch and the Company expect to enter into a consulting arrangement under which Ms. Bloch will continue to provide services to the Company in a limited capacity following the effective date of her retirement. 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. Additionally, the increasing demand for qualified personnel may make it more difficult for us to attract and retain qualified employees. Changing demographics and labor work force trends may make it difficult for us to replace departing employees at our manufacturing and other facilities and we may experience increased turnover rates. U.S. labor market conditions are currently challenging and labor shortages have been exacerbated during and following the COVID-19 pandemic. These conditions are expected to persist into 2023 and may lead to higher labor costs. If we fail to attract and retain qualified personnel, or if we experience labor shortages, we may experience higher costs and other difficulties. 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 2023 and 2038. 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 2023 and 2038. 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 is 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 are subject to international regulation as medical devices under the Medical Devices Directive and, once our CE Mark under MDD expires in May 2024 will be subject to the new European Union Medical Device Regulation ("MDR"). 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 adsorber 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 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 and/or DrugSorb-ATR 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 and DrugSorb-ATR 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, DrugSorb-ATR 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, DrugSorb-ATR 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 or marketing approval 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 adsorber. 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.

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.

Weakness in the global economy, and in particular in the United States and Europe, could negatively impact our revenue and operating results.

The United States and Europe and other economies may suffer from uncertainty, volatility, disruption, and other adverse conditions, such as inflation or the rising cost of energy, and these conditions have adversely impacted and may continue to adversely impact the business community and the financial markets. Adverse economic and financial market conditions may negatively affect our markets, thereby negatively impacting our revenue and operating results. As a result, if economic and financial market conditions weaken or deteriorate, then our revenue and operating results, including our ability to grow and expand our business and operations, could be materially and adversely affected.

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, 2022, 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, or the rapidly evolving conflict between Russia and Ukraine, 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, our inability to timely engage with and collect payment from customers in Russia and other affected regions, or otherwise affect our ability to do business. Additionally, global events such as the current COVID-19 coronavirus pandemic and the conflict in Ukraine, that have or could, 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 (iv) our inability to timely engage with and collect payment from our customers or (v) our inability to access capital markets, our business and results of operations could be materially and adversely affected. For example, in response to the conflict between Russia and Ukraine, the United States has imposed and may further impose, and other countries may additionally impose, broad sanctions or other restrictive actions against governmental and other entities in Russia. CytoSorb is currently distributed in Russia. While the existing sanctions do not currently prohibit the distribution of CytoSorb in Russia, additional sanctions may be imposed in the future that could prevent us from selling CytoSorb in this or other affected regions. Additionally, further escalation of geopolitical tensions could have a broader impact that extends into other markets where we do business. 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 or distribute our products, including Russia, 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 $4.23 and as low as $1.03 per share between January 1, 2022 and December 31, 2022 on Nasdaq. On March 7, 2023, the closing price of our common stock, as reported on Nasdaq, was $3.80. 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 clinical data, analyst or media reports;
- 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, 2022, two shareholders hold 10.4% of our shares and our directors and officers hold 6.7% 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 56,364,000 shares remain available for issuance as of December 31, 2022 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 December 30, 2021 we entered into an Open Market Sale Agreement with Jefferies LLC (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 $25,000,000. 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 one facility in Princeton, New Jersey and two facilities in Berlin, Germany as follows:

1. In March 2021, we entered into a lease agreement for a new 48,511 square foot operating facility at 305 College Road East, Princeton, New Jersey, which contains office, laboratory, manufacturing and warehouse space. The lease commenced in April 2021 and expires in March 2037. As of February 2023, our monthly rent payment is approximately $114,000.

2. Our office facility leases in Berlin, Germany requires combined base rent payments amounting to approximately $12,100 per month. The initial lease term of both leases ends August 31, 2026. In addition, the Company is obligated to monthly operating expenses of approximately $3,000 per month. Both leases have a five-year option to renew that would extend the lease term to August 31, 2031.

3. Our warehouse facility lease in Berlin, Germany commenced on April 1, 2021 and requires monthly payments of base rent of approximately $7,800 and other costs of approximately $240 and has a term of five years. The lease also has an option to extend the lease term for an additional five-year period through March 31, 2031.

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.

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 13, 2023, there were approximately 11,200 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.

Issuer Purchases of Securities

There were no repurchases of the Company's securities during the year ended December 31, 2022.

Recent Sales of Unregistered Securities

We had no sales of unregistered securities in 2022 that have not been previously disclosed in a Current Report on Form 8-K or Quarterly Report on Form 10-Q.

Item 6. [Reserved]

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, 2022, 2021 and 2020 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 the treatment of life-threatening conditions in the intensive care ("ICU") and cardiac surgery using blood purification via our proprietary polymer adsorption technology. We have a number of products commercialized and in development based on this technology platform. Our flagship product, CytoSorb®, is already commercialized, and is being used to reduce deadly uncontrolled inflammation and dangerous substances in hospitalized patients around the world, with the goal of preventing or treating multiple organ failure, bleeding, and other potentially fatal complications. Organ failure is the cause of nearly half of all deaths in the ICU, with little to improve clinical outcome. CytoSorb, is approved in the European Union ("EU") as an effective extracorporeal cytokine absorber, designed to reduce the "cytokine storm" or "cytokine release syndrome" that could otherwise cause massive inflammation, organ failure and death in common critical illnesses such as sepsis, burn injury, trauma, lung injury, cytokine release syndrome due to cancer immunotherapy, and pancreatitis. These are conditions where the mortality is extremely high, yet few to 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 Device 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 U.S. FDA has granted U.S. Emergency Use Authorization ("EUA") of CytoSorb for use in critically ill patients with COVID-19 infection and respiratory failure. In May 2020, we received a CE-Mark label expansion for CytoSorb for the removal of rivaroxaban during cardiothoracic surgery requiring cardiopulmonary bypass. In August 2021, the Company announced that it was granted a second Breakthrough Device Designation for its DrugSorb-ATR Antithrombotic Removal System by the FDA to remove the direct oral anticoagulants, rivaroxaban and apixaban. The Company has initiated a pivotal randomized, controlled clinical trial in the U.S. and Canada, called the STAR-T trial, evaluating the use of DrugSorb-ATR during cardiothoracic surgery to remove ticagrelor to prevent or reduce perioperative bleeding complications in pursuit of U.S. FDA and Health Canada marketing approval.

CytoSorb is used during and after cardiac surgery to remove inflammatory mediators, such as cytokines, activated complement, 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 195,000 human treatments to date in critical illnesses and in cardiac surgery. CytoSorb has received CE-Mark label expansions for the removal of bilirubin (liver disease), myoglobin (trauma) and both ticagrelor and rivaroxaban during cardiothoracic surgery. CytoSorb has also received FDA Emergency Use Authorization in the United States for use in critically-ill COVID-19 patients with imminent or confirmed respiratory failure, in defined circumstances. The EUA will be effective until a declaration is made that the circumstances justifying the EUA have terminated or until revoked by the FDA. CytoSorb has been used globally in more than 7,650 human treatments to date in COVID-19 patients. CytoSorb has also been granted FDA Breakthrough Designation for the removal of ticagrelor in a cardiopulmonary bypass circuit during emergent and urgent cardiothoracic surgery. CytoSorb was also granted a second FDA Breakthrough Device designation for the removal of the Direct Oral Anticoagulants (DOACs) apixaban and rivaroxaban in a cardiopulmonary bypass circuit to reduce the likelihood of serious perioperative bleeding during urgent cardiothoracic 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 18 issued U.S. patents and multiple international patents, with applications pending both in the U.S. and internationally. We have numerous other product candidates under development based upon this unique blood purification technology, including CytoSorb XL, K^+ontrol, HemoDefend-RBC, HemoDefend-BGA, ContrastSorb, DrugSorb, DrugSorb-ATR and others.

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.

- DrugSorb-ATR — an investigational extracorporeal antithrombotic removal system based on the same polymer technology as CytoSorb that is being evaluated in the U.S. STAR-T and future STAR-D pivotal randomized, controlled trials to reduce the level of antithrombotic drugs, ticagrelor, apixaban and rivaroxaban to reduce bleeding complications in patients undergoing cardiothoracic surgery while on these drugs.

- ECOS-300CY — an adsorption cartridge approved in the E.U. for use with *ex vivo* organ perfusion systems to remove cytokines and other inflammatory mediators in the organ perfusate, with the goal of maintaining or improving solid organ function prior to transplant. In 2021, commercialization of PerSorb™ and Aferetica's PerLife™ *ex vivo* organ perfusion system commenced in Italy.

- 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, the U.S. Air Force, U.S. Special Operations Command, and others.

Results of Operations

Comparison of the year ended December 31, 2022 and 2021

Revenues:

For the year ended December 31, 2022, we generated total revenue, which includes product revenue and grant income, of approximately $34,689,000 as compared to revenues of approximately $43,166,000 for the year ended December 31, 2021, a decrease of approximately $8,477,000, or 20%. Revenue from product sales was approximately $29,360,000 for the year ended December 31, 2022, as compared to approximately $40,109,000 in the year ended December 31, 2021, a decrease of approximately $10,749,000 or 27%. Direct sales decreased by approximately $8,983,000 and distributor sales decreased by approximately $1,766,000 during the year ended December 31, 2022 as compared to the year ended December 31, 2021. Sales to hospitals in the United States under the EUA granted by the FDA amounted to approximately $300,000 for the year ended December 31, 2022, as compared to approximately $1,690,000 in 2021. Though difficult to quantify, we estimate that approximately $300,000 and approximately $6,300,000 of total product sales during the years ended December 31, 2022 and 2021 was due to the demand for CytoSorb to treat COVID-19 patients. In addition, as a result of the decrease in the average exchange rate of the Euro to the U.S. dollar, 2022 product sales were negatively impacted by approximately $3,127,000. For the year ended December 31, 2022, the average exchange rate of the Euro to the U.S. dollar was $1.05 as compared to an average exchange rate of $1.18 for the year ended December 31, 2021.

Grant income was approximately $5,329,000 for the year ended December 31, 2022 as compared to approximately $3,057,000 for the year ended December 31, 2021, an increase of approximately $2,272,000, or 74%. During the year ended December 31, 2021, our research and development employees were either deployed to work-from-home status or reassigned to assist in activities related to increasing the production of CytoSorb. In 2022, research and development employees were assigned primarily to grant related activities.

Cost of Revenue:

For the years ended December 31, 2022 and 2021, cost of revenue was approximately $13,956,000 and $11,047,000, respectively, an increase of approximately $2,909,000. This increase was due to an increase in grant cost of revenue of approximately $2,210,000 due to the increase in billable hours charged to our grant related projects. Product cost of revenues increased approximately $698,000 during the year ended December 31, 2022 as compared to the year ended December 31, 2021. This increase was primarily due to an equipment failure of a refrigeration unit at our new manufacturing facility that caused a net write-off (after insurance proceeds) of approximately $300,000 of work-in-process inventory (see Note 2 to the financial statements) and inefficiencies associated with lower production due to a decrease in production volume and inefficiencies associated with relocating our production activities to the new facility. Product gross margins were approximately 70% for the year ended December 31, 2022 and approximately 80% for the year ended December 31, 2021.

Gross Profit:

Gross profit was approximately $20,733,000 for the year ended December 31, 2022, a decrease of approximately $11,385,000 or 35%, versus gross profit of $32,118,000 in 2021. This decrease is attributed to lower sales, the inventory write-off related to an equipment failure and inefficiencies associated with the process of relocating our production activities to the new facility as discussed above.

Research and Development Expenses:

Our research and development costs were approximately $15,119,000 and $16,381,000 for the years ended December 31, 2022 and 2021, respectively, a decrease of approximately $1,262,000, or 8%. This decrease was due to a decrease in clinical trial related costs of approximately $2,448,000, due primarily to the temporary pause of our STAR-D clinical trial in the U.S. and the discontinuation of the Hep-On-Fire clinical trial in Germany, a decrease in rent expense to research and development of approximately $685,000 related to our new facility and a decrease in non-grant related research and development costs of approximately $187,000. These decreases were offset by an increase in salaries related to our clinical trial activities of approximately $1,694,000 due to the hiring of additional clinical expertise and an increase in other research and development labor costs of approximately $364,000 related to the hiring of additional scientific expertise.

Legal, Financial and Other Consulting Expenses:

Our legal, financial and other consulting costs were approximately $2,848,000 and $2,732,000 for the years ended December 31, 2022 and 2021, respectively, an increase of approximately $116,000, or 4%. This increase was due to an increase in legal fees of approximately $685,000 due to the abandonment of certain issued patents and patent applications and an increase in accounting fees of approximately $169,000. These increases were offset by a decrease in consulting fees of approximately $396,000 and a decrease in hiring fees of approximately $342,000.

Selling, General and Administrative Expenses:

Our selling, general and administrative expenses were approximately $34,288,000 and $35,750,000 for the years ended December 31, 2022 and 2021, respectively, a decrease of approximately $1,462,000, or 4%. This decrease was due to a decrease of salary and commission costs of approximately $594,000 due to a reduction in commissions due to lower sales, a decrease in royalty expense of approximately $915,000 due to lower sales, a decrease in non-cash restricted stock expense of approximately $1,771,000 related to restricted stock units granted to the Company's executive officers, a decrease in non-cash stock compensation expense of approximately $597,000 and a decrease in other general and administrative expenses of approximately $324,000. These decreases were offset by an increase sales and marketing costs, which include advertising and conference attendance, of approximately $797,000, an increase in travel and entertainment costs of approximately $530,000 and an increase in occupancy costs of approximately $1,412,000 related to the rent expense on our new manufacturing facility.

Gain (Loss) on Foreign Currency Transactions:

For the year ended December 31, 2022, the loss on foreign currency transactions was approximately $2,449,000, as compared to a loss on foreign currency transactions of approximately $2,578,000 for the year ended December 31, 2021. The 2022 loss is directly related to the decrease of the exchange rate of the Euro as of December 31, 2022 as compared to December 31, 2021. The exchange rate of the Euro to the U.S. dollar was $1.07 per Euro at December 31, 2022 as compared to $1.14 per Euro at December 31, 2021. The 2021 loss is directly related to the decrease in the exchange rate of the Euro as of December 31, 2021, as compared to December 31, 2020. The exchange rate of the Euro to the U.S. dollar was $1.14 per Euro at December 31, 2021 as compared to $1.22 per Euro at December 31, 2020.

Benefit from Income Taxes:

Our benefit from income taxes was approximately $1,093,000 and $736,000 for the years ended December 31, 2022 and 2021, 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, 2021 and 2020

Revenues:

For the year ended December 31, 2021, we generated total revenue, which includes product revenue and grant income, of approximately $43,166,000 as compared to revenues of approximately $41,005,000 for the year ended December 31, 2020, an increase of approximately $2,161,000, or 5%. Revenue from product sales was approximately $40,109,000 for the year ended December 31, 2021, as compared to approximately $39,453,000 in the year ended December 31, 2020, an increase of approximately $656,000 or 2%. Direct sales increased by approximately $361,000 and distributor sales increased by approximately $295,000 during the year ended December 31, 2021 as compared to the year ended December 31, 2020. Sales to hospitals in the United States under the EUA granted by the FDA amounted to approximately $1,690,000 for the year ended December 31, 2021, as compared to approximately $1,341,000 in 2020. Though difficult to quantify, we estimate that approximately $6.3 million and $9.4 million of total product sales during the years ended December 31, 2021 and 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 $1,207,000. For the year ended December 31, 2021, the average exchange rate of the Euro to the U.S. dollar was $1.18 as compared to an average exchange rate of $1.14 for the year ended December 31, 2020.

Cost of Revenue:

For the years ended December 31, 2021 and 2020, cost of revenue was approximately $11,047,000 and $11,052,000, respectively, a decrease of approximately $5,000. Product cost of revenues decreased approximately $1,447,000 during the year ended December 31, 2021 as compared to the year ended December 31, 2020. This decrease was related to certain costs associated with the rapid ramp-up of production during the year ended December 31, 2020 that did not recur during the year ended December 31, 2021. These decreases were offset by the negative impact of non-recurring costs related to prior years tariffs as a result of an audit by the German Customs Authorities of approximately $732,000 and the offsetting non-recurring positive impact of the Employee Retention Tax Credit of approximately $388,000, both of which were recorded in the first quarter of 2021. Product gross margins were approximately 80% for the year ended December 31, 2021 and approximately 76% for the year ended December 31, 2020.

Gross Profit:

Gross profit was approximately $32,118,000 for the year ended December 31, 2021, an increase of approximately $2,166,000 or 7%, over gross profit of $29,952,000 in 2020. This increase is attributed to the reasons discussed above.

Research and Development Expenses:

Our research and development costs were approximately $16,381,000 and $8,811,000 for the years ended December 31, 2021 and 2020, respectively, an increase of approximately $7,570,000, or 86%. This increase was due to an increase in clinical trial and related costs of approximately $4,670,000, due primarily to the start-up of our STAR-T and STAR-D clinical trials in the U.S. and our PROCYSS and Hep-On-Fire clinical trials in Germany, an increase in salaries related to our clinical trial activities of approximately $1,620,000 due to the hiring of additional clinical expertise, an increase in rent expense of approximately $943,000 related to rent expense on our new facility, an increase in other research and development labor costs of approximately $294,000 related to the hiring of additional scientific expertise and an increase in other research and development costs of approximately $43,000.

Legal, Financial and Other Consulting Expenses:

Our legal, financial and other consulting costs were approximately $2,732,000 and $3,048,000 for the years ended December 31, 2021 and 2020, respectively, a decrease of approximately $316,000, or 10%. This decrease was due to due to a decrease in hiring fees of approximately $319,000, a decrease in legal fees of approximately $263,000, and a decrease in accounting fees of approximately $28,000. These increases were offset by an increase in consulting fees of approximately $294,000 related to certain corporate initiatives.

Selling, General and Administrative Expenses:

Our selling, general and administrative expenses were approximately $35,750,000 and $28,464,000 for the years ended December 31, 2021 and 2020, respectively, an increase of approximately $7,286,000, or 26%. This increase is related to an increase in salaries, commissions and related costs of approximately $4,476,000, an increase in non-cash restricted stock expense of approximately $989,000 related to restricted stock units granted to the Company's executive officers, an increase in non-cash stock option compensation expense of approximately $507,000, an increase in commercial insurance of approximately $280,000, an increase in sales and marketing costs, which include advertising and conference attendance of approximately $1,152,000 and an increase in travel and entertainment costs of approximately $121,000. These increases were offset by a decrease in contracted public relations costs of approximately $210,000 and a decrease in other general and administrative expenses of approximately $29,000.

Interest Expense, Net:

For the year ended December 31, 2021, interest income, net was approximately $28,000, as compared to interest expense, net of approximately $1,201,000 for the year ended December 31, 2020. This decrease in net interest expense of approximately $1,229,000 was the result of the payoff of our outstanding term loans with Bridge Bank in December of 2020.

Gain (Loss) on Foreign Currency Transactions:

For the year ended December 31, 2021, the loss on foreign currency transactions was approximately $2,578,000, as compared to a gain on foreign currency transactions of approximately $2,607,000 for the year ended December 31, 2020. The 2021 loss is directly related to the decrease of the exchange rate of the Euro at December 31, 2021 as compared to December 31, 2020. The exchange rate of the Euro to the U.S. dollar was $1.14 per Euro at December 31, 2021 as compared to $1.22 per Euro at December 31, 2020. The 2020 gain is directly related to the increase in 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, 2019 as compared to $1.12 per Euro at December 31, 2019.

Benefit from Income Taxes:

Our benefit from income taxes was approximately $736,000 and $1,127,000 for the years ended December 31, 2021 and 2020, 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.

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, 2022, we had current assets of approximately $33,760,000 including cash, cash equivalents and restricted cash on hand of approximately $23,832,000 and had current liabilities of approximately $9,715,000. All of the $25 million of our total shelf amount allocated to our ATM facility was available as of December 31, 2022. On December 27, 2022, we drew down the first $5 million tranche of the Term C loans available under the terms of our Amended Loan and Security Agreement with Bridge Bank (see below). Also, we expect to receive approximately $1,093,000 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 half of 2023.

As of December 31, 2022, cash, cash equivalents and restricted cash were $23.8 million compared to $53.8 million as of December 31, 2021. After taking into account the $5 million related to our debt drawdown, our 2022 cash burn was approximately $35.0 million. This cash burn was due to lower-than-expected sales volumes, product gross margins that were lower due to decreased production volumes, and operating efficiencies associated with the move to our new manufacturing facility, capital expenditures of approximately $6.3 million related to our new facility and other factors (e.g. a delay in realizing savings from cost cutting due to notice periods and labor laws in Europe). A reduction in product gross margins from 80% in 2021 to 70% in 2022, unfavorably impacted our cash burn by approximately $2.9 million. We expect product gross margins to return to previous levels as we transition production fully to the new facility by the end of this year, end the lease at our Deer Park Drive facility, and begin to capture anticipated manufacturing efficiencies driven by expected improvement in market conditions and increased product demand.

We are also managing our resources proactively, continuing to invest in key areas such as our U.S. clinical program. while driving cost-cutting throughout our Company. At the beginning of Q2 2022, we began instituting tighter cost controls and have reduced our headcount (including full and part-time employees and consultants) internationally by 10%, with the goal of reducing our cash burn. In addition, we have shifted our R&D headcount to funded grant programs, where we have an $11.5 million backlog as of December 31, 2022. Some of our costs savings of our headcount reduction are not yet visible in our results due to notice periods and labor laws in Europe but will be reflected in our 2023 operating budget. Meanwhile, we are working diligently to prioritize activities that we believe have a near-term return on investment and advance our strategic priorities, which cutting non-core or non-essential activities and spend. Our goal is, through a combination of driving an increase in sales and gross margin, and cutting costs, to significantly reduce our cash burn and to extend our operating runway with the resources we have.

Based upon the foregoing, we believe that we have sufficient cash to fund the Company’s operations beyond twelve months from the issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Loan and Security Agreement

The Company and its wholly-owned subsidiary, CytoSorbents Medical, Inc. (together, the "Borrower"), are parties to that certain Loan and Security Agreement ("Original Agreement") with Bridge Bank, a division of Western Alliance Bank, (the "Bank"), which was most recently amended on January 19, 2022 (the "Fourth Amendment Date") under that certain Fourth Amendment to the Amended and Restated Loan and Security Agreement (the "Fourth Amendment" and the Original Agreement, as so amended, the "Loan Agreement"). Under the Loan Agreement, the Bank has agreed to loan a tranche of term loans in the aggregate amount of $15 million, which are available for the Company to draw down at its sole discretion in three tranches of $5 million each at any time during the period commencing on the Fourth Amendment Date and ending on the earlier of (i) December 31, 2022 and (ii) the occurrence of an Event of Default (as defined in the Loan Agreement) (the "Term C Loan"). On December 27, 2022, the Company drew down the first $5 million tranche of the Term C loans available under the terms of the Fourth Amendment. On December 28, 2022 (the "Fifth Amendment Date"), the Company entered into the Fifth Amendment of its Amended Loan and Security Agreement with Bridge Bank. The Fifth Amendment extends the draw period under the Fourth Amendment to the earlier of (i) March 1, 2023 and (ii) the occurrence of an Event of Default. On March 9, 2023, the Company entered into the Sixth Amendment of its Amended Loan and Security Agreement. The Sixth Amendment further extends the draw period to March 24, 2023. For further discussion regarding the Loan Agreement and the Term C Loan, please see Note 7 – Long Term Debt to our Consolidated Financial Statements, included elsewhere in this Annual Report on Form 10-K.

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 with various agencies of the United States government. 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 and are included in accrued expenses and other current liabilities in the consolidated balance sheet. 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 our leased facility in Princeton, New Jersey and two leased facilities in Berlin, Germany as follows:

- In March 2021, we entered into a lease agreement for a new 48,511 square foot operating facility at 305 College Road East, Princeton, New Jersey, which contains office, laboratory, manufacturing and warehouse space. The lease commenced in April 2021 and expires in March 2037. As of February 2023, our monthly base rent is approximately $114,000.

- Our office facility leases in Berlin, Germany requires combined base rent payments amounting to approximately $12,100 per month. The initial lease term of both leases ends August 31, 2026. In addition, the Company is obligated to monthly operating expenses of approximately $3,000 per month. Both leases have a five-year option to renew that would extend the lease term to August 31, 2031.

- Our warehouse facility lease in Berlin, Germany commenced on April 1, 2021 and requires monthly payments of base rent of approximately $7,800 and other costs of approximately $240 and has a term of five years. The lease also has an option to extend the lease term for an additional five-year period through March 31, 2031.

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, 2022, 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, 2022. 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, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspection.

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 2023 annual meeting of stockholders scheduled to be held on June 6, 2023, 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 2023 annual meeting of stockholders scheduled to be held on June 6, 2023, which we intend to file within 120 days of the end of our fiscal year.

To the extent required, 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 2023 annual meeting of stockholders scheduled to be held on June 6, 2023, 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 2023 annual meeting of stockholders scheduled to be held on June 6, 2023, 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 2023 annual meeting of stockholders scheduled to be held on June 6, 2023, 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 2023 annual meeting of stockholders scheduled to be held on June 6, 2023, 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 2023 annual meeting of stockholders scheduled to be held on June 6, 2023, 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 2022 annual meeting of stockholders scheduled to be held on June 6, 2023, 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 April 8, 2021).
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 filed on March 10, 2022).
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+	Lease Agreement between Princeton Corporate Plaza LLC and the Registrant dated as of March 9, 2000 (incorporated by reference to Exhibit 10.4 to the Registrant's Annual Report on Form 10-K filed on March 31, 2015).
10.6	Third Amendment to Lease Agreement between Princeton Corporate Plaza LLC and the Registrant dated as of December 12, 2014 (incorporated by reference to Exhibit 10.5 to the Registrant's Annual Report on Form 10-K filed on March 31, 2015).
10.7	Fourteenth Amendment to Lease Agreement by and between the Registrant and Princeton Corporate Plaza, LLC, dated April 1, 2016 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on May 9, 2016).
10.8	Amended and Restated Fourteenth Amendment to Lease Agreement by and between the Registrant and Princeton Corporate Plaza LLC, dated August 5, 2016 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on May 9, 2016).
10.9	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).
10.10	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).
10.11*	Assignment and Assumption of Certain Royalty Rights, dated as of November 22, 2022, by and among Robert Shipley Living Trust, ROKK, LLC, and CytoSorbents Medical, Inc.
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	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).
10.18	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).
10.19	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).
10.20	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).
10.21	Fourth Amendment to the Amended and Restated Loan and Security Agreement, dated as of January 19, 2022, 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 January 20, 2022).
10.22	Fifth Amendment to the Amended and Restated Loan and Security Agreement, dated as of December 28, 2022, 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 29, 2022).
10.23	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).
10.24	Success Fee Letter, dated as of January 19, 2022, 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 January 20, 2022).
10.25†	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).
10.26†	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).
10.27	Open Market Sale AgreementSM, dated as of December 30, 2021, by and between CytoSorbents Corporation and Jefferies LLC (incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K, filed with the SEC on December 30, 2021).

10.28	Marketing Agreement, dated as of August 1, 2022, by and between CytoSorbents Corporation and Fresenius Medical Care Deutschland GmbH (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on November 3, 2022).
10.29	Lease, dated as of March 26, 2021, by and between 300 CR LLC and CytoSorbents Medical, Inc. (incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K, filed with the SEC on March 31, 2021).
10.30*	Sixth Amendment to the Amended and Restated Loan and Security Agreement, dated as of March 8, 2023, by and among CytoSorbents Corporation, CytoSorbents Medical, Inc. and Western Alliance Bank.
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, 2021, formatted in Extensible Business Reporting Language (XBRL): (1) Consolidated Balance Sheets at December 31, 2022 and December 31, 2021, (iii) Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2022, 2021 and 2020, (iii) Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Equity/(Deficit) for the years ended December 31, 2022, 2021 and 2020, (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2022, 2021 and 2020, 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, 2023.

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, 2023
/s/ Kathleen P. Bloch Kathleen P. Bloch	Chief Financial Officer (Principal Financial and Accounting Officer)	March 9, 2023
/s/ Al Kraus Al Kraus	Chairman of the Board	March 9, 2023
/s/ Alan D. Sobel Alan D. Sobel	Director	March 9, 2023
/s/ Edward R. Jones Edward R. Jones	Director	March 9, 2023
/s/Michael G. Bator Michael G. Bator	Director	March 9, 2023

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, 2022.

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 over financial reporting. 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, 2023

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, 2022 and 2021, 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, 2022, 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, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, 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, 2022, based on criteria established in *Internal Control-Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

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

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated 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 consolidated 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 separate opinions 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, board of directors, and consultants as compensation for their service. The Company recorded approximately $3,424,000 of stock-based compensation expense during the year ended December 31, 2022. 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 of performance achieved. In 2022, the Company granted 2,528,800 of such awards and recorded stock-based compensation expense related to these performance awards of approximately $180,440.

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. 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 the Company's 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 through review of source documents, press releases, and board minutes 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 this matter.

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

/s/ WithumSmith+Brown, PC

East Brunswick, New Jersey
March 9, 2023
PCAOB ID Number 100

CYTOSORBENTS CORPORATION
CONSOLIDATED BALANCE SHEETS

December 31,	2022	2021
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 22,144,567	$ 52,137,707
Grants and accounts receivable, net of allowance for doubtful accounts of $76,041 and $60,539 at December 31, 2022 and 2021, respectively	5,664,941	4,523,430
Inventories	3,461,586	4,766,098
Prepaid expenses and other current assets	2,488,597	2,871,655
Total current assets	33,759,691	64,298,890
Property and equipment - net	10,743,032	5,150,886
Restricted cash	1,687,459	1,687,459
Right-of-use asset	12,603,901	13,423,472
Other assets	4,437,447	4,958,575
Total Assets	$ 63,231,530	$ 89,519,282
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 1,655,173	$ 2,805,235
Accrued expenses and other current liabilities	7,950,440	10,314,341
Lease liability – current portion	108,939	570,566
Total current liabilities	9,714,552	13,690,142
Lease liability, net of current portion	13,142,005	13,250,943
Long-term debt	5,000,000	—
Total Liabilities	27,856,557	26,941,085
Commitments and Contingencies (Note 10)		
Stockholders' Equity:		
Preferred Stock, Par Value $0.001, 5,000,000 shares authorized; no shares issued and outstanding at December 31, 2022 and 2021	—	—
Common Stock, Par Value $0.001, 100,000,000 shares authorized; 43,635,715 and 43,478,487 shares issued and outstanding at December 31, 2022 and 2021, respectively	43,635	43,478
Additional paid-in capital	287,000,021	283,194,429
Accumulated other comprehensive income	2,329,195	525,585
Accumulated deficit	(253,997,878)	(221,185,295)
Total stockholders' equity	35,374,973	62,578,197
Total Liabilities and Stockholders' Equity	$ 63,231,530	$ 89,519,282

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, 2022	Year ended December 31, 2021	Year ended December 31, 2020
Revenue:			
CytoSorb sales	$ 28,572,709	$ 39,996,700	$ 39,342,102
Other sales	787,201	111,867	110,400
Total product sales	29,359,910	40,108,567	39,452,502
Grant income	5,328,899	3,056,960	1,552,099
Total revenue	34,688,809	43,165,527	41,004,601
Cost of revenue	13,955,752	11,047,350	11,052,409
Gross profit	20,733,057	32,118,177	29,952,192
Operating expenses:			
Research and development	15,118,907	16,380,930	8,810,561
Legal, financial and other consulting	2,847,899	2,731,515	3,048,242
Selling, general and administrative	34,288,130	35,750,477	28,463,723
Total operating expenses	52,254,936	54,862,922	40,322,526
Loss from operations	(31,521,879)	(22,744,745)	(10,370,334)
Other income (expense):			
Interest (expense), net	132,597	28,007	(1,201,067)
Gain (loss) on foreign currency transactions	(2,448,583)	(2,577,913)	2,607,139
Miscellaneous expense	(67,303)	—	—
Total other income (expense), net	(2,383,289)	(2,549,906)	1,406,072
Loss before benefit from income taxes	(33,905,168)	(25,294,651)	(8,964,262)
Benefit from income taxes	1,092,585	736,003	1,127,074
Net loss attributable to common stockholders	$ (32,812,583)	$ (24,558,648)	$ (7,837,188)
Basic and diluted net loss per common share	$ (0.75)	$ (0.57)	$ (0.20)
Weighted average number of shares of common stock outstanding	43,573,215	43,359,186	38,818,990
Comprehensive loss:			
Net loss	$ (32,812,583)	$ (24,558,648)	$ (7,837,188)
Other comprehensive income (loss):			
Foreign currency translation adjustment	1,803,610	2,259,663	(2,260,056)
Comprehensive loss	$ (31,008,973)	$ (22,298,985)	$ (10,097,244)

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, 2022, 2021 and 2020

	Common Stock		Paid-In	Accumulated Other Comprehensive	Accumulated	Stockholders'
	Shares	Par value	Capital	Income (Loss)	Deficit	Equity
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 income, foreign currency 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
Stock-based compensation - employees, consultants and directors	—	—	4,020,819	—	—	4,020,819
Issuance of common stock - offerings, net of fees incurred	—	—	(90,000)	—	—	(90,000)
Issuance of restricted stock options	106,662	107	928,310	—	—	928,417
Proceeds from exercise of stock options	139,102	139	805,060	—	—	805,199
Cashless exercise of stock options	10,724	10	(2,842)	—	—	(2,832)
Other comprehensive income, foreign currency translation adjustment	—	—	—	2,259,663	—	2,259,663
Net loss	—	—	—	—	(24,558,648)	(24,558,648)
Balance at December 31, 2021	43,478,487	43,478	283,194,429	525,585	(221,185,295)	62,578,197
Stock-based compensation - employees, consultants and directors	—	—	3,423,517	—	—	3,423,517
Legal/audit fees related to ATM offering	—	—	(40,358)	—	—	(40,358)
Issuance of restricted stock options	144,728	145	379,946	—	—	380,091
Other comprehensive loss, foreign currency translation adjustment	—	—	—	1,803,610	—	1,803,610
Stock issued to vendor in lieu of cash payment	12,500	12	42,487	—	—	42,499
Net loss	—	—	—	—	(32,812,583)	(32,812,583)
Balance at December 31, 2022	43,635,715	$ 43,635	$ 287,000,021	$ 2,329,195	$ (253,997,878)	$ 35,374,973

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

CYTOSORBENTS CORPORATION
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31, 2022	Year ended December 31, 2021	Year ended December 31, 2020
Cash flows from operating activities:			
Net loss	$ (32,812,583)	$ (24,558,648)	$ (7,837,188)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash compensation	376,574	2,183,317	1,193,949
Depreciation and amortization	882,621	731,578	660,788
Amortization of right-of-use asset	249,008	398,035	—
Bad debt expense (recovery)	(8,354)	(512)	(102,310)
Loss on disposal of fixed assets	132,303	—	—
Impairment of patents	635,606	—	—
Foreign currency transaction (gains) losses	2,448,583	2,577,913	(2,607,139)
Stock-based compensation	3,423,517	4,020,819	3,513,671
Amortization of loan acquisition costs	—	—	322,812
Changes in operating assets and liabilities:			
Grants and accounts receivable	(1,288,422)	420,578	(326,860)
Inventories	945,352	(2,350,547)	(461,512)
Prepaid expenses and other current assets	(22,187)	280,915	(1,076,849)
Other assets	52,678	(135,857)	—
Accounts payable and accrued expenses	(3,248,978)	2,426,810	1,107,352
Net cash used in operating activities	(28,234,282)	(14,005,599)	(5,613,286)
Cash flows from investing activities:			
Purchases of property and equipment	(6,087,365)	(3,641,248)	(708,395)
Patent costs	(368,211)	(640,013)	(967,823)
Net cash used in investing activities	(6,455,576)	(4,281,261)	(1,676,218)
Cash flows from financing activities:			
Proceeds from long-term debt	5,000,000	—	1,410,900
Repayment of long-term debt	—	—	(16,410,900)
Final fee on long-term debt	—	—	(375,000)
Payment of loan acquisition costs	—	—	—
Equity contributions - net of fees incurred	(40,358)	(90,000)	80,214,008
Proceeds from exercise of stock options	—	805,199	1,509,322
Proceeds from exercise of warrants	—	—	—
Net cash provided by financing activities	4,959,642	715,199	66,348,330
Effect of exchange rates on cash	(262,924)	(24,774)	130,357
Net change in cash, cash equivalents and restricted cash	(29,993,140)	(17,596,435)	59,189,183
Cash, cash equivalents and restricted cash at beginning of year	53,825,166	71,421,601	12,232,418
Cash, cash equivalents and restricted cash at end of year	$ 23,832,026	$ 53,825,166	$ 71,421,601
Supplemental disclosure of cash flow information:			
Cash paid during the year for interest	$ —	$ —	$ 1,127,647
Supplemental disclosure of non-cash financing activities:			
Issuance of common stock to vendor in lieu of cash payment	$ 42,499	—	—
Capital expenditures included in accounts payable	$ 359,965	—	—
Settlement of accrued bonuses with restricted stock units	$ 380,091	$ 928,417	$ 657,780

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

CYTOSORBENTS CORPORATION
Notes to Consolidated Financial Statements
December 31, 2022

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, CytoSorbents Poland Sp. z.o.o., CytoSorbents Medical UK Limited, and CytoSorbents France SAS, the 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. As of December 31, 2022, the Company's cash, cash equivalents and restricted cash balances were approximately $23.8 million, which the Company expects will fund the Company's operations beyond twelve months from the issuance of these consolidated financial statements. 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 the treatment of life-threatening conditions in intensive care and cardiac surgery using blood purification. 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 the Company's clinical trial activities in the United Kingdom. In March 2022, the Company formed CytoSorbents Medical UK Limited to provide marketing and direct sales services in the United Kingdom and the Republic of Ireland. In October 2022, the Company formed CytoSorbents France SAS to provide marketing and direct sales services in France. CytoSorb, the Company's flagship product, was approved in the European Union ("EU") in March 2011 and is currently being marketed and distributed in more than 75 countries around the world, as an effective extracorporeal cytokine absorber, designed to reduce the "cytokine storm" or "cytokine release syndrome" seen in critical illnesses that may result in massive inflammation, organ failure, and patient death. 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 that can lead to post-operative complications, including multiple organ failure. In January 2020, CytoSorb received EU CE Mark label expansion to include the removal of ticagrelor during cardiopulmonary bypass in patients undergoing cardiothoracic surgery. In May 2020, CytoSorb also received EU CE Mark label expansion to include rivaroxaban removal for the same indication.

In April 2020, CytoSorb received United States Food and Drug Administration ("FDA") Emergency Use Authorization ("EUA") of CytoSorb for use in adult critically-ill COVID-19 patients with imminent or confirmed respiratory 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 for its DrugSorb-ATR Antithrombotic Removal System 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 CytoSorbents' technology 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 July 2021, the Company received full approval of its Investigative Device Exemption ("IDE") to conduct the pivotal STAR-T (Safe and Timely Antithrombotic Removal – Ticagrelor) double-blind randomized control trial ("RCT") for up to 120 patients in the United States to support FDA marketing approval.

In August 2021, the Company announced that it was granted a second Breakthrough Device designation for its DrugSorb-ATR Antithrombotic Removal System by the FDA. This Breakthrough Device designation covers the removal of the Direct Oral Anticoagulants (DOACs) apixaban and rivaroxaban in a cardiopulmonary bypass circuit to reduce the likelihood of serious perioperative bleeding during urgent cardiothoracic surgery. In October 2021, the Company also received full FDA approval of an IDE application to conduct a double-blind, randomized, controlled clinical study for up to 120 patients entitled, "Safe and Timely Antithrombotic Removal – Direct Oral Anticoagulants (STAR-D)," in the United States to support FDA marketing approval.

If FDA marketing approval is obtained for either the removal of ticagrelor or direct oral anticoagulants indications, the device would be marketed as DrugSorb-ATR in the United States. The DrugSorb-ATR Antithrombotic Removal System is based on the same polymer technology as CytoSorb.

In May 2022, the Company announced that the Company entered into a 3-year preferred supplier agreement with Asklepios, making CytoSorb available without restrictions to all of the approximate 170 healthcare facilities across 14 states throughout Germany at which Asklepios operates. This includes Asklepios Klinik St. Georg in Hamburg, Germany, which pioneered the use of CytoSorb to remove antithrombotic drugs during cardiothoracic surgery, and is well-known for their seminal publication on CytoSorb use for this application during emergency cardiac surgery in patients at high risk of bleeding.

In June 2022, the Company announced that, following a successful pilot program in three countries, the Company signed an expanded non-exclusive agreement with Nikkiso Europe GmbH ("Nikkiso") to distribute Nikkiso's PureADJUST stand-alone hemoperfusion pump and accessories in a total of 14 countries. In addition to securing the rights to sell Nikkiso's stand-alone pump and accessories in Germany, Austria, and Luxembourg, the Company entered into an expanded multi-country reseller agreement with Nikkiso covering the following countries: Belgium, Bosnia and Herzegovina, Croatia, Finland, France, Iceland, Lichtenstein, Poland, Serbia, Slovenia and Switzerland. The Company will also be able to provide field support services in these countries.

In August 2022, the Company entered into a Marketing Agreement (the "Marketing Agreement") with Fresenius Medical Care Deutschland GmbH ("Fresenius"), which expands the Company's strategic partnership with Fresenius by establishing a multi-stage global collaboration to combat life-threatening diseases in critical care. The Marketing Agreement provides for the combined marketing and promotion of CytoSorb with Fresenius' critical care products by Fresenius' marketing organization worldwide, excluding the United States. The Marketing Agreement has an initial term of three years, with an automatic renewal for an additional two years at the end of such initial term, subject to earlier termination by either of the parties (the "Term"). Compared to the prior co-marketing agreement between the parties, the Marketing Agreement intends to increase the commitments from both parties and to ensure an ongoing and consistent level of marketing and promotional activity specifically focused around CytoSorb, where Fresenius will actively market and promote CytoSorb as the featured blood purification therapy for removal of cytokines, bilirubin, and myoglobin on its critical care platforms. Specifically, the Marketing Agreement provides that various Fresenius-led in-person, virtual, social media, and web-based marketing programs and events will feature the CytoSorb therapy and highlight the cooperation between the two companies in the field of critical care during the Term. To help support the increased marketing and promotional efforts of the expanded collaboration, CytoSorbents has agreed to subsidize a portion of the marketing costs through a royalty payment to Fresenius Medical Care based on CytoSorb sales in the intensive care unit on Fresenius Medical Care platforms, excluding the United States. In addition to strengthening and expanding the global marketing of CytoSorb, the Company and Fresenius also plan to work together to bring new innovative solutions to the market. The Marketing Agreement also includes the certification of compatibility of CytoSorb for usage on Fresenius' current critical care platforms. Certain initial activities have been completed with the formal launch of this program expected to occur sometime in 2023.

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 18 issued U.S. patents and multiple international patents, with applications pending both in the U.S. and internationally, including HemoDefend, ContrastSorb, DrugSorb, DrugSorb-ATR and others. These patents and patent applications are directed to various compositions and methods of use related to the Company's blood purification technologies and are expected to expire between 2023 and 2038, absent any patent term extensions. Management believes that any near-term expiring patents will not have a significant impact on the Company's 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, CytoSorbents Poland Sp. z.o.o., CytoSorbents Medical UK Limited and CytoSorbents France SAS, 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 $(2,448,000), $(2,578,000) and $2,607,000 for the years ended December 31, 2022, 2021 and 2020, 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 stockholders' 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.

The following table provides a reconciliation of cash and cash equivalents and restricted cash and cash equivalents to amounts shown in the consolidated balance sheets and consolidated statements of cash flows:

	December 31,	
	2022	2021
Cash and cash equivalents	$ 22,144,567	$ 52,137,707
Restricted cash	1,687,459	1,687,459
Total cash, cash equivalents and restricted cash	$ 23,832,026	$ 53,825,166

Restricted Cash

The Company's total restricted cash in the amount of $1,687,459 consists of cash of $1,467,459 that the Company is obligated to maintain as collateral for the outstanding letter of credit with Bridge Bank that was provided to the landlord of the College Road facility as security and cash of $220,000 that the Company is obligated to maintain as collateral for the credit limit on the Company's credit card account.

Grants and Accounts Receivable

Grants receivable represent amounts due from U.S. government agencies and are included in grants and accounts Receivable in the accompanying consolidated balance sheets.

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 in 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, 2022 and 2021, the Company's inventory was comprised of finished goods, which amounted to $1,567,871 and $3,084,606, respectively, work in process which amounted to $1,280,368 and $1,322,736, respectively, and raw materials which amounted to $613,347 and $358,756, 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.

In September 2022, the Company experienced an equipment failure of a refrigeration unit at its new College Road manufacturing facility. This equipment stored various items of work-in-process inventory. The Company determined all the items that were stored in this unit were required to be scrapped. The value of this inventory was approximately $599,000. Accordingly, this inventory was written off and was included in cost of goods sold at the time of the loss in September 2022. The Company filed a claim with its insurance carrier related to this loss. In December 2022, the claim was approved in the amount of approximately $299,000 and, accordingly, has been recorded as a reduction to cost of goods sold in the accompanying consolidated statement of operations and comprehensive loss.

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. During the year ended December 31, 2022, the Company wrote-off patent costs of approximately $636,000 related to the impairment of certain issued patents and pending patent applications in certain specific jurisdictions, the abandonment of certain patent defense costs that are no longer being pursued and the abandonment of certain pending patent application costs in the ordinary course of business.

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 with various agencies of the U.S. government. 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 and are included in accrued expenses and other current liabilities in the consolidated balance sheets. 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 $582,000, $615,000 and $285,000 in 2022, 2021 and 2020, respectively, and is included in selling, general, and administrative expenses in 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. In 2017, 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 as of December 31, 2022 or 2021. 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., CytoSorbents UK Limited, CytoSorbents Medical UK Limited and CytoSorbents France file an annual corporate tax return, a VAT return and a trade tax return in Germany, Switzerland, Poland, France 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, liabilities at the date of the balance sheet, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from these estimates. The valuation of options granted, allowance for doubtful accounts and recoverability of patents are significant estimates 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 the Company’s revenues are from product sales in Germany. Substantially all of the Company’s 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, 2022, two distributors accounted for approximately 27% of outstanding grants and accounts receivables. As of December 31, 2021, one distributor accounted for approximately 12% of outstanding grants and accounts receivables. For the years ended December 31, 2022, 2021 and 2020, 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 net loss per share is computed by dividing loss attributable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net loss 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 net loss 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 $297,000, $276,000 and $560,000 for the years ended December 31, 2022, 2021 and 2020, respectively.

Effect of Recent Accounting Pronouncements

In November 2021, the Financial Accounting Standards Board (the “FASB”), issued Accounting Standards Update No. 2021-10 entitled, “Government Assistance (Topic 832) Disclosures by Business Entities about Government Assistance” (the “ASU”). This ASU will require enhanced disclosures related to the Company’s contracts with the U.S. government. The ASU is effective for annual periods beginning after December 15, 2021. The Company implemented the provisions of this ASU during 2022.

In June 2016, the FASB, issued ASU No. 2016-13 entitled, “Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments”. This ASU provides guidance on the calculation of credit losses, which includes the allowance for doubtful accounts on trade accounts receivable. The updated guidance is effective for public entities for fiscal years beginning after December 15, 2022. The Company is evaluating the impact of the updated guidance but does not believe that this will have a significant impact on its financial statements.

3. REVENUE:

The following table disaggregates the Company's revenue by customer type and geographic area for the year ended December 31, 2022:

	Direct	Distributors/ Strategic Partners	United States Government Agencies	Total
Product sales:				
United States	$ 787,201	$ 181,750	$ —	$ 968,951
Germany	12,566,437	—	—	12,566,437
All other countries	4,705,580	11,118,942	—	15,824,522
Total product revenue	18,059,218	11,300,692	—	29,359,910
Grant income:				
United States	—	—	5,328,899	5,328,899
Total revenue	$ 18,059,218	$ 11,300,692	$ 5,328,899	$ 34,688,809

The following table disaggregates the Company's revenue by customer type and geographic area for the year ended December 31, 2021:

	Direct	Distributors/ Strategic Partners	United States Government Agencies	Total
Product sales:				
United States	$ 189,167	$ 1,500,700	$ —	$ 1,689,867
Germany	21,006,432	—	—	21,006,432
All other countries	5,846,256	11,566,012	—	17,412,268
Total product revenue	27,041,855	13,066,712	—	40,108,567
Grant income:				
United States	—	—	3,056,960	3,056,960
Total revenue	$ 27,041,855	$ 13,066,712	$ 3,056,960	$ 43,165,527

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 revenue	26,681,329	12,771,173	—	39,452,502
Grant income:				
United States	—	—	1,552,099	1,552,099
Total revenue	$ 26,681,329	$ 12,771,173	$ 1,552,099	$ 41,004,601

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 U.S., 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 FDA. Direct sales outside the United States relate to sales to hospitals located in Germany, Switzerland, Austria, Belgium, Luxembourg, Poland, the Netherlands, Sweden, Denmark, Norway and the United Kingdom. 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 to 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 numerous grant contracts from various agencies of the U.S. government. The purpose of these grant contracts is to perform various research and development activities. The type of research required is outlined in each contract. These contracts 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.

These government contracts have terms ranging from three months to four years. The Company may apply for an extension of the term of the contract in order to complete its research and development activities but would not receive additional funding during the extension period in excess of the original contract. See Note 2 regarding the accounting policies related to these contracts.

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 government 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, 2022	December 31, 2021
Contract receivables, which are included in grants and accounts receivable	$ 3,822,452	$ 3,000,708
Contract liabilities, which are included in accrued expenses and other current liabilities	$ 1,694,906	$ 2,251,177

Contract receivables represent balances due from product sales to distributors amounting to $2,944,031 and $2,265,159 at December 31, 2022 and 2021, respectively, and billed and unbilled amounts due on government contracts amounting to $878,421 and $735,549 at December 31, 2022 and 2021, respectively.

Contract liabilities represent the value of free of charge goods and credit rebates earned in accordance with the terms of certain direct customer agreements, which amounted to $178,134 and $303,824 at December 31, 2022 and 2021, respectively, and deferred grant revenue related to the billing on fixed price government contracts in excess of costs incurred, which amounted to $1,516,772 and $1,947,343 at December 31, 2022 and 2021, respectively.

4. PROPERTY AND EQUIPMENT, NET:

Property and equipment - net, consist of the following:

December 31,	2022	2021	Depreciation/ Amortization Period
Furniture and fixtures	$ 1,306,267	$ 1,424,476	7 years
Equipment and computers	5,131,934	5,863,673	3 to 7 years
Leasehold improvements	6,201,523	2,623,356	Lesser of term of lease or estimated useful life
	12,639,724	9,911,505	
Less accumulated depreciation and amortization	1,896,692	4,760,619	
Property and Equipment, Net	$ 10,743,032	$ 5,150,886	

Depreciation expense for the years ended December 31, 2022, 2021 and 2020 amounted to $688,565, $571,156 and $553,946 respectively.

5. OTHER ASSETS:

Other assets consist of the following:

December 31,	2022	2021
Patent applications pending	$ 2,466,341	$ 2,717,701
Patents issued	2,773,191	2,641,603
Less accumulated amortization of patents issued	(848,999)	(657,320)
Patents, net	4,390,533	4,701,984
Security deposits	46,914	256,591
Total	$ 4,437,447	$ 4,958,575

Amortization expense amounted to $194,056, $160,422 and $106,842 for the years ended December 31, 2022, 2021 and 2020, respectively.

Amortization expense for the next five years will be approximately $201,000 for the year ending December 31, 2023; approximately $201,000 for the year ending December 31, 2024; approximately $201,000 for the year ending December 31, 2025; approximately $200,000 for the year ending December 31, 2026 and approximately $196,000 for the year ending December 31, 2027.

6. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES:

Accrued expenses and other current liabilities consist of the following:

December 31,	2022	2021
Accrued salaries and commissions	$ 2,862,930	$ 3,270,715
Deferred revenue	1,516,772	1,947,353
Clinical studies	1,115,123	1,767,826
Accrued accounts payable	850,630	1,044,088
Professional fees	622,353	314,068
Accrued royalties	592,398	769,262
Customer rebates	166,065	214,119
Travel and entertainment	99,316	88,850
Board of Director fees	97,426	71,381
Sales, payroll and income taxes payable	21,871	785,818
Interest	5,556	—
Congresses	—	40,861
	$ 7,950,440	$ 10,314,341

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 "Third Amendment 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, if needed. On January 19, 2022 (the "Fourth Amendment Closing Date"), the Company closed on the Fourth Amendment (the "Fourth Amendment") of its Amended Loan and Security Agreement with Bridge Bank. Under the terms of the Amendment, the Company received a commitment from Bridge Bank to provide a new term loan of up to $15 million, if needed and entered into the Fourth Amendment Success Fee Letter (the "2022 Success Fee Letter"). On December 28, 2022 (the "Fifth Amendment Date"), the Company entered into the Fifth Amendment of its Amended Loan and Security Agreement with Bridge Bank. The Fifth Amendment extends the draw period under the Fourth Amendment to the earlier of (i) March 1, 2023 and (ii) the occurrence of an Event of Default. On March 9, 2023, the Company entered into the Sixth Amendment of its Amended Loan and Security Agreement. The Sixth Amendment further extends the draw period to March 24, 2023.

The Fourth Amendment provides a tranche of term loans (the "Term C Loans") in the aggregate amount of $15 million, which are available for the Company to draw down at its sole discretion in three tranches of $5 million each at any time during the period commencing on the Fourth Amendment Date and ending on the earlier of (i) December 31, 2022 and (ii) the occurrence of an Event of Default (as defined in the Amended Loan and Security Agreement). The Term C Loans 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 immediately preceding the month in which the interest will accrue) plus 1.25%. Pursuant to the Fourth Amendment, interest on the Term C Loans is subject to an interest rate cap of 8.00%. On December 27, 2022, the Company drew down the first $5 million tranche of the Term C loans available under the terms of the Fourth Amendment. Under the terms of the Fourth Amendment, commencing on February 1, 2023, the Company is required to make monthly payments of interest only through December 2023. The interest-only period will be further extended through June 2024 provided the Company has met both the required reserves test and the seventy-five percent test, as set forth in the Fourth Amendment, as of November 30, 2023. Commencing on January 1, 2024, if the Company does not meet both the required reserves test and the seventy-five percent test, the Company shall make equal monthly payments of principal of $208,333, together with accrued and unpaid interest. Commencing on July 1, 2024, if the Company meets both the required reserves test and the seventy-five percent test, the Company shall make equal monthly payments of principal of $277,778, together with accrued and unpaid interest. In either event, all unpaid principal and accrued and unpaid interest shall be due and payable in full on December 1, 2025.

On the Fourth Amendment Closing Date, the Company was required to pay a non-refundable closing fee of approximately $18,750, which was amortized as a monthly charge to interest expense. On the Third Amendment Closing Date, the Company paid a non-refundable closing fee of $75,000, which was amortized as a charge to interest expense. 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 the Term Loan funded upon the earlier of the (i) the maturity date or (ii) termination of the Term Loans via acceleration or prepayment.

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.

2022 Success Fee Letter:

Pursuant to the 2022 Success Fee Letter, the Borrower will pay to the Bank a success fee equal to (i) 1% of $5 million if the Company draws down the first tranche of the Term C Loan and is payable only if the Company's stock price equals or exceeds $8 for five consecutive trading days; (ii) 1.5% of $5 million if the Company draws down the second tranche of the Term C Loan and is payable only if the Company's stock price equals or exceeds $10 for five consecutive trading days; and (iii) 2% of $5,000,000 if the Company draws down the third tranche of the Term C Loan and is payable only if the Company's stock price equals or exceeds $12 for five consecutive trading days (together, the "Success Fee"). Borrower may pay the Success Fee in cash or in shares of common stock, at Borrower's sole discretion. The right of Bank to receive the Success Fees and the obligation of the Borrower to pay the Success Fees hereunder shall terminate on the date that is fifth anniversary of the funding date of the last Term C Loans made but shall survive the termination of the Loan Agreement and any prepayment of the Term C Loans.

Long-term debt consists of the following as of December 31, 2022:

Principal amount	$ 5,000,000
Less Current maturities	—
Long-term debt net of current maturities	$ 5,000,000

Principal payments of long-term debt are due as follows during the years ending December 31:

2023	$ —
2024	2,500,000
2025	2,500,000
Total	$ 5,000,000

8. LEASES:

The Company leases its operating facilities in both the United States and Germany under operating lease agreements. In March 2021, CytoSorbents Medical Inc. entered into a lease agreement for a new operating facility at 305 College Road East, Princeton, New Jersey, which contains office, laboratory, manufacturing and warehouse space. The lease commenced on June 1, 2021. The Early Term commenced on June 1, 2021 and lasted until September 30, 2021. The lease also contains two five-year renewal options; however, the Company has determined that it is not likely that they will exercise these options. Commencing on September 30, 2021, the remaining lease term will last for 15.5 years. The lease requires monthly rental payments of $25,208 for the Initial Early Term, $88,254 for the Early Term and initial monthly payments of approximately $111,171 in the first year of the remaining term. Following the first year of the remaining term, the annual base rent will increase by approximately 2.75% annually over the remaining term. The lease also contains six months of rent abatement (months 1, 2, 3, 25, 26 and 27 of the remaining lease term). In addition to the base rent, payments of operating expenses and real estate taxes will be required. These payments are to be based on actual amounts incurred during 2021 multiplied by the Company's share of the total building space (92.3%). The landlord will also provide an allowance of approximately $1,455,000 related to certain building improvements as outlined in the lease. In April 2021, the Company provided the landlord with a letter of credit in the amount of approximately $1,467,000 as security. The Company has determined that this lease should be treated as an operating lease in accordance with the provisions of Accounting Standards Codification ("ASC") 842. On April 1, 2021, the Company recorded a Right-of-Use asset and related lease liability of approximately $11.6 million, which represents the estimated present value of the lease payments at the commencement date discounted at the Company's incremental borrowing rate of 9.8%. In addition, due to the six months of rent abatement and annual base rent escalations during the remaining lease term that commenced on September 30, 2021, the Company will recognize rent expense on this lease on a straight-line basis over the remaining term of the lease for the difference between the rent expense recognized and the required payments under the lease.

In April 2021, the Company entered into a Twentieth Amendment to Lease with the landlord at the existing Monmouth Junction facility which became effective May 31, 2021. This amendment extended the term of the lease for the Company's previous facility to May 31, 2022. The Company's base rent was approximately $35,000 per month. In addition, the Company was obligated to pay monthly operating expenses of approximately $30,000 per month. Under the terms of this amendment, the Company vacated a portion of the space as of May 31, 2022. The Company continued to lease the remaining space until December 31, 2022, at which time the lease terminated and the Company vacated the space. The Company's base rent for the remaining space was approximately $20,000 per month. Monthly operating expenses were approximately $11,000 per month. In addition, the Company agreed to increase its security deposit by approximately $54,000 to a total of $150,000. At the end of the lease term, the entire security deposit was paid to the landlord for the purpose of making any needed repairs to the vacated premises, and the Company has no further obligation to pay for repairs to the vacated premises. Effective April 1, 2021, the Company adjusted its incremental borrowing rate to the incremental borrowing rate used in the College Road lease and recalculated the right of use asset and lease liability under the amended terms of this lease. In addition, the Company also adjusted the incremental borrowing rate and related right of use asset and lease liability on the existing Germany office lease effective April 1, 2021.

In September 2021, the Company extended its two operating leases for its office facility in Germany. These leases require combined base rent payments amounting to approximately $12,100 per month. The initial lease term of both leases ends August 31, 2026. In addition, the Company is obligated to monthly operating expenses of approximately $3,000 per month. Both leases have a five-year option to renew that would extend the lease term to August 31, 2031. 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.

In January 2021, CytoSorbents Europe GmbH entered into a lease for 1,068 square meters of additional warehouse space. The lease commenced on April 1, 2021 and requires monthly payments of base rent of $7,784 and other costs of approximately $239 and has a term of five years. The lease also has an option to extend the lease term for an additional five-year period through March 31, 2031. The Company has determined that this lease should be treated as an operating lease in accordance with the provisions of ASC 842. On April 1, 2020, the Company recorded a Right-of-Use asset and related lease liability at the estimated present value of the lease payments at the commencement date of approximately $594,000.

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 all expected renewals for all periods 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 9.8%, 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,	
	2022	2021
Right-of-use asset	$ 12,603,901	$ 13,423,472
Total lease liability	$ 13,250,944	$ 13,821,509
Less current portion	(108,939)	(570,566)
Lease liability, net of current portion	$ 13,142,005	$ 13,250,943

The maturities of the lease liabilities are as follows as of December 31, 2022:

2023	$ 1,266,346
2024	1,656,678
2025	1,695,677
2026	1,735,747
2027	1,776,920
Thereafter	17,232,300
Total lease payments	25,363,668
Present value discount	12,112,724
Total	$ 13,250,944

For the years ended December 31, 2022, 2021 and 2020, operating cash flows paid in connection with operating leases amounted to approximately $2,935,000, $1,968,000 and $937,000, respectively.

As of December 31, 2022 and 2021, the weighted average remaining lease term was 12.4 years and 14.3 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, 2022, 2021 and 2020 is as follows:

	Year Ended December 31,		
	2022	2021	2020
Domestic	$ (21,155,203)	$ (18,829,797)	$ (5,682,628)
Foreign	(12,749,965)	(6,464,854)	(3,281,634)
Total	$ (33,905,168)	$ (25,294,651)	$ (8,964,262)

The benefit from income taxes consists of the following:

	Year Ended December 31,		
	2022	2021	2020
State Tax, including sale of New Jersey losses & credits	$ 1,092,585	$ 736,003	$ 1,127,074
Foreign tax provision	—	—	—
	$ 1,092,585	$ 736,003	$ 1,127,074

The Company has deemed any foreign earnings will be indefinitely reinvested. Currently, foreign operations have resulted in an accumulated deficit. The Company will continue to analyze their stance if their circumstances change in the future.

As of December 31, 2022, the Company had federal net operating loss ("NOL") carryforwards of approximately $87.4 million, state NOL carry forwards of approximately $5.5 million, and foreign NOL carry forwards of approximately $42.7 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 2022 and 2037. The federal NOL carryforwards of $39.6 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 $5.5 million, if not utilized, will begin to expire in 2042. As of December 31, 2022, the Company had Federal and state research and development tax credit carryforwards of approximately $3.7 million and $0.3 million, respectively, available to reduce future tax liabilities, which will begin to expire at various dates starting in 2023.

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.

We record tax benefits related to uncertain tax positions taken or expected to be taken on a tax return when such benefits meet a more likely than not threshold. We recognize interest related to unrecognized tax benefits in interest expense and penalties in operating expenses. Currently, the Company is not accounting for any uncertain tax positions.

U.S. Tax Reform

Due to The Tax Cuts and Jobs Act of 2017 (TCJA) there was a change in the deductibility of research and experimental expenditures that took effect for taxable periods that begin after December 31, 2021. Prior to January 1, 2022, the Company expensed research and experimental expenditures under §174(a) in the year that books recognized the expense. The Company has adopted §174(b) for taxable years 2022 and beyond. Domestic and foreign research and experimental expenditures will be capitalized and amortized over a period no less than 60 months and 180 months, respectively.

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 $1,093,000 from the approved sale of the 2021 state NOL and research and development credits in the first half of 2023.

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

	Year Ended December 31,		
	2022	2021	2020
Deferred tax assets:			
Net operating loss carry forward	$ 31,570,846	$ 27,190,654	$ 22,301,154
Stock options	500,975	1,203,272	305,982
Research and development credit carryforward	3,982,147	2,687,591	2,194,211
Accruals and others	24,121	232,665	135,330
Lease liability	3,724,840	3,997,114	289,287
§174(b) research and development	3,331,625	—	—
Gross deferred tax assets	43,134,554	35,311,296	25,225,964
Less valuation allowance	(39,303,451)	(31,242,130)	(24,794,474)
	3,831,103	4,069,166	431,490
Deferred tax liability:			
Fixed assets	(288,145)	(183,941)	(431,490)
Right of Use Asset	(3,542,958)	(3,885,225)	—
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, 2022, 2021 and 2020 were $8,061,321, $6,447,656, and $1,936,732, 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,		
	2022	2021	2020
Federal statutory rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	(2.8)	(2.0)	(9.5)
Foreign rate differential	3.4	2.3	3.3
Permanent items	(1.5)	(6.5)	(2.0)
Rate change and true-up	0.6	11.8	17.0
Change in valuation allowance	(22.8)	(25.5)	(21.6)
R&D credit	2.1	1.7	4.4
Sale of state R&D credit and NOL	3.2	—	—
Effective income tax rate	3.2 %	2.8 %	12.6 %

10. COMMITMENTS AND CONTINGENCIES:

Payroll Tax Examination

In December 2021, the Company was notified that its European subsidiary, CytoSorbents Europe GmbH, would be subject to an audit of their payroll tax and social cost filings for the four-year period from 2018 through 2021. The Company has determined that payroll taxes and social costs were not paid on certain employee expense reimbursements as is required by German tax rules. Accordingly, the Company accrued approximately $598,000 as an estimate of this liability as of December 31, 2021. In January 2023, the Company received an assessment from the German tax authorities for the payroll tax audit of approximately $90,000. In addition, it was determined that the Company would owe additional social security and VAT taxes related to this matter of approximately $83,000. Accordingly, the Company has adjusted its accrual related to this payroll tax audit to approximately $173,000 as of December 31, 2022. This liability is included in accrued expenses and other current liabilities in the consolidated balance sheet as of December 31, 2022.

The expense related this examination is included in selling, general and administrative expenses on the consolidated statements of operations and comprehensive loss.

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 expired 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.In January 2022, these employment agreements automatically renewed for an additional 1 year. 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.

On September 30, 2022, Ms. Bloch notified the Company of her intention to retire effective March 31, 2023. A search has been initiated for Ms. Bloch's replacement. Ms. Bloch and the Company expect to enter into a consulting arrangement under which Ms. Bloch will continue to provide services to the Company in a limited capacity following the effective date of her retirement.

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 perpetual royalty of 3% on all gross revenues received by the Company from the sale of its CytoSorb device which such rights were assigned to an existing investor in 2017. For the years ended December 31, 2022, 2021 and 2020, the Company recorded royalty expenses of approximately $849,000, $1,193,000, and $1,172,000, respectively. These expenses are included in selling, general and administrative expenses in the consolidated statements of operations and comprehensive loss.

On August 1, 2022, the Company entered into the Marketing Agreement with Fresenius, which expands the Company's strategic partnership with Fresenius by establishing a multi-stage global collaboration to combat life-threatening diseases in critical care. The Marketing Agreement has an initial term of three years, with an automatic renewal for an additional two years at the end of such initial term, subject to earlier termination by either of the parties (the "Term") To help support the increased marketing and promotional efforts of the expanded collaboration, the Company has agreed to subsidize a portion of the marketing costs through royalty payments to Fresenius. Initially, the Marketing Agreement provides for royalty payments equal to 0.9% of the Company's net sales of CytoSorb products made during the Term (excluding net sales in the United States). This initial royalty rate was determined based on certain assumptions regarding the percentage of the Company's sale of CytoSorb products that are used with the Fresenius critical care platforms in the intensive care unit outside of the United States but is subject to adjustment if the Company determines that the underlying assumptions have changed significantly. For the year ended December 31, 2022, the Company did not record any expense related to this agreement as Fresenius did not commence any marketing activities as defined by the agreement.

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 date of the agreement. For the years ended December 31, 2022, 2021 and 2020 per the terms of the license agreement, the Company recorded licensing expenses of

approximately $1,416,000, $1,988,000 and $1,954,000, 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.

Shelf Registration

On July 14, 2021, the Company filed a registration statement on Form S-3 with the SEC, which was amended on July 20, 2021 and declared effective by the SEC on July 27, 2021 (as amended, the "2021 Shelf"). The 2021 Shelf 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

On December 30, 2021, the Company entered into an Open Market Sale Agreement (the "Sale Agreement") with Jefferies LLC (the "Agent"), pursuant to which the Company could 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 Agent, as the Company's sales agent. All shares of the Company's common stock offered and sold, or to be offered and sold under the Sale Agreement, would have been issued and sold pursuant to the Company's 2021 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.

Subject to the terms of the Sales Agreement, the Agent is 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 Agent 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. There were no sales pursuant to the Amended Sale Agreement during the years ended December 31, 2022 and 2021, respectively. In addition, during the year ended December 31, 2021, the Company paid approximately $90,000 related to the Amended Sale Agreement.

Stock Option Plans

As of December 31, 2022, 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, 2022, there were shares remaining to purchase approximately 3,713,000 and 258,000 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 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, 2022, 2021 and 2020 amounted to approximately $3,424,000, $4,021,000, and $3,514,000, 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, 2022, 2021 and 2020 is as follows:

	Shares	Weighted Average Exercise per Share	Weighted Average Remaining Contractual Life (Years)
Outstanding January 1, 2020	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
Granted	2,051,980	$ 8.78	9.30
Forfeited	(138,037)	$ 6.73	—
Expired	(21,756)	$ 7.46	—
Exercised	(171,413)	$ 5.73	—
Outstanding, December 31, 2021	6,885,978	$ 7.09	7.15
Granted	2,721,205	$ 1.99	9.60
Forfeited	(1,270,155)	$ 8.65	—
Expired	(227,204)	$ 7.71	—
Exercised	—	$ —	—
Outstanding, December 31, 2022	8,109,824	$ 5.11	6.91

The fair value of each stock option was estimated using the Black-Scholes pricing model which takes the following factors into account.

Year - Ended	Grant Date Exercise Price Range	Expected Life of the Stock Option	Current Price of the Underlying Stock and its Expected Volatility Range	Expected Dividends	Risk Free Interest Rate Range
December 31, 2020	$ 5.00 - $10.58 per share	6 years	61.7% to 69.8 %	0 %	0.28% to 0.96 %
December 31, 2021	$ 4.26 - $11.39 per share	6 years	58.2% to 60.7 %	0 %	0.47% to 1.39 %
December 31, 2022	$ 1.11 - $3.91 per share	6 years	59.3% to 67.9 %	0 %	1.52% to 4.20 %

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, 2022 of $1.55 and the exercise price of the shares.

Options Outstanding				
Range of Exercise Price	Number Outstanding at December 31, 2022	Weighted Average Exercise Price	Weighted Average Remaining Life (Years)	Aggregate Intrinsic Value
$1.11 - $13.20	8,109,824	$ 5.11	6.91	$ 7,280

Options Exercisable		
Number Exercisable at December 31, 2022	Weighted Average Exercise Price	Aggregate Intrinsic Value
4,623,085	$ 6.32	$ 1,250

The summary of the status of the Company's non-vested options for the year ended December 31, 2022, is as follows:

	Shares	Weighted Average Grant Date Fair Value
Non-vested, January 1, 2022	2,994,846	$ 4.68
Granted	2,721,205	1.99
Forfeited	(1,270,155)	8.65
Vested	(959,157)	3.65
Non-vested, December 31, 2022	3,486,739	$ 2.10

As of December 31, 2022, the Company had approximately $4,745,000 of total unrecognized compensation cost related to stock options which will, on average, be amortized over 43 months.

Awards of Stock Options:

On August 10, 2022, the Board of Directors granted options to purchase 1,163,800 shares of common stock to the Company's employees which will be awarded based upon each employee's 2022 individual performance evaluation. Once awarded, these options will vest one quarter on February 15, 2023, one quarter on February 15, 2024, one quarter on February 15, 2025 and one quarter on February 15, 2026. The grant date fair value of these unvested options amounted to approximately $1,381,000. The Company has recorded approximately $180,440 in stock option expense related to these options for the year ended December 31, 2022.

On August 10, 2022, the Board of Directors granted options to purchase 772,905 shares of common stock to the Company's employees. These options will vest one eighth on the six-month anniversary of the grant date, one eighth on the first anniversary of the grant date, one quarter on second anniversary of the grant date, one quarter on third anniversary of the grant date and one quarter on fourth anniversary of the grant date. The grant date fair value of these unvested options amounted to approximately $917,000. The Company has recorded approximately $89,662 in stock option expense related to these options for the year ended December 31, 2022.

On August 10, 2022, the Board of Directors granted options to purchase 113,850 shares of common stock to members of the Company's Board of Directors. These options will vest one quarter on the grant date, one quarter on September 30, 2022, one quarter on December 31, 2022, and one quarter on March 31, 2023. The grant date fair value of these unvested options amounted to approximately $135,000. The Company has recorded approximately $101,336 in stock option expense related to these options for the year ended December 31, 2022.

On August 10, 2022, the Board of Directors granted options to purchase 473,750 shares of common stock to certain senior managers of the Company. These options will vest one quarter on the grant date, one quarter on the first anniversary of the grant date, one quarter on second anniversary of the grant date, one quarter on third anniversary of the grant date. The grant date fair value of these unvested options amounted to approximately $562,000. The Company has recorded approximately $160,944 in stock option expense related to these options for the year ended December 31, 2022.

On August 10, 2022, the Board of Directors granted options to purchase 1,365,000 shares of common stock to certain senior managers of the Company which will only vest upon the achievement of certain specific, predetermined milestones related to the Company's long-term performance goals. The grant date fair value of these unvested options amounted to approximately $1,620,000. As of December 31, 2022, none of these milestones has been met. Accordingly, no charge for these options has been recorded in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2022.

On April 12, 2021, the Board of Directors granted options to purchase 1,323,400 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. 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 $7,042,000. On March 1, 2022, Board of Directors determined that the Company met approximately 19% of these milestones, and accordingly, the Company has recorded $314,000, and $273,000 in stock option expense related to these options for the years ended December 31, 2022, and 2021, respectively.

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. The grant date fair value of these unvested options amounted to approximately $3,883,000. On April 12, 2021, Board of Directors determined that the Company met approximately 88% of these milestones, and accordingly, the Company has recorded $951,000 and $1,070,000 in stock option expense related to these options for the years ended December 31, 2022, and 2021, respectively.

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, 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
Granted 2021	—	—	396,000	396,000	
Forfeited 2021	—	—	(132,000)	(132,000)	
December 31, 2021	277,200	724,500	1,709,500	2,711,200	$ 11,359,928
Granted 2022	69,300	55,000	373,750	498,050	
Forfeited 2022	—	—	(318,750)	(318,750)	
December 31, 2022	346,500	779,500	1,764,500	2,890,500	$ 4,480,275

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 statement of operations and comprehensive loss through the year ended December 31, 2022.

Performance-Based Awards of Restricted Stock Units:

Pursuant to a review of the compensation of the senior management of the Company and management's performance in 2020, on February 28, 2020, the Board of Directors granted 168,100 restricted stock units to certain senior managers of the Company. 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, 2022 and 2021, the Company recorded (income) expense of approximately $(65,000) and $528,000, respectively, related to these restricted stock unit awards.

Pursuant to a review of the compensation of the senior management of the Company and management's performance in 2021, on April 12, 2021, the Board of Directors granted 235,765 restricted stock units to certain senior managers of the Company. These awards were valued at approximately $2,120,000 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, 2022 and 2021, the Company recorded a charge of approximately $226,000 and $1,207,000, respectively, related to these restricted stock unit awards.

On August 10, 2022, certain named executive officers and senior managers were granted 288,500 restricted stock units. These awards were valued at approximately $563,000 at the date of issuance, based upon the market price of the Company's common stock at the date of the grant, and vested (or will 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 year ended December 31, 2022 and 2021, the Company recorded expense of approximately $260,000 and $0, respectively, related to these restricted stock unit awards.

Additionally, in 2021 and 2020 certain employees were offered 91,750 restricted stock units as a condition of their employment. These awards were valued at approximately $713,868 at the date of issuance. 46,750 of these restricted stock units vest upon the earlier of a Change in Control or one third after the second anniversary of the award, one third on the third anniversary of the award, and one third on the fourth anniversary of the award. The other 45,000 of these restricted stock units vest upon the earlier of a Change in Control or four years from the date of the award. For the years ended December 31, 2022 and 2021, the Company recorded (income) expense of approximately $(16,000) and $178,000, respectively, related to these restricted stock unit awards.

The following table outlines the restricted stock unit activity for the year ended December 31, 2022:

	Shares	Weighted Average Grant Date Fair Value
Non-vested, January 1, 2022	304,962	$ 8.08
Granted	288,500	$ 1.95
Forfeited	(45,000)	$ 8.35
Vested	(236,370)	$ 5.38
Non-vested, December 31, 2022	312,092	$ 4.42

Warrants:

As of December 31, 2022, the Company had no warrants outstanding.

12. NET LOSS PER SHARE:

Basic net loss per share and diluted net loss per share for the years ended December 31, 2022, 2021 and 2020 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 11,312,000, 9,902,000 and 7,786,000 incremental shares at December 31, 2022, 2021 and 2020, respectively, have been excluded from the computation of diluted net 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.Prior to 2021, the Company provided 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 $442,000, $355,000 and $59,200 for the years ended December 31, 2022, 2021 and 2020, respectively.

14. QUARTERLY FINANCIAL RESULTS (UNAUDITED):

Summarized quarterly data for 2022, 2021 and 2020 are as follows:

	For the Quarters Ended			
	March 31	June 30	September 30	December 31
2022:				
Total revenue	$ 8,691,424	8,495,558	8,111,353	9,390,474
Gross margin	6,413,788	4,944,856	3,617,377	5,757,036
Loss from operations	(7,791,135)	(8,357,050)	(9,017,338)	(6,356,356)
Net loss attributable to common stockholders	(8,966,398)	(10,879,222)	(12,200,837)	(766,128)
Net loss per share, basic and diluted	(0.21)	(0.25)	(0.28)	(0.02)
2021				
Total revenue	$ 10,598,847	$ 12,024,069	$ 9,760,416	$ 10,782,195
Gross margin	7,847,403	9,313,852	7,297,470	7,659,452
Loss from operations	(2,852,191)	(4,924,733)	(5,406,000)	(9,561,821)
Net loss attributable to common stockholders	(4,167,821)	(4,677,530)	(6,406,285)	(9,307,012)
Net loss per share, basic and diluted	(0.10)	(0.11)	(0.15)	(0.25)
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

ASSIGNMENT AND ASSUMPTION OF CERTAIN ROYALTY RIGHTS

This ASSIGNMENT AND ASSUMPTION OF CERTAIN ROYALTY RIGHTS (this "Assignment"), dated as of November 22, 2022 (the "Assignment Date"), is entered into by and among the Robert Shipley Living Trust (the "Shipley Trust"), ROKK, LLC ("ROKK, LLC") and CytoSorbents Medical, Inc. Each individual entity party to this Assignment is referred to as a "Party" and collectively as the "Parties."

RECITALS

WHEREAS, on August 11, 2003, RenalTech International, LLC ("RenalTech"), who is the predecessor entity to CytoSorbents Medical, Inc., and Guillermina Vega Montiel ("Montiel") entered into that certain letter agreement (the "Royalty Letter Agreement") pursuant to which RenalTech agreed to pay a royalty of 3.0% of all gross revenues received by RenalTech from sales of the CytoSorb Device (the "Royalties") in the areas of sepsis, cardio-pulmonary bypass, organ donation, chemotherapy and inflammation control;

WHEREAS, Montiel and the Shipley Trust entered into that certain Assignment and Assumption of Certain Royalty Rights, dated as of February 28, 2017, pursuant to which Montiel assigned all of Montiel's rights, title and interest in and to the Royalties under the Royalty Letter Agreement to the Shipley Trust, and the Shipley Trust accepted such assignment and agreed to assume and perform all obligations of Montiel under the Royalty Letter Agreement, effective as of February 28, 2017; and

WHEREAS, pursuant to this Assignment, the Shipley Trust desires to assign all of its rights, title and interest in and to the Royalties under the Royalty Letter Agreement to ROKK, LLC and ROKK, LLC desires to accept the assignment thereof.

NOW THEREFORE, in consideration of the Recitals set forth above, the terms and provisions of this Assignment and for other good and valuable consideration, the receipt, adequacy and sufficiency of which are hereby acknowledged, the Parties hereby covenant and agree as follows:

AGREEMENT

1. Assignment and Assumption

As of the Assignment Date, the Shipley Trust does hereby assign all of its rights, title and interest in and to the Royalties under the Royalty Letter Agreement to ROKK, LLC. As of the Assignment Date, ROKK, LLC hereby accepts the foregoing assignment and assumes all of the obligations of the Shipley Trust under the Royalty Letter Agreement.

2. Successors and Assigns

This Assignment shall be binding upon and inure to the benefit of the Parties' respective successors and assigns. The agreements contained herein constitute the entire understanding between the Parties with respect to the subject matter hereof, and supersede all prior agreements, written or oral, which are inconsistent herewith.

3. Modification and Waiver

No supplement, modification, waiver, or amendment of this Assignment shall be binding unless executed in writing by each of the Parties hereto. No waiver of any of the provisions of this Assignment

shall be deemed or shall constitute a waiver of any other provision hereof nor shall any such waiver constitute a continuing waiver.

4. Governing Law

The validity and effect of this Assignment and the rights and obligations of the Parties hereunder shall be governed by and construed and enforced in accordance with the laws of the State of Delaware, without regard to its conflict of law provisions.[1]

5. Counterparts

This Assignment may be executed in counterparts, each of which shall be deemed to be an original, but all of which together shall constitute one and the same instrument. A facsimile or an electronic copy of a signature is valid as an original.

6. Further Assurances

The Parties agree to execute and deliver any and all documents and to take such further actions as shall reasonably be required to effectuate the intent and transactions contemplated by this Assignment.

IN WITNESS WHEREOF, the Parties, intending to be legally bound, have duly executed this Assignment as of the Assignment Date.

ROBERT SHIPLEY LIVING TRUST

Name: Mary Shipley Ley

Title: Trustee

ROKK, LLC

Name: Mary Shipley Ley

Title: Managing Member

Acknowledged by:

CYTOSORBENTS MEDICAL, INC.

Name: Kathleen P. Bloch

Title: Chief Financial Officer

ASSIGNMENT AND ASSUMPTION OF CERTAIN ROYALTY RIGHTS

THIS ASSIGNMENT AND ASSUMPTION OF CERTAIN ROYALTY RIGHTS (this "**Assignment**") dated as of February 28, 2017 (the "**Closing Date**"), is entered into by and between Guillermina Vega Montiel ("**Assignor**"), and Robert Shipley Living Trust ("**Assignee**")

RECITALS:

A) On August 11, 2003, RenalTech International, LLC ("**RenalTech**"), who is the predecessor corporation to CytoSorbents Medical, Inc., and Assignor entered into an agreement whereby in exchange for certain payments from Assignor, RenalTech agreed to pay a royalty of 3.0% of all gross revenues received from sales of the CytoSorb Device (the "**Royalties**") in the areas of sepsis, cardio-pulmonary bypass, organ donation, chemotherapy and inflammation control ("**Royalty Agreement**"), as more fully described in the Royalty Agreement attached hereto as Exhibit A;

B) Pursuant to this Agreement, Assignor desires to assign its interest in the Royalties to Assignee, and Assignee desires to accept the assignment thereof, upon the terms and conditions of this Assignment;

NOW THEREFORE, in consideration of the Recitals set forth above, the terms and provisions of this Assignment and other good and valuable consideration, the receipt, adequacy and sufficiency of which are hereby acknowledged, Assignor and Assignee hereby covenant and agree as follows:

1. Assignment. Effective as of the date hereof, Assignor hereby sells, assigns, transfers, and sets over unto Assignee all of Assignor's right, title and interest in and to the Royalties as described in the Royalty Agreement.

2. Acceptance and Assumption. Assignee hereby accepts this Assignment and agrees to assume and perform all obligations of the Royalty Agreement; provided, however, that Assignee shall not have any liability and does not assume any obligation under the Royalty Agreement.

3. Successors and Assigns. This Assignment shall be binding on and inure to the benefit of the parties hereto, their heirs, executors, administrators, successors in interest and assigns.

4. Governing Law. This Assignment shall be governed by and construed in accordance with the laws of the State of New Jersey.

1 of 2

5. Counterparts. This Assignment may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, when taken together, shall constitute one and the same document.

IN WITNESS WHEREOF, Assignor and Assignee have executed this Assignment the day and year first above written.

ASSIGNOR:

Guillermina Vega Montiel

ASSIGNEE:

Robert Shipley Living Trust

RenalTech
INTERNATIONAL

RenalTech International, LLC
320 East 65th Street, Suite 11B
New York, NY 10021
Telephone: 212-717-8644
Facsimile: 212-717-8643
www.renaltech.com
E-mail: info@renaltech.com

Guillermina Vega Montiel
P.O. Box 894
Nogales, AZ 85628

August 11, 2003

Dear Guillermina,

This letter shall summarize the points of our discussion from 8/5 regarding the agreed incentive structure for your further investment in RenalTech.:

a. You will purchase $4 million of Membership Units from RenalTech at a price of $3.25 per Unit with a ratchet provision that gives you the lower price if within the next 12 months, after this investment, Membership Units are sold at a lower price.

b. RenalTech will grant you a royalty of 3% on all gross revenues received by RenalTech from the sales of the CytoSorb Device in the areas of sepsis, cardio-pulmonary bypass, organ donation, chemotherapy and inflammation control. The term "revenue" shall include all product sales revenue as well as license fees and proceeds from the sale of RenalTech's Cytosorb intellectual property.

c. You will arrange to (1) immediately wire $1.5mm to Renal Tech's Citibank account #41358084 for purposes of conducting the FDA clinical trials for the BetaSorb ;

(2) wire an additional $1mm by August 25, to provide working capital;

(3) wire an additional $1.5 mm by October 15.

d While not contractually committed to do so, you will consider investing an additional $1 million at the same price as stated above provided the Company is, in your opinion, making satisfactory progress. This right to invest the additional $1mm at $3.25+ratchet to lower price shall be exercisable through February 28, 2004.

Please sign and return a copy of this letter (by fax) to indicate your agreement

Agreed to:

RenalTech International, LLC

By:

SIXTH AMENDMENT TO THE AMENDED AND RESTATED LOAN AND SECURITY AGREEMENT

THIS SIXTH AMENDMENT to the Amended and Restated Loan and Security Agreement (this "**Amendment**") is made effective as of March 8, 2023 (the "**Sixth Amendment Date**") and made by and among **WESTERN ALLIANCE BANK**, an Arizona corporation ("**Bank**") and **CYTOSORBENTS CORPORATION**, a Delaware corporation and **CYTOSORBENTS MEDICAL, INC.**, a Delaware corporation (individually and collectively, jointly and severally "**Borrower**").

WHEREAS, Bank and Borrower have entered into that certain Amended and Restated Loan and Security Agreement, dated as of March 29, 2018 (as amended, supplemented, restated or otherwise modified from time to time, the "**Loan Agreement**") pursuant to which Bank has provided to Borrower certain loans in accordance with the terms and conditions thereof; and

WHEREAS, Bank and Borrower desire to amend certain provisions of the Loan Agreement as provided herein and subject to the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the promises, covenants and agreements contained herein, and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, Bank and Borrower hereby agree as follows:

1. Capitalized terms used herein but not otherwise defined shall have the respective meanings given to them in the Loan Agreement.

2. Section 1.1 of the Loan Agreement is hereby amended by adding the following definition thereto in alphabetical order:

   "Sixth Amendment Date" is March 8, 2023.

3. Section 1.1 of the Loan Agreement is hereby amended by amending and restating the following definition therein as follows:

   "Third Draw Period" means the period commencing on the Fourth Amendment Date and ending on the earlier of (i) March 24, 2023 and (ii) the occurrence of an Event of Default; provided further that no Term C Loan as would cause the aggregate principal amount of Term C Loans to exceed Five Million Dollars ($5,000,000.00) shall be made during the Third Draw Period unless on the Funding Date of such Term C Loan, the Required Reserves Test is met and on or before the Funding Date of such Term C Loan (but no earlier than ten (10) days prior to the Funding Date), the Seventy Five Percent Test is met.

4. Limitation of Amendment.

   a. The amendments set forth above are effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right, remedy or obligation which the Bank or Borrower may now have or may have in the future under or in connection with any Loan Document, as amended hereby.

   b. This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents, except as herein amended, are hereby ratified and confirmed and shall remain in full force and effect.

5. To induce the Bank to enter into this Amendment, Borrower hereby represents and warrants to the Bank as follows:

a. Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct in all material respects as of such date), and (b) no Event of Default has occurred and is continuing;

b. Borrower has the power and due authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

c. The organizational documents of Borrower delivered to the Bank on the Effective Date, and updated pursuant to subsequent deliveries by the Borrower to the Bank, if any, remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

d. The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, will not constitute an event of default under any material agreement with a Person binding on Borrower, or a breach of any provision contained in the Articles of Incorporation or Bylaws of Borrower; and

e. This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and by general equitable principles.

6. Except as expressly set forth herein, the Loan Agreement shall continue in full force and effect without alteration or amendment. This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements.

7. This Amendment shall be deemed effective as of the Amendment Date upon the due execution and delivery to the Bank of this Amendment by each party hereto.

8. This Amendment may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, taken together, shall constitute one and the same instrument.

9. This Amendment and the rights and obligations of the parties hereto shall be governed by and construed in accordance with the laws of the State of California.

[*Balance of Page Intentionally Left Blank*]

IN WITNESS WHEREOF, the parties hereto have caused this Sixth Amendment to the Amend and Restated Loan and Security Agreement to be executed as of the date first set forth above.

CYTOSORBENTS CORPORATION, A DELAWARE CORPORATION

By: DocuSigned by: Kathleen P. Bloch

Name: Kathleen P. Bloch

Title: Chief Financial Officer

CYTOSORBENTS MEDICAL, INC., A DELAWARE CORPORATION

By: DocuSigned by: Kathleen P. Bloch

Name: Kathleen P. Bloch

Title: Chief Financial Officer

WESTERN ALLIANCE BANK, AN ARIZONA CORPORATION

By: DocuSigned by: Christian Ebert

Name: Christian Ebert

Title: Vice President

DocuSign

Certificate Of Completion

Envelope Id: 322987CAFFCE4C0AA445762265F5C225
Status: Completed
Subject: Western Alliance Bank – Loan Documents_Cytosorbents
Source Envelope:
Document Pages: 3
Signatures: 3
Certificate Pages: 4
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
Kaeleen Weber-Turner
1 E Washington St Ste 1400
Phoenix, AZ 85004
KWeber-Turner@westernalliancebank.com
IP Address: 38.29.192.249

Record Tracking

Status: Original
3/9/2023 12:26:34 PM
Holder: Kaeleen Weber-Turner
KWeber-Turner@westernalliancebank.com
Location: DocuSign

Signer Events	Signature	Timestamp
Kathleen P. Bloch kbloch@cytosorbents.com Chief Financial Officer CytoSorbents Corporation Security Level: Email, Account Authentication (None), Authentication	DocuSigned by: Kathleen P. Bloch E9CC9D995260496... Signature Adoption: Pre-selected Style Using IP Address: 69.248.11.122	Sent: 3/9/2023 12:28:56 PM Viewed: 3/9/2023 12:31:44 PM Signed: 3/9/2023 12:31:59 PM

Authentication Details
ID Check:
Transaction: 31020865162555
Result: passed
Vendor ID: LexisNexis
Type: iAuth
Recipient Name Provided by: Recipient
Information Provided for ID Check: Address, SSN9, SSN4, DOB
Performed: 3/9/2023 12:31:37 PM

Question Details:
passed person.known.single.fake
passed vehicle.historical.association.real
passed county.lived.single.real
passed property.city.real
passed corporate.association.real
passed corporate.association.real

Electronic Record and Signature Disclosure:
Accepted: 3/9/2023 12:31:44 PM
ID: 4b9aa82b-a392-4988-94e4-e214206703b3

Christian Ebert christian.ebert@bridgebank.com Vice President Security Level: Email, Account Authentication (None)	DocuSigned by: Christian Ebert 8E5B2B6D8D0449F... Signature Adoption: Pre-selected Style Using IP Address: 38.29.192.249	Sent: 3/9/2023 12:32:00 PM Viewed: 3/9/2023 12:33:12 PM Signed: 3/9/2023 12:33:22 PM

Electronic Record and Signature Disclosure:
Accepted: 3/9/2023 12:33:12 PM
ID: fcef229f-aa11-4f8d-8f7b-66cba39cb1ba

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	3/9/2023 12:28:56 PM
Certified Delivered	Security Checked	3/9/2023 12:33:12 PM
Signing Complete	Security Checked	3/9/2023 12:33:22 PM
Completed	Security Checked	3/9/2023 12:33:22 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

ELECTRONIC COMMUNICATIONS, RECORD AND SIGNATURES

You agree that Western Alliance Bank ("we," "us," "our," or similar terms) may use electronic communications to enter into agreement and contracts between ourselves and you and otherwise to establish terms and conditions for products and services you receive from or through us. Electronic agreements may be provided to you though such things as hyperlinks or "click-through" agreements on our web site. Your consent to or agreement with the electronic communication in these circumstances may occur by your clicking "agreed" or similar terms, or by your subsequent use of a product or service, or otherwise as may be specified in the communication or as provided by law (subject to any limitations set forth in the communication). Your signature and agreement may be obtained by us electronically and includes mouse clicks, key strokes, your use of passwords or other authentication systems, or as is otherwise set forth in the particular electronic communication.

You agree not to contest the authorization for, or validity or enforceability of, our electronic records and documents, or the admissibility of copies thereof, under any applicable law related to whether certain agreements, files or records are to be in writing or signed by the party to be bound thereby. Records and electronically "signed" documents, if introduced as evidence on paper in any judicial or other proceedings, will be admissible to the same extent and under the same conditions as other documentary business records. Upon our request, you agree to manually sign or place your signature on any paper original of any record or "signed" document which we provide to you containing your purported signature.

If you choose not to agree to these terms, it will not limit our ability to otherwise communicate with you electronically, to the extent not prohibited by applicable law. However, it may slow the speed at which we can complete certain steps and complete transactions with you.

We reserve the right, from time to time, to deliver one or more communications in paper form instead of electronic form by mailing or emailing a communication to the last known mailing or email address on our records for you. In the event that we do so, we may continue to provide communications to you in electronic form.

If you download or print any confidential materials, be sure that you store them in a secure environment, just as you would paper-based bank records.

Getting paper copies

You may obtain paper copies of any of the communications the Bank provides to you electronically by sending your written request to **Western Alliance Bank, Atten: Treasury Management Support, One East Washington Street, Suite 1400, Phoenix, AZ 85004**. If you request a paper-based copy, the Bank will provide the first copy to you free of any Bank fees or charges. Although we do not currently impose a fee or other charge for additional paper copies of electronic communications, we reserve the right to impose a fee or charge in the future and to change such fee at any time.

Required hardware and software

In order for you to access and retain the electronic communications, you will need a computer with sufficient memory to store electronic records as well as a working connection to the internet. The requirements are as follows:

Operating System	Microsoft Internet Explorer	Apple Safari®	Mozilla Firefox®
Windows Vista®	9.0	4.0, 5.0	33.0, 34.0
Windows 7	10.0, 11.0	N/A	33.0, 34.0

Windows 8	10.0	N/A	33.0, 34.0
Windows 8.1	11.0	N/A	33.0, 34.0
Mac OS X 10.9 (Maverick™)	N/A	6.01	33.0, 34.0

Hardware:	**Browser configured to support:**
• 1 GHz Celeron processor	• 128-bit encryption
• 1024x768 SVGA resolution at 256 colors	• JavaScript
• 500 MB RAM	• Cookies
• 128 Kbps (slowest DSL) or better	• Cascading Style Sheets
	• Browser page cache should be set to get a new version every visit to the page

In addition, you will need to have Adobe® Reader installed on your device to be able to view and/or save the electronic documents.

Access, Retention and Agreement Acknowledgement

By checking the 'I Agree' box, I confirm and acknowledge each of the following:

- I can access and read this ELECTRONIC COMMUNICATIONS, RECORDS AND SIGNATURES document;
- I can print or electronically store and save this document, for future reference and access; and
- I agree to all of the terms of this ELECTRONIC COMMUNICATIONS, RECORDS AND SIGNATURES document.

Western Alliance Bank. Member FDIC.

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 France SAS	France
CytoSorbents UK Limited***	United Kingdom

*Wholly-owned subsidiary of CytoSorbents Corporation

**Wholly-owned subsidiary of CytoSorbents Europe GmbH

***Wholly-owned 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 report dated March 9, 2023 relating to the consolidated financial statements of CytoSorbents Corporation (the "Company") as of December 31, 2022 and 2021 and for each of the three years in the period ended December 31, 2022 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, 2023

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, 2023

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, 2023

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, 2022 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, 2023

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, 2022 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, 2023

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.