Cytosorbents Corp
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PROSPECTUS SUPPLEMENT
(To Prospectus dated July 29, 2015)

68,791 Shares of Common Stock

This prospectus supplement relates to the issuance by us of 68,791 shares of our common stock to Western Alliance Bancorporation, a Delaware corporation (NYSE: WAL) (Western Alliance), in consideration for certain outstanding obligations as described herein.

On June 30, 2016, we, along with our wholly-owned subsidiary, CytoSorbents Medical, Inc., entered into a Loan and Security Agreement with Western Alliance Bank, an Arizona corporation and subsidiary of Western Alliance (the Bank). In connection therewith, we executed a Success Fee Letter in favor of the Bank (the Success Fee Letter). Under the Success Fee Letter, we agreed to pay the Bank a success fee equal to 6.37% of the total amount of the term loans funded by the Bank under the Loan and Security Agreement (the Success Fee) upon the first Liquidity Event (as defined in the Success Fee Letter) to occur after the date of the Success Fee Letter.

On May 17, 2018, the Success Fee became due and payable, and, on May 18, 2018, the Bank assigned all of its rights and obligations under the Success Fee Letter, including its right to receive payment of the Success Fee, to Western Alliance for no consideration.

As permitted under the Success Fee Letter, we have elected to issue 68,791 shares of our common stock to Western Alliance in lieu of paying the Success Fee in cash. The number of shares to be issued was calculated, in accordance with the terms of the Success Fee Letter, by dividing $637,000, the aggregate amount payable by us in respect of the Success Fee, by $9.26, the volume weighted average price per share of our common stock for the five successive business days commencing on May 11, 2018 and ending on May 17, 2018. We expect to issue the shares to Western Alliance on or about May 22, 2018. Following such issuance, we will have no further obligations under the Success Fee Letter. We will not receive any proceeds from the issuance of the shares.

Our common stock is listed on the Nasdaq Capital Market under the symbol CTSO. The last reported sale price of our common stock on the Nasdaq Capital Market on May 21, 2018 was $10.55 per share.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-11 of this prospectus supplement and page 10 of the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to

the contrary is a criminal offense.

The date of this prospectus supplement is May 22, 2018

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You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with different information, and we do not take any responsibility for, and can provide no assurance as to the reliability of, any information that others may provide you. We are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should not assume that the information contained in this prospectus supplement or the accompanying prospectus is accurate on any date other than the date set forth on the front of the document or that any information we have incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate on any date other than the date of the applicable document

incorporated by reference.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we have filed with the Securities and Exchange Commission (the SEC) using a shelf registration process under the Securities Act of 1933, as amended (the Securities Act).

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of our common stock and adds to and updates the information contained in the accompanying prospectus. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus, you should rely on the information in this prospectus supplement.

This prospectus supplement and the accompanying prospectus contain summaries of certain provisions contained in some of the documents described herein and therein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of the documents referred to herein have been filed, or will be filed or incorporated by reference as exhibits to the registration statement, and you may obtain copies of those documents as described below under Where You Can Find More Information and Incorporation of Certain Information by Reference.

This prospectus includes our trademarks and trade names, such as CytoSorb®, BetaSorb™, HemoDefend™ and VetResQ™, which are protected under applicable intellectual property laws and are the property of CytoSorbents Corporation and its subsidiaries. This prospectus 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 prospectus 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.

Unless the context otherwise requires, references in this prospectus to we, us, our, or the Company refer to CytoSorbents Corporation, a Delaware corporation, and its subsidiaries.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in, or incorporated by reference into, this prospectus supplement or the accompanying prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should carefully read this entire prospectus supplement and the accompanying prospectus, including each of the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, before making an investment decision.

We are a leader in critical care immunotherapy, investigating and commercializing our CytoSorb blood purification technology to reduce deadly uncontrolled inflammation in hospitalized patients around the world, with the goal of preventing or treating multiple organ failure in life-threatening illnesses and cardiac surgery. Organ failure is the cause of nearly half of all deaths in the intensive care unit (ICU), with little to improve clinical outcome. CytoSorb, our flagship product, is approved in the European Union (EU) as a safe and effective extracorporeal cytokine filter and is designed to reduce the cytokine storm that could otherwise cause massive inflammation, organ failure and death in common critical illnesses such as sepsis, burn injury, trauma, lung injury, and pancreatitis. These are conditions where the mortality is extremely high, yet no effective treatments exist. In addition, CytoSorb can be used in other inflammatory conditions such as cardiac surgery, autoimmune disease flares, and potentially for cancer, cytokine release syndrome in cancer immunotherapy, and cancer cachexia, a common syndrome that affects cancer patients, where cytokines play a major role in the cause of inflammation. CytoSorb has been used globally in more than 40,000 human treatments to date. Our purification technologies are based on biocompatible, highly porous polymer beads that can actively remove toxic substances from blood and other bodily fluids by pore capture and surface adsorption. We have numerous products under development based upon this unique blood purification technology. As of March 31, 2018, the technology is protected by 15 issued and 2 allowed but not yet issued U.S. patents, multiple issued foreign patents and multiple applications pending both in the U.S. and internationally. Our intellectual property consist of composition of matter, materials, methods of production, systems incorporating the technology and multiple medical uses with expiration dates ranging from 2 to 15 years.

In March 2011, CytoSorb, as an extracorporeal cytokine filter indicated for use in clinical situations where cytokines are elevated, was CE marked in the EU, 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 all 28 countries of the EU. In addition, many countries outside the EU accept CE mark approval for medical devices, but may also require registration with or without additional clinical studies. The broad approved indication enables CytoSorb to be used on-label in diseases where cytokines are elevated including, but not limited to, critical illnesses such as those mentioned above, autoimmune disease flares, cancer cachexia, and many other conditions where cytokine-induced inflammation plays a detrimental role.

Cytokines are small proteins that normally stimulate and regulate the immune response. However, in certain diseases, particularly life-threatening conditions commonly seen in the ICU, such as sepsis and infection, trauma, acute respiratory distress syndrome (ARDS), severe burn injury, liver failure, and acute pancreatitis, cytokines are often

produced in vast excess a condition often called cytokine storm. Left unchecked, this cytokine storm can lead to a severe maladaptive SIRS that can then cause cell death, multiple organ dysfunction syndrome, and multiple organ failure. Failure of vital organs such as the heart, lungs, and kidneys, accounts for nearly half of all deaths in the ICU, despite the wide availability of supportive care therapies, or life support, such as dialysis, mechanical ventilation, extracorporeal membrane oxygenation,

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and vasopressors. By replacing the function of failed organs, these supportive care therapies can initially help to keep patients alive, but do not help patients recover faster, and in many cases can increase the risk of dangerous complications. Unlike these supportive care therapies, the goal of the CytoSorb cytokine filter is to proactively prevent or treat organ failure by reducing cytokine storm and reducing the maladaptive SIRS response. In doing so, CytoSorb targets the reduction in the severity of patient illness and the need for intensive care, while potentially improving clinical outcome and saving healthcare costs.

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

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

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

In late June 2012, following the establishment of our wholly owned European subsidiary, CytoSorbents Europe GmbH, we began the commercial launch of CytoSorb in Germany with the hiring of Dr. Christian Steiner as Vice President of Sales and Marketing and three additional sales representatives. The fourth quarter of 2012 represented the first full quarter of direct sales with the full sales team in place. During this period, we expanded our direct sales efforts to include both Austria and Switzerland. At the end of 2017, we had hundreds of KOLs in our commercialized territories worldwide in critical care, cardiac surgery, and blood purification, who were either using CytoSorb or supporting its use in clinical practice or clinical trials.

In March 2016, we established CytoSorbents Switzerland GmbH, a wholly-owned subsidiary of CytoSorbents Europe GmbH, to conduct marketing and direct sales in Switzerland. This subsidiary began operations during the second quarter of 2016. In 2017, we further expanded our direct sales efforts into Belgium and Luxemburg. As of May 1, 2018, our European sales, marketing and clinical support team included 19 direct sales people, one contract sales person, and 15 sales support staff.

We have complemented our direct sales efforts with sales to distributors and/or corporate partners. In 2013, we reached agreements with distributors in the United Kingdom, Ireland, Turkey, Russia and the Netherlands. In 2014, we announced distribution of CytoSorb in the Middle East, including Saudi Arabia, the United Arab Emirates, Kuwait, Qatar, Bahrain, and Oman (the Gulf Cooperative Council) and Yemen, Iraq, and Jordan through an exclusive agreement with Techno Orbits. In December 2014, we entered into an exclusive agreement with Smart Medical Solutions S.R.L., to distribute CytoSorb for critical care applications in Romania and the neighboring Republic of Moldova. In 2015, we announced exclusive distribution agreements with Aferetica SRL to distribute CytoSorb in Italy, AlphaMedix Ltd. to distribute CytoSorb in Israel, TekMed Pty Ltd. to distribute CytoSorb in Australia and New Zealand, and Hoang Long Pharma to distribute CytoSorb in Vietnam. In June 2016, we announced an exclusive distribution agreement with Palex Medical SA to distribute CytoSorb in Spain and Portugal. In September 2016, we

announced an exclusive agreement with Armaghan Salamat Kish Group (Arsak) to distribute CytoSorb in Iran. In October 2016, we announced an exclusive agreement with Foxx Medical Chile SpA to distribute CytoSorb in Chile. In July 2017, we announced an exclusive agreement with Droguería, Ramón, González, Revilla (DRGR) S.A. to distribute CytoSorb in Panama.

We have been working to expand the number and scope of our strategic partnerships. In September 2013, we entered into a strategic partnership with Biocon Ltd. (Biocon), India s largest biopharmaceuticals

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company, with an initial distribution agreement for India and select emerging markets, under which Biocon has the exclusive commercialization rights for CytoSorb initially focused on sepsis. In October 2014, the partnership with Biocon was expanded to include all critical care applications and cardiac surgery. In addition, Biocon committed to higher annual minimum purchases of CytoSorb to maintain distribution exclusivity and committed to conduct and publish results from multiple investigator initiated studies and patient case studies. In December 2017, the Biocon partnership was further expanded to include exclusive distribution of CytoSorb in Malaysia. Under the terms of the agreement, Biocon has committed to minimum annual purchases in Malaysia to maintain exclusivity this territory. In addition, the term of the original agreement was extended to December 2022

In December 2014, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & Co KGaA (Fresenius) to commercialize the CytoSorb therapy. Under the terms of this agreement, Fresenius has exclusive rights to distribute CytoSorb for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership 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. Fresenius launched the product in these six countries in May 2016. In January 2017, the Fresenius partnership was expanded. The terms of the revised three-year agreement extend 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. In addition, we have entered into a new comprehensive co-marketing agreement with Fresenius. Under the terms of the agreement, CytoSorbents and Fresenius will jointly market CytoSorb to Fresenius critical care customer base in all countries where CytoSorb is being actively commercialized. CytoSorb will continue to be sold by our direct sales force or through our international network of distributors and partners, while Fresenius will sell all ancillary products to their customers. Fresenius will also provide a written endorsement 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 late 2017 and is continuing, with implementation of the co-marketing program in additional countries planned for the future.

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

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

Overall, we have established either direct sales or distribution (via distributors or strategic partners) of CytoSorb in 45 countries worldwide. Registration of CytoSorb is typically required in each of these countries prior to active commercialization. With CE mark approval, this can be typically achieved within several months in EU countries. Outside of the EU, the process is more variable and can take several months to more than a year due to different requirements for documentation and clinical data. Variability in the timing of registration affects the initiation of active commercialization in these countries, which affects the timing of expected CytoSorb sales. We actively support all of our distributors and strategic partners in the product registration process. We cannot generally predict the timing of these registrations, and there can be no guarantee that we will ultimately achieve registration in countries where we

have established distribution. For example, in August 2014 we announced exclusive distribution of CytoSorb in Taiwan with Hemoscien Corporation (Hemoscien). However, in March 2015, due to the complexity we encountered with Taiwanese product registration, we elected to terminate our agreement with Hemoscien. Outside of the EU, CytoSorb is actively being commercialized in Turkey, India, Australia, New Zealand, Russia, South Africa, Serbia, Norway, Vietnam, Chile, Iceland, Saudi Arabia and Panama. We cannot guarantee that we will generate

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meaningful sales in the countries where we have established registration, due to other factors such as market adoption and reimbursement. We are currently actively evaluating other potential distributor and strategic partner networks in other major countries that accept CE mark approval.

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

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

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

In addition, we now have more than 60 investigator-initiated studies planned, enrolling or completed in Germany, Austria, Switzerland, the Netherlands, Hungary, the United Kingdom, India, and the U.S. Approximately 20 of these studies are currently enrolling patients. Others have been completed. These trials, which are funded and supported by well-known university hospitals and KOLs, are the equivalent of Phase II clinical studies. They have provided and will continue to provide invaluable information regarding the success of the device in the treatment of sepsis, cardiac surgery, trauma, and many other indications, and if successful, will be integral in helping to drive additional usage and adoption of CytoSorb.

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

In February 2015, the U.S. Food and Drug Administration (the FDA) approved our Investigational Device Exemption (IDE) application to commence a planned U.S. cardiac surgery feasibility study called REFRESH I (REduction of FREe Hemoglobin) amongst 20 patients and three U.S. clinical sites. The FDA subsequently approved an amendment to the protocol, expanding the trial to be a 40 patient randomized

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controlled study (20 treatment, 20 control) in eight clinical centers. REFRESH I represented the first part of a larger clinical trial strategy intended to support the approval of CytoSorb in the U.S. for intra-operative use during cardiac surgery.

The REFRESH I study was designed to evaluate the safety and feasibility of CytoSorb when used intra-operatively in a heart-lung machine to reduce plasma free hemoglobin (pfHb) and cytokines in patients undergoing complex cardiac surgery. The study was not powered to measure effect on clinical outcomes. The length, complexity and invasiveness of these procedures cause hemolysis and inflammation, leading to high levels of plasma free hemoglobin, cytokines, activated complement, and other substances. These inflammatory mediators are correlated with the incidence of serious post-operative complications such as kidney injury, renal failure and other organ dysfunction. The goal of CytoSorb is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications. Enrollment was completed with 46 patients. A total of 38 patients were evaluable for pfHb and completed all aspects of the study.

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

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

In December 2017, the FDA approved our IDE application for our REFRESH 2-AKI study. The REFRESH 2-AKI study is a pivotal trial designed to provide the key safety and efficacy data needed to support United States regulatory approval for the use of CytoSorb in cardiac surgery, which we are planning to pursue via the premarket approval pathway. The IDE approval allows us to aggressively move forward with our clinical trial sites to complete the final steps prior to the official start of the study. The REFRESH 2-AKI pivotal study will assess the effectiveness of intraoperative CytoSorb blood treatment on postoperative acute kidney injury (AKI), the primary endpoint of the study and one of the most common adverse events in patients undergoing complex cardiac surgery. The REFRESH 2-AKI trial is a randomized, controlled, multi-center, clinical trial designed to evaluate intraoperative CytoSorb use as a therapy to reduce the incidence and severity of AKI, as measured by Kidney Disease Improving Global Outcomes (KDIGO) criteria, following complex cardiac surgery. The trial will enroll up to 400 patients at increased risk of cardiovascular surgery associated AKI, undergoing elective, non-emergent open heart surgery for either valve replacement, or aortic reconstruction with hypothermic cardiac arrest. We have initiated discussions with previous trial sites that participated in the REFRESH I study that are familiar with the CytoSorb device and intraoperative use during CPB. We believe using sites that previously participated in REFRESH I will accelerate the process of site startup and launch of REFRESH 2. In April 2018, we announced first patient enrollment into the pivotal U.S. REFRESH 2-AKI trial. We are ramping the trial and working to add additional centers experienced in the conduct of clinical trials in complex cardiac surgery. We anticipate that this study will take at least two years to complete, and could take longer if enrollment challenges or other factors causing delays are encountered.

The German government is funding a 250 patient, multi-center randomized, controlled study (REMOVE) using CytoSorb during valve replacement open heart surgery in patients with infective endocarditis. The study enrolled its first patient in January 2018.

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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 (DARPA), the U.S. Army, U.S. Special Operations Command, and others.

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

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

HemoDefend is a development-stage blood purification technology platform designed to safeguard and protect the blood supply. Continued development of the product is being supported through a $1.5 Phase II SBIR contract funded by the National Heart, Lung and Blood Institute, a division of the NIH, and U.S. Special Operations Command. We seek to license the HemoDefend platform and have not yet received regulatory approval in any markets. HemoDefend consists of a mixture of proprietary porous polymer beads that target the removal of contaminants that can cause transfusion reactions or cause disease in patients receiving the tens of millions of transfused blood products administered worldwide each year. These contaminants include, for example, foreign antibodies, antigens, cytokines, free hemoglobin, bioactive lipids, toxins, drugs, and other inflammatory mediators that either were from the donor or accumulated during blood storage. The goal of the HemoDefend technology is to reduce these contaminants in transfused blood products to reduce transfusion reactions, to keep new blood fresh, and to improve the quality and safety of blood.

The HemoDefend beads are intended to be used in multiple configurations, including as a common in-line filter between the blood bag and the patient as well as a patent-pending Beads in a Bag treatment configuration, where the beads are placed directly into a blood storage bag. Once blood is put into this bag, the beads begin to automatically

remove contaminants from the blood, and are designed to continue purifying blood throughout the entire blood storage period. The use of neutrally buoyant beads eliminates the need for mixing and is compatible with current blood storage conditions. Integrated filters in the bag prevent beads from leaving the bag during the transfusion process. The base polymer meets ISO 10993 standards for

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biocompatibility, hemocompatibility, genotoxicity, cytotoxicity, acute sensitivity and complement activation and can therefore directly contact blood for extended periods of time. In addition, the beads are inert and stable at a wide range of temperatures, and do not contain any antibodies, biologics, ligands, or drugs. Because of this, the beads have a very long shelf life that is consistent with blood storage bag manufacturing standards. No special equipment or handling is required, making it well-suited for mainstream and military applications, as well as for use in less developed countries that are not well-equipped to test and process blood products.

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

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

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

Our BetaSorb device is intended to remove beta2, -microglobulin and other mid-molecular weight toxins from the blood of patients suffering from chronic kidney failure who rely on long term dialysis therapy to sustain their life. Standard high-flux hemodialysis is very effective in removing small uremic toxins, but much less effective in removing these mid-molecular weight toxins that functional kidneys normally remove. BetaSorb utilizes an adsorbent polymer packed into a similarly shaped and constructed cartridge as utilized for our CytoSorb product, although the polymers used in the two devices are physically different, with one optimized for short-term critical care use and the

other specifically designed for the needs of long-term chronic usage. The BetaSorb device also incorporates industry standard connectors at either end of the device, which connect directly into the extra-corporeal circuit (bloodlines) in series with a dialyzer. To date, we have manufactured the BetaSorb device on a limited basis for testing purposes, including for use in clinical studies.

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

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

Corporate History

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

On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. As a result of this reverse stock split, shares of our common stock outstanding were reduced by approximately 96%. 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 by merging with and into our recently formed, wholly-owned Delaware subsidiary. At the effective time of the merger, (i) we merged with and into our Delaware subsidiary, (ii) our separate corporate existence in Nevada ceased to exist, (iii) the Delaware subsidiary became the surviving corporation, (iv) the certificate of incorporation, as amended and restated, and the bylaws of the Delaware subsidiary became our certificate of incorporation and bylaws, and (v) each share of our common stock outstanding immediately prior to the effective time was converted into one fully-paid and non-assessable share of our common stock as a Delaware corporation. The reverse stock split, the merger and the Agreement and Plan of Merger were approved by our Board of Directors and stockholders representing a majority of our then-outstanding common stock.

All references to us, we, or the Company, on or after December 3, 2014, refer to CytoSorbents Corporation, a Delaware corporation.

Our executive offices are located at 7 Deer Park Drive, Suite K, Monmouth Junction, New Jersey 08852, and our telephone number is (732) 329-8885. Our website address is *http://www.cytosorbents.com*. We have included our

website address as an inactive textual reference only. We 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 prospectus supplement or the accompanying prospectus.

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THE OFFERING

Common stock offered by us

68,791 shares of our common stock to be issued to Western Alliance in full satisfaction of our obligations under the Success Fee Letter.

Common stock to be outstanding after this offering

30,043,159 shares, based on 29,974,368 shares outstanding as of March 31, 2018, and excludes as of such date:

862,560 shares of our common stock issuable upon exercise of outstanding warrants;

3,996,142 shares of our common stock issuable upon exercise of outstanding stock options under our equity incentive plan, at a weighted average exercise price of $5.43 per share; and

165,805 shares of our common stock subject to vesting of performance stock units and restricted stock units.

Use of proceeds

We will not receive any proceeds from the issuance of the shares to Western Alliance.

Risk factors

Investing in our common stock involves a high degree of risk. See risk factors described under the caption Risk Factors in this prospectus supplement, as well as the other information set forth in this prospectus supplement and the accompanying prospectus, and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Nasdaq Capital Market symbol

CTSO.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information set forth in this prospectus supplement and the accompanying prospectus, and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, before deciding to purchase shares of our common stock. If any of the events, contingencies, circumstances or conditions described in the risks below actually occurs, our business, financial condition or results of operations could be seriously harmed. The trading price of our common stock could, in turn, decline and you could lose all or part of your investment.

Risks Related to our Business and our Industry

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

We have experienced substantial operating losses since inception. As of March 31, 2018, we had an accumulated deficit of approximately $155,295,000, which included net losses of approximately $2,982,000 and $1,525,000 for the three months ended March 31, 2018 and 2017, respectively. Due in part to these losses, our audited consolidated financial statements have been prepared assuming we will continue as a going concern, and the auditors report on those financial statements express substantial doubt about our ability to continue as a going concern. Our losses have resulted principally from costs incurred in the research and development of our polymer technology and general and administrative expenses. We intend to conduct significant additional research, development, and clinical study activities which, together with expenses incurred for the establishment of manufacturing arrangements and a marketing and distribution presence and other general and administrative expenses, are expected to result in continuing operating losses for the foreseeable future. The amount of future losses and when, if ever, we will achieve profitability are uncertain. Our ability to achieve profitability will depend, among other things, on continued adoption and usage of our products in the market, obtaining additional regulatory approvals in markets not covered by the CE mark, establishing sales and marketing arrangements with third parties, satisfactory reimbursement in key territories, and raising sufficient funds to finance our activities. No assurance can be given that our product development efforts will be successful, that our current CE mark will enable us to achieve profitability, that additional regulatory approvals in other countries will be obtained, that any of our products will be manufactured at a competitive cost and will be of acceptable quality, that reimbursement will be available or satisfactory, that we will be able to achieve profitability or that profitability, if achieved, can be sustained, or our ability to raise additional capital when needed or on terms acceptable to us. Our failure with respect to any or all of these matters would have a material adverse effect on our business, operating results, financial condition and prospects.

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

As of March 31, 2018, we had current assets of approximately $24,515,000, including cash on hand of approximately $21,090,000 and current liabilities of approximately $3,986,000. For the three months ended March 31, 2018, our cash burn was approximately $2,600,000. Our current and historical cash burn is not necessarily indicative of our future use of cash and cash equivalents.

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

- rate of sales growth and adoption of our products in the marketplace;
- product gross margin;
- continued progress and cost of our research and development programs;
- progress with pre-clinical studies and clinical studies;
- the time and costs involved in obtaining regulatory clearance in other countries and/or for other indications;