

Cytosorbents Corp
Form 424B5
May 22, 2018

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-205806**

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

TABLE OF CONTENTS

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

	Page
<u>About this Prospectus Supplement</u>	<u>S-1</u>
<u>Prospectus Supplement Summary</u>	<u>S-2</u>
<u>The Offering</u>	<u>S-10</u>
<u>Risk Factors</u>	<u>S-11</u>
<u>Special Note Regarding Forward-Looking Statements</u>	<u>S-23</u>
<u>Use of Proceeds</u>	<u>S-24</u>
<u>Plan of Distribution</u>	<u>S-25</u>
<u>Where You Can Find More Information</u>	<u>S-26</u>
<u>Incorporation of Certain Information by Reference</u>	<u>S-26</u>
<u>Legal Matters</u>	<u>S-27</u>
<u>Experts</u>	<u>S-27</u>

PROSPECTUS	Page
<u>About this Prospectus</u>	<u>1</u>
<u>About CytoSorbents Corporation</u>	<u>2</u>
<u>Risk Factors</u>	<u>10</u>
<u>Forward-Looking Statements</u>	<u>19</u>
<u>Use of Proceeds</u>	<u>20</u>
<u>Description of the Securities We May Offer</u>	<u>21</u>
<u>Description of Capital Stock</u>	<u>22</u>
<u>Description of Debt Securities</u>	<u>26</u>
<u>Description of Warrants</u>	<u>26</u>
<u>Description of Units</u>	<u>29</u>
<u>Legal Ownership of Securities</u>	<u>32</u>
<u>Selling Stockholder</u>	<u>35</u>
<u>Plan of Distribution</u>	<u>36</u>
<u>Where You Can Find More Information</u>	<u>39</u>
<u>Incorporation of Certain Documents by Reference</u>	<u>40</u>
<u>Legal Matters</u>	<u>41</u>
<u>Experts</u>	<u>41</u>

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.

S-i

TABLE OF CONTENTS

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®, BetaSM, HemoDefenTM and VetResTM, 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 TM, ® 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.

S-1

TABLE OF CONTENTS

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,

S-2

TABLE OF CONTENTS

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 Luxembourg. 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

Edgar Filing: Cytosorbents Corp - Form 424B5

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

S-3

TABLE OF CONTENTS

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

S-4

TABLE OF CONTENTS

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

S-5

TABLE OF CONTENTS

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.

S-6

TABLE OF CONTENTS

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

S-7

TABLE OF CONTENTS

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.

S-8

TABLE OF CONTENTS

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.

S-9

TABLE OF CONTENTS

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.

S-10

TABLE OF CONTENTS

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;

S-11

TABLE OF CONTENTS

costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims;
costs of developing sales, marketing and distribution channels;
market acceptance and reimbursement of our products; and
cost for training physicians and other health care personnel.

We have an effective shelf registration statement with the SEC which enables us to raise up to \$100 million in equity financing. We entered into a Controlled Equity Offering SM Sales Agreement (the Sales Agreement) with Cantor Fitzgerald & Co. in November 2015 for the offer and sale of up to an aggregate of \$25,000,000 of shares of our common stock. During the three months ended March 31, 2018, we sold a total of 782,328 shares of our common stock at an average price of \$7.97 per share, under the terms of the Sales Agreement, generating net proceeds of approximately \$6.0 million. From April 1, 2018 through May 2, 2018 we sold an additional 27,088 shares of our common stock at an average price of \$8.29 per share, generating net proceeds of approximately \$218,000.

On March 29, 2018, we entered into an Amended and Restated Loan and Security Agreement (the Restated Loan and Security Agreement) with the Bank, which amended and restated, in its entirety, the Loan and Security Agreement, dated as of June 30, 2016 (the Prior Loan and Security Agreement), previously in effect between us and the Bank. Under the Restated Loan and Security Agreement, the Bank agreed to loan us up to an aggregate of \$15 million, to be disbursed in two tranches: (1) one tranche of \$10 million, which was funded on the Closing Date (as defined in the Restated Loan and Security Agreement) and used to refinance our outstanding indebtedness under the Prior Loan and Security Agreement, and (2) a second tranche of \$5 million, which may be disbursed at our request prior to March 31, 2019, provided certain conditions are met.

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

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

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

We have historically been engaged primarily in research and development activities and have generated limited revenues to date. With the launch of our CytoSorb product in the EU and abroad, there can be no assurance that we will be able to successfully manage the balance of our research and development operations with our planned commercial enterprise. Potential investors should be aware of the problems, delays, expenses and difficulties frequently encountered by an enterprise in balancing development, which include unanticipated problems relating to testing, product registration, regulatory compliance and manufacturing, with commercialization, which includes problems with market adoption, reimbursement, marketing problems and additional costs. Our products and product candidates will require significant additional research and testing, and we will need to overcome significant regulatory burdens prior to commercialization in other countries, such as the U.S., and for ongoing compliance for our CE mark. We will also need to raise additional funds to complete additional clinical studies and obtain regulatory approvals in

other countries before we can begin selling our products in markets not covered by our CE mark. In addition, we may be required to spend significant funds on building out our commercial operations. There can be no assurance that after the expenditure of substantial funds and efforts, we will successfully develop and commercialize any products, generate any significant revenues or ever achieve and maintain a substantial level of sales of our products.

S-12

TABLE OF CONTENTS

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

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

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

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

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

If users of our products are unable to obtain adequate reimbursement from third-party payers, or if reimbursement is

As of May 2, 2018, we had 89 full-time employees and several temporary employees. Our success will depend to a significant degree upon the continued services of our key management team and advisors, including, Dr. Phillip P.

Chan, our Chief Executive Officer; Kathleen P. Bloch, our Chief Financial Officer; Vincent Capponi, our Chief Operating Officer, and Dr. Eric R. Mortensen, our Chief Medical Officer. Although these individuals have long-term employment and consulting agreements, there can be no assurance that key management personnel or other members of our management team and advisors will continue to provide services to us. In addition, our success will depend on our ability to attract and retain other highly skilled personnel. We may be unable to recruit such personnel on a timely basis, if at all. Management and other employees may voluntarily terminate their employment with us at any time. The

loss of services of key personnel, or the inability to attract and retain additional qualified personnel, could result in delays in development or approval of our products, loss of sales and diversion of management resources.

S-13

TABLE OF CONTENTS

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

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

the receipt of regulatory clearance of marketing claims for the uses that we are developing;
the establishment and demonstration of the advantages, safety and efficacy of our polymer technology;
pricing and reimbursement policies of government and third-party payers such as insurance companies,
health maintenance organizations and other health plan administrators;

competition;

our ability to attract corporate partners, including medical device companies, to assist in commercializing our products; and

our ability to effectively market our products.

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

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

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

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable

Acceptance of our medical devices in the marketplace is uncertain, and failure to achieve market acceptance will pr

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

TABLE OF CONTENTS

meaningfully protect our products or product candidates, effectively prevent competitors and third parties from commercializing competitive products or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative products in a non-infringing manner.

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

We cannot be certain that our patents and patent rights will be effective in protecting our products, product candidates and technologies. In addition, certain of our existing patents expire between 2020 and 2033. Failure to protect such assets may have a material adverse effect on our business, operations, financial condition and prospects.

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

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

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

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

Several years ago we engaged in discussions with the Dow Chemical Company, which had indicated a strong interest in being our polymer manufacturer. After a Dow representative on our Advisory Board resigned, Dow filed and received several patents naming our former Advisory Board member as an inventor. In management's view, the Dow patents improperly incorporate our technology and should not have been granted to Dow. The existence of these Dow patents could result in a potential dispute with Dow in the future. In the event such a dispute arises, we may be forced

We may face litigation from third parties claiming that our products infringe on their intellectual property rights, or se

to spend significant time and resources to defending our position. There can be no assurances that such efforts will be successful and not have a material adverse effect on our business, operating results, financial condition and prospects.

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

We rely on patent, trademark, trade secret and other intellectual property protection in the discovery, development, manufacturing, and sale of our products and product candidates. In particular, patent protection is important in the development and eventual commercialization of our products and product candidates.

S-15

TABLE OF CONTENTS

Patents covering our products and product candidates normally provide market exclusivity, which is important in order for our products and product candidates to become profitable.

Certain of our patents expire between 2020 and 2033. While we are seeking additional patent coverage which may protect the technology underlying these patents, there can be no assurances that such additional patent protection will be granted, or if granted, that these patents will not be infringed upon or otherwise held enforceable. Even if we are successful in obtaining a patent, patents have a limited lifespan. In the United States, the natural expiration of a utility patent typically is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our products and product candidates, we may be open to competition from generic versions of such methods and devices.

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

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

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

We have commenced the process of seeking regulatory approvals of our products and product candidates, but the

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

To date, we have conducted limited clinical studies on our CytoSorb product. There can be no assurance that we will successfully complete additional clinical studies necessary to receive additional regulatory approvals in markets not covered by the CE mark. While studies conducted by us and others have produced results we believe to be encouraging and indicative of the potential efficacy of our products and technology, data already obtained, or in the future obtained, from pre-clinical studies and clinical studies do not necessarily predict the results that will be obtained from later pre-clinical studies and clinical studies. Moreover, pre-clinical and clinical data are susceptible to varying interpretations, which could delay, limit or prevent additional regulatory approvals. A number of companies in the medical device and pharmaceutical industries have suffered significant setbacks in advanced clinical studies, even after promising results in earlier studies. The failure to adequately demonstrate the safety and effectiveness of an intended product under development could delay or prevent regulatory clearance of the device, resulting in delays to

S-16

TABLE OF CONTENTS

commercialization, and could materially harm our business. Even though we have received approval to apply the CE mark to our CytoSorb device as a cytokine filter, there can be no assurance that we will be able to receive approval for other potential applications of CytoSorb, or that we will receive regulatory clearance from other targeted regions or countries.

We rely extensively on research and testing facilities at various universities and institutions, which could adversely affect us should we lose access to those facilities. At the same time, relationships with these individuals and entities are the subject of heightened scrutiny and may present the potential for future healthcare enforcement risk.

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

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

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

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

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

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

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

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.

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

S-17

TABLE OF CONTENTS

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

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

We expect to enter into agreements with third parties for the commercial marketing, and distribution of our products.

There can be no assurance that parties we may engage to market and distribute our products will:

satisfy their financial or contractual obligations to us;

adequately market our products; or

not offer, design, manufacture or promote competing products.

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

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

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

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

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

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

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

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

For the three months ended March 31, 2018, we derived a majority of our net product sales from sales in Germany. Despite modest European and global growth, there are many economic and political issues that could negatively impact the health of Germany's economy, the broader EU economy, and the world economy

TABLE OF CONTENTS

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

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

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

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

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

Our business could be harmed by adverse economic conditions in Germany, our primary geographical market, or by

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

S-19

TABLE OF CONTENTS

products must be made in compliance with these laws, tariffs, and regulations. If we fail to comply with these laws, tariffs, and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

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

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

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

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

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

Cyberattacks and other security breaches could compromise our proprietary and confidential information which could

Risks Connected to Our Securities

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

On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. Immediately after the reverse stock split, we changed our state of incorporation from the State of Nevada to the State of Delaware pursuant to an Agreement and Plan of Merger, dated December 3, 2014, pursuant to

S-20

TABLE OF CONTENTS

which we merged with and into our recently formed, wholly-owned Delaware subsidiary. On December 17, 2014, we received approval for up-listing to the Nasdaq Capital Market (Nasdaq), and our common stock began trading on Nasdaq on December 23, 2014 under the symbol CTSO. Our common stock closed as high as \$7.05 and as low as \$6.55 per share between January 1, 2018 and March 31, 2018 on Nasdaq. On May 18, 2018, the closing price of our common stock, as reported on Nasdaq, was \$10.55. Historically, medical device company securities such as our common stock have experienced extreme price fluctuations. Some of the factors leading to this volatility include, but are not limited to:

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

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

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

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

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, pursuant to which we merged with and into our recently formed, wholly-owned Delaware subsidiary. Pursuant to the Agreement and Plan of Merger effecting the merger, we adopted the certificate of incorporation, as amended and restated, and bylaws of our Delaware subsidiary as our certificate of incorporation and bylaws at effective time of the merger. As a result, our certificate of incorporation, as amended and restated, authorizes the issuance of up to 5,000,000 shares of blank check preferred stock, with such designation rights and preferences as may be determined from time to time by the Board of Directors.

Currently, our certificate of incorporation, as amended and restated, which was effective December 3, 2014, authorizes the issuance of up to 50,000,000 shares of common stock, of which 19,951,207 shares remain available for issuance as of May 21, 2018 and may be issued by us without stockholder approval.

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

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

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

S-21

TABLE OF CONTENTS

establish advance notice requirements for nominations for election to the Board of Directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

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

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

Our common stock is thinly traded on Nasdaq 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.

In November 2015, we entered the Sales Agreement with Cantor Fitzgerald & Co. to offer shares of our common stock from time to time through at-the-market offerings, pursuant to which we offer and sell shares of our common stock for an aggregate offering price of up to \$25 million. We are not obligated to make or continue to make any sale of shares of our common stock under the at-the-market offerings. 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.

TABLE OF CONTENTS

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained in, or incorporated by reference into, this prospectus supplement or the accompanying prospectus constitute forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). Forward-looking statements frequently, but not always, use the words may, estimate, projects, intends, plans, believes, anticipates or similar words. Forward-looking statements include all statements involving matters that are not historical facts and include, without limitation, statements concerning our business strategy, outlook, objectives, future milestones, plans, intentions, goals, and future financial condition, including the period of time for which our existing resources will enable us to fund our operations.

All forward-looking statements are based on management's present expectations of future events and are subject to a number of assumptions that could cause actual results to differ materially from those described in the forward-looking statements. Forward-looking statements should be evaluated together with the many risks and uncertainties that affect our business and market, including those risks and uncertainties discussed in the following documents:

the risk factors described in this prospectus supplement under the caption Risk Factors ;
our most recent annual report on Form 10-K;
our quarterly reports on Form 10-Q; and
our other SEC filings.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in, or incorporated by reference into, this prospectus supplement or the accompanying prospectus might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only of the date the statement is made. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements after the date on which the statement is made, whether as a result of new information, future events or otherwise, except as may be required by applicable law. All subsequent forward-looking statements attributable to us are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

S-23

TABLE OF CONTENTS

USE OF PROCEEDS

The shares are being issued to Western Alliance in full satisfaction of our obligations under the Success Fee Letter. We will not receive any proceeds from the issuance of the shares. We will bear all costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus supplement, including, but not limited to, all registration and filing fees and fees and expenses of our counsel and accountants.

S-24

TABLE OF CONTENTS

PLAN OF DISTRIBUTION

The shares offered hereby will be issued to Western Alliance in full satisfaction of our obligations under the Success Fee Letter, and no broker, dealer or underwriter has been engaged in connection with the issuance. Western Alliance will act independently of us in making decisions with respect to the timing, manner and size of each resale of such shares.

S-25

TABLE OF CONTENTS

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other documents with the SEC under the Exchange Act. You may read and copy any materials that we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800 SEC-0330. Our reports, proxy statements and other documents filed electronically with the SEC are available at the website maintained by the SEC at <http://www.sec.gov>. You can read and copy reports and other information concerning us at the offices of the Financial Industry Regulatory Authority, located at 1735 K Street, Washington D.C. 20006. We also make available free of charge on or through our Internet website, <http://www.cytosorbents.com>, our annual, quarterly and current reports, and, if applicable, amendments to those reports, filed or furnished pursuant to Section 13(a) of the Exchange Act, as soon as reasonably practicable after we electronically file such reports with the SEC. Information on our website is not a part of this prospectus supplement or the accompanying prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus supplement information that we file with the SEC, which means we can disclose important information to you by referring you to other documents that contain that information. The information we incorporate by reference is considered to be part of this prospectus supplement and information we later file with the SEC will automatically update and supersede the information in this prospectus supplement. The following documents filed by us with the SEC pursuant to Section 13 of the Exchange Act and any future filings under Sections 13(a), 13(c), 14 or 15 (d) of the Exchange Act, except for information furnished under Item 2.02 or 7.01 of current report on Form 8 K, or exhibits related thereto, made after the date of the initial registration statement and prior to effectiveness of the registration statement and before the termination of the offering are incorporated by reference herein:

our annual report on Form 10-K for the fiscal year ended December 31, 2017, filed on March 8, 2018;
the information specifically incorporated by reference into our annual report from our definitive proxy statement on Schedule 14A, filed on April 25, 2018;

our quarterly report on Form 10-K for the quarter ended March 31, 2018, filed on May 8, 2018;
our current reports on Form 8-K, filed on March 5, 2018, March 20, 2018 and April 4, 2018; and
our description of our common stock contained in the Registration Statement on Form 8-A12B filed with the Securities and Exchange Commission on December 17, 2014.

Any statement contained in this prospectus supplement, the accompanying prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement or the accompanying prospectus will be deemed to be modified or superseded to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We will provide, upon written or oral request, at no cost, to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus. You may request a copy of these filings by writing us at CytoSorbents Corporation, 7 Deer Park Drive, Suite K, Monmouth Junction, New Jersey 08852. Our telephone

number is (732) 329-8885. A copy of all documents that are incorporated by reference into this prospectus can also be found on our website by accessing <http://www.cytosorbents.com>.

S-26

TABLE OF CONTENTS

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by DLA Piper LLP (US), Short Hills, New Jersey.

EXPERTS

The consolidated financial statements of CytoSorbents Corporation appearing in CytoSorbents Corporation's annual report on Form 10-K for the year ended December 31, 2017, and the effectiveness of CytoSorbents Corporation's internal control over financial reporting as of December 31, 2017 have been audited by WithumSmith+Brown, PC, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

S-27

TABLE OF CONTENTS

Prospectus

\$100,000,000

**Common Stock, Preferred Stock,
Debt Securities, Warrants and Units**

2,500,000

**Shares of Common Stock
Offered by the Selling Stockholder**

CytoSorbents Corporation may offer from time to time in one or more offerings up to an aggregate of \$100,000,000 of the common stock, preferred stock, debt securities, warrants, and/or units described in this prospectus, separately or together in one or more combinations. The preferred stock, debt securities, and warrants may be convertible into or exercisable or exchangeable for common stock or preferred stock or other securities of CytoSorbents Corporation as identified in the applicable prospectus supplement.

In addition, the selling stockholder may offer and sell, from time to time, up to an aggregate of 2,500,000 shares of common stock under this prospectus. We will not receive any proceeds from sales of our common stock, if any, by the selling stockholder.

This prospectus provides a general description of the securities we or the selling stockholder may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities. This prospectus may not be used to consummate a sale of securities by us unless accompanied by the applicable prospectus supplement.

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 July 17, 2015 was \$6.80 per share. We may sell the shares of common stock through underwriters, through dealers, directly to one or more institutional purchasers or through agents.

\$100,000,000 Common Stock, Preferred Stock, Debt Securities, Warrants and Units 2,500,000 Shares 52Common

Investing in shares of our common stock involves risk. See Risk Factors beginning on page 10 of this prospectus. You should read this document and any prospectus supplement carefully before you invest.

This prospectus will allow us and the selling stockholder to offer for sale securities over time. We will provide a prospectus supplement each time we issue securities, which will inform you about the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference before you invest in any of our securities.

This prospectus may not be used to sell the securities unless accompanied by a prospectus supplement.

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 is July 29, 2015

TABLE OF CONTENTS

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	<u>1</u>
<u>ABOUT CYTOSORBENTS CORPORATION</u>	<u>2</u>
<u>RISK FACTORS</u>	<u>10</u>
<u>FORWARD-LOOKING STATEMENTS</u>	<u>19</u>
<u>USE OF PROCEEDS</u>	<u>20</u>
<u>DESCRIPTION OF THE SECURITIES WE MAY OFFER</u>	<u>21</u>
<u>DESCRIPTION OF CAPITAL STOCK</u>	<u>22</u>
<u>DESCRIPTION OF DEBT SECURITIES</u>	<u>26</u>
<u>DESCRIPTION OF WARRANTS</u>	<u>26</u>
<u>DESCRIPTION OF UNITS</u>	<u>29</u>
<u>LEGAL OWNERSHIP OF SECURITIES</u>	<u>32</u>
<u>SELLING STOCKHOLDER</u>	<u>35</u>
<u>PLAN OF DISTRIBUTION</u>	<u>36</u>
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	<u>39</u>
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	<u>40</u>
<u>LEGAL MATTERS</u>	<u>41</u>
<u>EXPERTS</u>	<u>41</u>

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission using a shelf registration process. Under this shelf registration process, we may offer and sell, from time to time, any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$100,000,000. In addition, the selling stockholder may offer and sell, from time to time, up to an aggregate of 2,500,000 shares of common stock under this prospectus.

This prospectus provides you with a general description of the securities we or the selling stockholder may offer. Each time we or the selling stockholder sell securities under this shelf registration, we will, to the extent required by law, provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the heading **Where You Can Find More Information** before making an investment decision.

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying supplement to this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or any accompanying prospectus supplement. This prospectus and any accompanying supplement to this prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and any accompanying supplement to this prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and any accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities sold on a later date.

This prospectus may not be used by us to consummate sales of our securities, unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

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.

TABLE OF CONTENTS

ABOUT CYTOSORBENTS CORPORATION

CytoSorbents is a leader in critical care immunotherapy commercializing its CytoSorb® blood purification technology to reduce deadly uncontrolled inflammation in hospitalized patients around the world, with the goal of preventing or treating multiple organ failure in life-threatening illnesses. Organ failure is the cause of nearly half of all deaths in the intensive care unit, with little to improve clinical outcome. CytoSorb®, the Company's flagship product, is approved in the European Union, or EU, as a safe and effective extracorporeal cytokine filter, 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 where cytokines play a major role in the cause of inflammation. CytoSorbents' 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. CytoSorbents has numerous products under development based upon this unique blood purification technology, protected by 32 issued U.S. patents and multiple applications pending, including HemoDefend™, ContrastSorb, DrugSorb, and others.

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

Our CE Mark enables CytoSorb® to be sold throughout all 28 countries of the EU. 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 intensive care unit, or 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 systemic inflammatory response syndrome, or SIRS, that can then cause cell death, multiple organ dysfunction syndrome or MODS, and multiple organ failure, MOF. Failure of vital organs such as the heart, lungs, and kidneys, accounts for nearly half of all deaths in the intensive care unit. This is despite the wide availability of supportive care therapies, or life support, such as dialysis, mechanical ventilation, extracorporeal membrane oxygenation, and vasopressors. By replacing the function of failed organs, these supportive care therapies can initially help to keep patients alive, but do not help patients recover faster, and in many cases can increase the risk of dangerous complications. Unlike these supportive care therapies, the goal of the CytoSorb® cytokine filter is to pro-actively 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 safe in this critically-ill population. Taking into account all 100 patients, the treatment was well-tolerated with no serious device related adverse events reported in more

TABLE OF CONTENTS

than 300 human treatments in the trial. Although the trial was not powered to demonstrate significant reduction in other clinical endpoints such as mortality, these were also included as secondary and exploratory endpoints in the trial.

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

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

Very high cytokine levels ($\text{IL-6} \geq 1,000 \text{ pg/mL}$ and/or $\text{IL-1ra} \geq 16,000 \text{ pg/mL}$) where 28-day mortality was 0% treated vs 63% control, $p=0.03$, $n=14$; and

Age ≥ 65 (14-day mortality: 0% treated vs 36% control, $p=0.04$, $n=21$).

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

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

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

In late June 2012, following the establishment of our European subsidiary, CytoSorbents Europe GmbH, a wholly-owned operating subsidiary of CytoSorbents Corporation, we began the commercial launch of CytoSorb® in Germany with the hiring of Dr. Christian Steiner as Vice President of Sales and Marketing and three additional sales representatives who joined us and completed their sales training in Q3 2012. The fourth quarter of 2012 represented the first quarter of direct sales with the full sales team in place. During this period, we expanded our direct sales efforts to include both Austria and Switzerland.

Fiscal 2013 represented the first full year of CytoSorb® commercialization. We focused our direct sales efforts in Germany, Austria and Switzerland with four sales representatives. The focus of the team was to encourage acceptance and usage by key opinion leaders, or KOLs, throughout these countries. By the end of 2014, we had more than 150 KOLs in critical care, cardiac surgery, and blood purification who were either

TABLE OF CONTENTS

using CytoSorb® or committed to using CytoSorb® in the near future. We believe these KOL relationships will be essential to drive adoption and recurrent usage of CytoSorb by the department, facilitate purchases by the hospital administration, arrange reimbursement, and generate data for papers and presentations. In addition, we now currently have more than 40 investigator initiated studies being planned in Germany, Austria, and the United Kingdom in multiple applications including sepsis, cardiac surgery, lung injury, trauma, pancreatitis, liver failure, kidney failure, and others, with many already enrolling patients. These studies are being supported by our European Director of Scientific Affairs. As of June 30, 2015, we have increased our sales force to includes six direct sales people, two contract sales people, and eight sales and distributor support staff.

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

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

In addition, in November 2014, we entered into an initial partnership agreement with a leading global medical device company in cardiac surgery and other cardiovascular diseases, to use CytoSorb® intra-operatively during cardiac surgery in France. Under the terms of the agreement, the partnership will commence with an initial six-month market evaluation period to determine various market parameters, to obtain clinical data, and to build key opinion leader support in France. Following a successful evaluation, the parties plan to jointly determine how to expand upon both the size and geographic footprint of its partnership.

In February 2015, we entered into a multi-country strategic partnership with Fresenius Medical Care AG & Co KGaA, or Fresenius, to commercialize the CytoSorb® therapy. Under the terms of this agreement, Fresenius has exclusive rights to distribute CytoSorb® for critical care applications in France, Poland, Sweden, Denmark, Norway, and Finland. The partnership will allow Fresenius to offer an innovative and easy way to use blood purification therapy for removing cytokines in patients that are treated in the intensive care unit. To promote the success of CytoSorb®, Fresenius will also engage in the ongoing clinical development of the product. This includes the support and publication of a number of small case series and patient case reports as well as the potential for future larger, clinical collaborations.

Overall, we have established either direct sales (as above) or distribution (via distributors or strategic partners) of CytoSorb in 29 countries worldwide. Registration of CytoSorb is typically required in each of these countries prior to active commercialization. With CE Mark approval, this can be typically achieved within several months in EU countries. Outside of the EU, the process is more variable and can take months to more than a year due to different requirements for documentation and clinical data. Variability in the timing of registration affects the initiation of active commercialization in these countries, which affects the timing of expected CytoSorb sales. We actively support

all of our distributors and strategic partners in the product registration process. Outside of the EU, CytoSorb is actively being commercialized in Turkey and India. CytoSorb is registered in Saudi Arabia, but is currently awaiting Saudi FDA approval, a proxy for the rest of the Gulf Cooperation Council, or GCC, countries. CytoSorb and its distribution partner in Russia have submitted all requested documentation for registration, and await a response from the Russian authorities. We cannot generally predict the timing of these registrations, and there can be no guarantee that we will

TABLE OF CONTENTS

ultimately achieve registration in countries where we have established distribution. For example, in August 2014 we announced exclusive distribution of CytoSorb® in Taiwan with Hemoscien Corporation. However, in March 2015, due to the complexity we encountered with Taiwanese product registration, we elected to terminate our agreement with Hemoscien. We also cannot guarantee that we will generate meaningful sales in the countries where we have established registration, due to other factors such as market adoption and reimbursement. We are currently actively evaluating other potential distributor and strategic partner networks in other major countries that accept CE Mark approval.

The market focus for CytoSorb® is the prevention or treatment of organ failure in life-threatening conditions, including commonly seen illnesses in the intensive care unit such as infection and sepsis, trauma, burn injury, ARDS, and others. Severe sepsis and septic shock, a potentially life-threatening systemic inflammatory response to a serious infection, accounts for approximately 10-20% 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 United States or Europe to treat it. As with other critical care illnesses, multiple organ failure is the primary cause of death in sepsis. When used with standard of care therapy, that includes antibiotics, the goal of CytoSorb® in sepsis is to reduce excessive levels of cytokines and other inflammatory toxins, to help reduce the SIRS response and either prevent or treat organ failure.

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

We are currently conducting a matched pairs analysis, dose ranging trial in Germany amongst eight clinical trial sites to evaluate the safety and efficacy of CytoSorb® when used continuously for seven days, each day with a new device.

Data from this dosing study are intended to help clinicians with additional treatment options for CytoSorb®, help support the positive clinical data from our first European Sepsis Trial, and help shape the trial protocol for a pivotal sepsis study.

In addition to the dosing study, we will rely on data generated in the more than 40 ongoing investigator initiated studies and company sponsored trials currently planned or enrolling in Germany, Austria and the United Kingdom, India, and the United States. Approximately 12 of these studies are currently enrolling patients. These trials, which are funded and supported by well-known university hospitals and KOLs, are the equivalent of Phase 2 clinical studies.

They will provide invaluable information regarding the success of the device in the treatment of sepsis, cardio-pulmonary bypass surgery, trauma, and many other indications, and if successful, will be integral in helping to drive additional usage and adoption of CytoSorb®.

In addition to sepsis and other critical care applications, cardiac surgery is emerging as an important potential application for CytoSorb® in the European market. There are approximately one million cardiac surgery procedures performed annually in the United States and EU including, for example, coronary artery bypass graft surgery, valve replacement surgery, heart and lung transplant, congenital heart defect repair, and left ventricular assist device, or LVAD, implantation. Cardiac surgery can result in inflammation and the production of high levels of inflammatory cytokines, as well as hemolysis, causing the release of free hemoglobin. These can lead to post-operative complications such as respiratory failure and acute kidney injury. CytoSorb® has a unique competitive advantage as the only cytokine and free hemoglobin removal technology that can be used during the operative procedure and can be easily installed in a bypass circuit in a heart-lung machine without the need for an additional pump. Direct cytokine

and hemoglobin removal with CytoSorb® enables it to replace the existing market for leukoreduction filters in cardiac surgery that attempt to indirectly reduce cytokines by capturing cytokine-producing leukocytes an inefficient and suboptimal approach.

In February 2015, the U.S. Food and Drug Administration, or FDA, approved our Investigational Device Exemption, or IDE, application to commence a planned cardiac surgery feasibility study in the United States. This single-arm study in 20 patients and three U.S. clinical sites represents the first part of a larger clinical

TABLE OF CONTENTS

trial strategy intended to support the U.S. approval of CytoSorb® for intra-operative use during cardiac surgery. The study is designed to evaluate the safety of CytoSorb® when used intra-operatively in a heart-lung machine to reduce plasma free hemoglobin and cytokines in patients undergoing complex cardiac surgery. The length, complexity and invasiveness of these procedures cause hemolysis and inflammation, leading to high levels of plasma free hemoglobin, cytokines, activated complement, and other substances. These inflammatory mediators directly correlate with the incidence of serious post-operative complications such as kidney injury and failure. The goal of CytoSorb® is to actively remove these inflammatory and toxic substances as they are being generated during the surgery and reduce complications.

Concurrently, we are funding a non-interventional study amongst a broader array of U.S. cardiac surgery centers that will assess adverse event rates (e.g., incidence of acute kidney injury and respiratory failure) and levels of free hemoglobin and other inflammatory mediators in patients undergoing complex cardiac surgery. These patients will be selected using similar inclusion and exclusion criteria to the feasibility study. The data from these two studies will help to rapidly validate assumptions in this surgical patient population and help to appropriately power a pivotal cardiac surgery trial in the United States.

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

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

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

In September 2012, we were awarded a Phase II Small Business Innovation Research, or SBIR, contract by the U.S. Army Medical Research and Material Command to evaluate our technology for the treatment of trauma and burn injury in large animal models. In 2013, we finalized the Phase II SBIR contract which provided for a maximum funding of approximately \$753,000 with the granting agency. This work is supported by the U.S. Army Medical Research and Material Command under an amendment to Contract W81XWH-12-C-0038. As of December 31, 2014, we received approximately \$649,000 in funding under this contract and no further amounts are expected from this contract.

In August 2012, we were awarded a \$3.8 million, five-year contract by DARPA for its Dialysis-Like Therapeutics program to treat sepsis. DARPA has been instrumental in funding many of the major technological and medical advances since its inception in 1958, including development of the Internet, the global positioning system, or GPS, and robotic surgery. The DLT program in sepsis seeks to develop a therapeutic blood purification device that is

capable of identifying the cause of sepsis (e.g. cytokines, toxins, pathogens, activated cells) and remove these substances in an intelligent, automated, and efficient manner. Our contract is for advanced technology development of its hemocompatible porous polymer technologies to remove cytokines and a number of pathogen and biowarfare toxins from blood. We are in Year 3 of the program and are currently working with the systems integrator, Battelle Laboratories, and its subcontractor NxStage Medical, who are responsible for integrating the technology developed by CytoSorbents and others into a final medical device design prototype, and evaluating this device in septic animals and eventually in human clinical trials in sepsis. Our work is supported by DARPA and SSC Pacific under

TABLE OF CONTENTS

Contract No. N66001-12-C-4199. As of December 31, 2014, we have received approximately \$2,818,000 to date and have approximately \$1,007,000 not yet billed under this contract.

In September 2013, the National Heart, Lung, and Blood Institute, or NHLBI, a division of the National Institutes of Health (NIH), awarded us a Phase I SBIR contract valued at \$203,351 to further advance our HemoDefend™ blood purification technology for packed red blood cell, or pRBC, transfusions. The University of Dartmouth collaborated with us as a subcontractor on the project, entitled Elimination of blood contaminants from pRBCs using HemoDefend™ hemocompatible porous polymer beads. The overall goal of this program is to reduce the risk of potential side effects of blood transfusions, and help to extend the useful life of pRBCs. As of December 31, 2014, we completed the Phase I program and have been invited to apply for the Phase II SBIR, which has now been submitted.

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

In addition to CytoSorb®, we are developing other products utilizing our adsorbent polymer technology that have not yet received regulatory approval including HemoDefend™, ContrastSorb, DrugSorb, BetaSorb™, and others. The HemoDefend™ technology platform is a development-stage blood purification system that can remove contaminants in transfused blood products, with the goal of reducing potentially fatal transfusion reactions and improving the quality of blood. ContrastSorb is designed to remove intravenous radiocontrast, or IV contrast, that is administered during interventional radiology procedures (e.g., coronary angiograms for heart disease) and computed tomography or computer axial tomography imaging (i.e., CT or CAT scans) that can cause kidney failure in high risk patients (e.g. those with pre-existing kidney disease, diabetes, hypertension, congestive heart failure, and old age). DrugSorb is designed to remove toxic drugs from blood, 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. Hemoperfusion, along with hemodialysis and hemofiltration, are the three major forms of blood purification. 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.

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

The HemoDefend™ beads are intended to be used in multiple configurations, including as a common in-line filter between the blood bag and the patient as well as a patent-pending Beads in a Bag treatment configuration, where the beads are placed directly into a blood storage bag. Once blood is put into this bag, the beads begin to automatically remove contaminants from the blood, and are designed to continue purifying blood throughout the entire blood storage period. The use of neutrally buoyant beads eliminates the need for mixing and is compatible with current blood storage conditions. Integrated filters in the bag prevent beads from leaving the bag during the transfusion process. The base polymer meets ISO 10993 standards for biocompatibility, hemocompatibility, genotoxicity, cytotoxicity, acute sensitivity and complement activation and can therefore directly contact blood for extended periods of time. In

addition, the beads are inert and stable at a wide range of temperatures, and do not contain any antibodies, biologics, ligands, or drugs. Because of this, the beads have a very long shelf life that is consistent with blood storage bag manufacturing

TABLE OF CONTENTS

standards. No special equipment or handling is required, making it well-suited for mainstream and military applications, as well as for use in less developed countries that are not well-equipped to test and process blood products.

ContrastSorb is a development-stage blood purification technology that is being optimized for the removal of IV contrast from blood in order to prevent contrast-induced nephropathy, CIN. Contrast-induced nephropathy 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 – 13%. For coronary intervention, the risk has been estimated to be as high as 20 – 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.

We had initially identified end stage renal disease, or ESRD, 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 BetaSorb™'s potential for usage 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

United States.

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 United States and Europe. The studies included approximately 345 treatments, with some

8

TABLE OF CONTENTS

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

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, and its business became our business. Following this 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 changed our state of incorporation from the State of Nevada to the State of Delaware.

On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. As a result of the reverse stock split shares of our common stock outstanding were reduced by approximately 96%. Based on the 582,097,092 shares of common stock outstanding as of December 3, 2014, the total number of shares of common stock outstanding after the reverse stock split, including accounting for fractional shares which were rounded up to the next whole number, were 23,284,040.

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

TABLE OF CONTENTS

RISK FACTORS

*You should carefully consider the following risk factors and the section entitled **Forward-Looking Statements** before you decide to invest in our securities.*

Described below are various risks and uncertainties that may affect our business. These risks and uncertainties are not the only ones we face. You should recognize that other significant risks and uncertainties may arise in the future, which we cannot foresee at this time. Also, the risks that we now foresee might affect us to a greater or different degree than expected. Certain risks and uncertainties, including ones that we currently deem immaterial or that are similar to those faced by other companies in our industry or business in general, may also affect our business. If any of the risks described below actually occur, our business, financial condition or results of operations could be materially and adversely affected.

Risks Related to our Industry and our Business

We may require additional capital in the future to fund our operations

As of March 31, 2015, we had current assets of approximately \$14,882,000, including cash on hand of approximately \$10,419,000 and short-term investments of approximately \$2,939,000 and current liabilities of approximately \$6,198,425. On January 14, 2015, we received approximately \$9,409,000 in net proceeds in connection with a registered offering of our common stock. Our cash burn was approximately \$2,800,000 for the three months ended March 31, 2015. Our current and historical cash burn is not necessarily indicative of our future use of cash and cash equivalents.

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

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

Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could be a material adverse effect on our business, operating results, financial condition and prospects.

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

We currently are in the process of commercializing our products, but there can be no assurance that we will be successful in developing commercial operations.

We have been engaged primarily in research and development activities and have generated limited revenues to date.

There can be no assurance that we will be able to successfully manage the transition to a commercial enterprise.

Potential investors should be aware of the problems, delays, expenses and difficulties frequently encountered by an enterprise in the early stage of development, which include unanticipated problems relating to development of proposed products, testing, regulatory compliance, manufacturing, competition, market adoption, product registration, reimbursement, marketing problems and additional costs

TABLE OF CONTENTS

and expenses that may exceed current estimates. Our proposed products 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 United States, and for ongoing compliance for our CE Mark. We will also need to raise significant additional funds to complete additional clinical studies and obtain regulatory approvals in other countries before we can begin selling our products in markets not covered by the 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.

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, 2015, we had an accumulated deficit of \$129,111,062, which included net losses of \$4,716,942 for the three months ended March 31, 2015 and \$975,083 for the three months ended March 31, 2014. In part due to these losses, our audited consolidated financial statements for the year ended December 31, 2014 have been prepared assuming we will continue as a going concern, and the auditors' report on those financial statements express substantial doubt about our ability to continue as a going concern. Our losses have resulted principally from costs incurred in the research and development of our polymer technology and general and administrative expenses. We intend to conduct significant additional research, development, and clinical study activities which, together with expenses incurred for the establishment of manufacturing arrangements and a marketing and distribution presence, and other general and administrative expenses, are expected to result in continuing operating losses for the foreseeable future. The amount of future losses and when, if ever, we will achieve profitability are uncertain. Our ability to achieve profitability will depend, among other things, on successfully completing the development of our technology and commercial products, obtaining additional requisite regulatory approvals in markets not covered by the CE Mark and for potential label extensions of our current CE Mark, establishing manufacturing and sales and marketing arrangements with third parties, and raising sufficient funds to finance our activities. No assurance can be given that our product development efforts will be successful, that our current CE Mark will enable us to achieve profitability, that additional regulatory approvals in other countries will be obtained, that any of our products will be manufactured at a competitive cost and will be of acceptable quality, or that we will be able to achieve profitability or that profitability, if achieved, can be sustained.

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

As of July 15, 2015, we currently have 48 full-time employees and several full-time temporary employees. Our success will depend to a significant degree upon the continued services of our key management and advisors, including Dr. Phillip Chan, our Chief Executive Officer; Kathleen P. Bloch, our Chief Financial Officer; Vincent Capponi, our Chief Operating Officer; and Dr. Robert Bartlett, our Chief Medical Officer, who works with us on a consulting basis. While we currently have employment agreements in place with Dr. Chan, Ms. Bloch, and Mr. Capponi, Dr. Bartlett does not have a long-term consulting arrangement in place. Although we are discussing formalizing our consulting arrangement with Dr. Bartlett, there can be no assurance that Dr. Bartlett, or other members of our management team under contract will continue to provide services to us. In addition, our success will depend on our ability to attract and retain other highly skilled personnel. We may be unable to recruit such personnel on a timely basis, if at all. Management and other employees may voluntarily terminate their employment with us at any time. The loss of services of key personnel, or the inability to attract and retain additional qualified personnel,

could result in delays in development or approval of our products, loss of sales and diversion of management resources.

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

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

TABLE OF CONTENTS

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 polymer products. Even with our approval to apply the CE Mark to our CytoSorb® device as a cytokine filter, our products may not achieve market acceptance in the European countries that recognize and accept the CE Mark. Additional approvals from other regulatory authorities (such as the U.S. Food and Drug Administration, or 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 the our polymer technology;
- pricing and reimbursement policies of government and third-party payers such as insurance companies, health maintenance organizations and other health plan administrators;
- our ability to attract corporate partners, including medical device companies, to assist in commercializing our products; and

- our ability to market our products.

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

Even with our approval to apply the CE Mark to our CytoSorb® device as a cytokine filter, there can be no assurance that the data from our limited clinical studies will be viewed as sufficient by the medical community to support the purchase of our products in substantial quantities or at all.

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

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

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

We have previously engaged in discussions with the Brotech Corporation and its affiliate, Purolite International, Inc. (collectively, "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

TABLE OF CONTENTS

United States District Court for the Eastern District of Pennsylvania approved a Stipulated Order and Settlement Agreement under which we and Purolite agreed to the settlement of the action. The Settlement Agreement provides us with the exclusive right to use our patented technology and proprietary know how relating to adsorbent polymers for a period of 18 years. Under the terms of the Settlement Agreement, we have agreed to pay Purolite royalties of 2.5% to 5% on the sale of certain of our products if and when those products are sold commercially.

More than a decade ago, we engaged in discussions with the Dow Chemical Company, which had indicated a strong interest in being our polymer manufacturer. After a Dow representative on our Advisory Board resigned, Dow filed and received several patents naming our former Advisory Board member as an inventor. In management's view, the Dow patents improperly incorporate our technology and should not have been granted to Dow. The existence of these Dow patents could result in a potential dispute with Dow in the future and additional expenses for us.

We have commenced the process of seeking regulatory approvals of our products, but the approval process involves lengthy and costly clinical studies and is, in large part, not within our control. The failure to obtain government approvals, internationally or domestically, for our polymer products, 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 regulatory approval in the EU under the CE Mark and the Medical Devices Directive. It is manufactured at our manufacturing facility in New Jersey under ISO 13485 Full Quality Systems certification. The manufacturing and marketing of our products will be subject to extensive and rigorous government regulation in the European market, the United States, in various states and in other foreign countries. In the United States and other countries, the process of obtaining and maintaining required regulatory approvals is lengthy, expensive, and uncertain. There can be no assurance that we will ever obtain the necessary additional approvals to sell our products in the United States or other non-EU countries. Even if we do ultimately receive FDA approval for any of our products, we will be subject to extensive ongoing regulation. While we have received approval from our Notified Body to apply the CE Mark to our CytoSorb® device, we will be subject to extensive ongoing regulation and auditing requirements to maintain the CE Mark.

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

We have commenced the process of seeking regulatory approvals of our products, but the approval process involves

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

To date, we have conducted limited clinical studies on our CytoSorb® product. There can be no assurance that we will successfully complete additional clinical studies necessary to receive additional regulatory approvals in markets not covered by the CE Mark. While studies conducted by us and others have produced results we believe to be encouraging and indicative of the potential efficacy of our products and technology, data already obtained, or in the future obtained, from pre-clinical studies and clinical studies do not necessarily predict the results that will be obtained from later pre-clinical studies and clinical studies. Moreover, pre-clinical and clinical data are susceptible to varying interpretations, which could delay, limit or prevent additional regulatory approvals. A number of companies in the medical device and pharmaceutical

TABLE OF CONTENTS

industries have suffered significant setbacks in advanced clinical studies, even after promising results in earlier studies. The failure to adequately demonstrate the safety and effectiveness of an intended product under development could delay or prevent regulatory clearance of the device, resulting in delays to commercialization, and could materially harm our business. Even though we have received approval to apply the CE Mark to our CytoSorb® device as a cytokine filter, there can be no assurance that we will be able to receive approval for other potential applications of CytoSorb®, or that we will receive regulatory clearance from other targeted regions or countries.

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

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

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

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

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

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

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

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

In March 2011, we received approval from our Notified Body to apply the CE Mark to our CytoSorb® device for commercial sale as a cytokine filter. Cytosorbents also achieved ISO 13485:2003 Full Quality Systems certification,

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.

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. CytoSorbents manufactures CytoSorb® at its manufacturing facilities in New Jersey for sale in the EU and for additional clinical studies. We will need to maintain compliance on an ongoing basis. We have limited experience in establishing, supervising and conducting commercial manufacturing. If we or the third-party manufacturers of our products fail to adequately establish, supervise and conduct all aspects of the manufacturing processes, we may not be able to commercialize our products.

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

TABLE OF CONTENTS

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

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

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

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

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

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

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

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

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

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

manufacturing, financial and managerial resources. These entities represent significant competition for us.

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

The continuing efforts of government and insurance companies, health maintenance organizations and other payers of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative partners and the availability of capital. For example, in certain foreign markets, pricing or profitability of medical devices is subject to government control. In the United States, given recent federal and state

TABLE OF CONTENTS

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, or HMOs. Third-party payers are increasingly challenging the prices charged for medical care. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and medical devices, as well as legislative proposals to reform health care or reduce government insurance programs, may all result in lower prices for our products. The cost containment measures that health care payers and providers are instituting and the effect of any health care reform could materially harm our ability to operate profitably.

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

Risks Connected to our Securities and this Offering

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 \$8.75 and as low as \$3.00 per share between January 1, 2014 and December 2, 2014 on the OTCQB. On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. Immediately after the reverse stock split, on December 3, 2014 we changed our state of incorporation from the State of Nevada to the State of Delaware pursuant to an Agreement and Plan of Merger, dated December 3, 2014, whereby we merged with and into our recently formed, wholly-owned Delaware subsidiary. On December 17, 2014, CytoSorbents received approval for up-listing to The NASDAQ Capital Market and its common stock began trading on the NASDAQ Capital Market on December 23, 2014. Our common stock closed as high as \$14.99 and as low as \$5.93 per share between December 23, 2014 and June 16, 2015. On June 16, 2015 the closing price of our common stock, as reported on the NASDAQ Capital Market was \$6.03. Historically, the over-the-counter markets for securities such as our common stock have experienced extreme price fluctuations. Some of the factors leading to this volatility include, but are not limited to:

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

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

If users of our products are unable to obtain adequate reimbursement from third-party payers, or if new restrictive le

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 our 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.

TABLE OF CONTENTS

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, which will adversely affect the rights of holders of our common stock.

On December 3, 2014, we effected a twenty-five-for-one (25:1) reverse split of our common stock. Immediately after the reverse stock split, on December 3, 2014 we changed our state of incorporation from the State of Nevada to the State of Delaware pursuant to an Agreement and Plan of Merger, dated December 3, 2014, whereby we merged with and into our recently formed, wholly-owned Delaware subsidiary. Pursuant to the Agreement and Plan of Merger effecting the merger, we adopted the certificate of incorporation, as amended and restated, and bylaws of our Delaware subsidiary as our certificate of incorporation and bylaws at effective time of the merger. As a result, our certificate of incorporation, as amended and restated, authorizes the issuance of up to 5,000,000 shares of blank check preferred stock, with such designation rights and preferences as may be determined from time to time by the Board of Directors. Currently, our certificate of incorporation, as amended and restated, which became effective on December 3, 2014, authorizes the issuance of up to 50,000,000 shares of common stock, of which approximately 25,141,000 shares remain available for issuance and may be issued by us without stockholder approval.

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

After giving effect to our merger into our wholly-owned Delaware subsidiary, provisions of our certificate of incorporation, as amended and restated, and our 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 our direction or management.

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, and any 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, and no assurances can be made about stock performance, liquidity, or maintenance of our NASDAQ listing.

Historically, our common stock was quoted on the OTCQB, which provided significantly less liquidity than a securities exchange (such as the New York Stock Exchange or the Nasdaq Stock Market). On December 17, 2014, our common stock was approved for trading on the NASDAQ Capital Market, or NASDAQ. Beginning on December 23,

2014, our common stock began trading on NASDAQ under the symbol CTSO. Although currently listed on NASDAQ, there can be no assurance that we will continue to meet NASDAQ's minimum listing requirements or that of any other national exchange. In addition, there can be no assurances that a liquid market will be created for our common stock. If we are unable to maintain listing on the NASDAQ or if a liquid market for our common stock does not develop, our common stock may remain thinly traded.

TABLE OF CONTENTS

Our use of the offering proceeds may not yield a favorable return on your investment.

We currently anticipate that the net proceeds from this offering will be used primarily to fund clinical studies, expand production capacity, support our sales and marketing efforts, to develop our products and for general corporate purposes. Pending the application of the net proceeds, we intend to invest the net proceeds in investment-grade or government, interest-bearing securities. Our management has broad discretion over how these proceeds are used and could spend the proceeds in ways with which you may not agree. Pending the use of the proceeds in this offering, we will invest them. However, the proceeds may not be invested in a manner that yields a favorable or any return.

TABLE OF CONTENTS

FORWARD-LOOKING STATEMENTS

This prospectus and documents incorporated by reference into this prospectus and any prospectus supplement or free writing prospectus may contain forward-looking statements within the meaning of the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, statements about our plans, objectives, representations and contentions and are not historical facts and typically are identified by use of terms such as may, should, could, expect, plan, anticipate, believe, estimate, potential, project, continue and similar words, although some forward-looking statements are expressed differently. You should be aware that the forward-looking statements included herein represent management's current judgment and expectations, but our actual results, events and performance could differ materially from those in the forward-looking statements. The following documents, among others, describe these assumptions, risks, uncertainties, and other factors. You should read and interpret any forward-looking statements together with the following documents:

our most recent Annual Report on Form 10-K, as amended, including the sections entitled Business, Risk Factors and Management's Discussion and Analysis of Financial Condition and Results of Operations;

the risk factors contained in this prospectus under the caption Risk Factors;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, filed May 11, 2015; and our other filings with the Securities and Exchange Commission.

Any forward-looking statement speaks only as to the date on which that statement is made. We assume no obligation to update any forward-looking statement to reflect events or circumstances that occur after the date on which the statement is made.

TABLE OF CONTENTS

USE OF PROCEEDS

Unless the applicable prospectus supplement states otherwise, we will retain broad discretion in the allocation of the net proceeds of this offering. We currently intend to use the net proceeds of this and any future issuances:

to fund clinical studies;
to increase production capacity;
to support our sales and marketing efforts;
to further develop our products; and

for general working capital and other general corporate purposes.

We have not determined the amount of net proceeds to be used for each of the specific purposes indicated. The amounts and timing of the expenditures may vary significantly depending on numerous factors, such as the commercial success of our products and any potential future products, the progress of our research and development efforts, technological advances and the competitive environment for our products. Accordingly, we will have broad discretion to use the proceeds as we see fit. Pending such uses, we intend to invest the net proceeds in interest-bearing, investment grade or government securities.

We believe it is prudent to have an effective shelf registration statement on file with the SEC to preserve flexibility to raise capital if and when needed. We have no specific plans to raise money at this time.

We will not receive the proceeds from any sale of our common stock made by the selling stockholder.

TABLE OF CONTENTS

DESCRIPTION OF THE SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize the material terms and provisions of the various types of securities that we or the selling stockholder may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If we so indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include in the prospectus supplement information, where applicable, about material U.S. federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

We may offer and sell from time to time, in one or more primary offerings, our common stock, preferred stock, debt securities, warrants or units, or any combination of the foregoing. The selling stockholder may offer and sell from time to time up to 2,500,000 shares of our common stock in one or more secondary offerings.

In this prospectus, we refer to the common stock, preferred stock, debt securities, warrants or units, or any combination of the foregoing securities to be sold by us in a primary offering collectively as securities. The total dollar amount of all securities that we may issue under this prospectus, not including the total dollar amount of our common stock that may be offered by selling stockholders, will not exceed \$100,000,000.

This prospectus may not be used by us to consummate a sale of securities unless it is accompanied by a prospectus supplement.

TABLE OF CONTENTS

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. It may not contain all the information that is important to you. For the complete terms of our common stock and preferred stock, please refer to our amended and restated certificate of incorporation and restated bylaws, which are incorporated by reference into the registration statement which includes this prospectus. The Delaware General Corporation Law may also affect the terms of these securities. While the terms we have summarized below will apply generally to any future common stock and preferred stock that we may offer, we will describe the particular terms of any series of these securities in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any security we offer under that prospectus supplement may differ from the terms we describe below.

Common Stock

Under our amended and restated certificate of incorporation, we have authority to issue 50,000,000 shares of our common stock, par value \$0.001 per share. As of June 16, 2015, 24,858,844 shares of our common stock were issued and outstanding. When we issue shares of our common stock under this prospectus, the shares will be fully paid and nonassessable and, unless specified in the applicable prospectus supplement, will not have or be subject to any rights of first refusal or similar rights.

Voting. For all matters submitted to a vote of stockholders, each holder of our common stock is entitled to one vote for each share registered in his or her name. Except as may be required by law and in connection with some significant actions, such as mergers, consolidations, or amendments to our amended and restated certificate of incorporation that affect the rights of stockholders, holders of our common stock vote together as a single class. There is no cumulative voting in the election of our directors, which means that, subject to any rights to elect directors that are granted to the holders of any class or series of preferred stock, a plurality of the votes cast at a meeting of stockholders at which a quorum is present is sufficient to elect a director.

Dividends. Subject to preferential dividend rights of any other class or series of stock, the holders of shares of our common stock are entitled to receive dividends, including dividends of our stock, as and when declared by our board of directors, subject to any limitations applicable by law and to the rights of the holders, if any, of our preferred stock.

Liquidation. In the event we are liquidated, dissolved or our affairs are wound up, after we pay or make adequate provision for all of our known debts and liabilities, each holder of our common stock will be entitled to share ratably in all assets that remain, subject to any rights that are granted to the holders of any class or series of preferred stock.

Other Rights and Restrictions. Subject to the preferential rights of any other class or series of stock, all shares of our common stock have equal dividend, distribution, liquidation and other rights, and have no preference, appraisal or exchange rights, except for any appraisal rights provided by Delaware law. Furthermore, holders of our common stock have no conversion, sinking fund or redemption rights, or preemptive rights to subscribe for any of our securities. Our restated certificate of incorporation and bylaws do not restrict the ability of a holder of our common stock to transfer his or her shares of our common stock.

The rights, powers, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any series of preferred stock which we may designate and issue in the

future.

Listing. Our common stock is listed on the NASDAQ Capital Market under the symbol CTSO.

Transfer Agent and Registrar. The transfer agent for our common stock is American Stock Transfer & Trust Company.

TABLE OF CONTENTS

Preferred Stock

Under our amended and restated certificate of incorporation, we have authority, subject to limitations prescribed by law and without further stockholder approval, to issue from time to time up to 5,000,000 shares of preferred stock, par value \$0.001 per share, in one or more series and to fix the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon the preferred stock, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of the common stock.

The issuance of preferred stock could adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation. The issuance could have the effect of decreasing the market price of our common stock. The issuance of preferred stock also could have the effect of delaying, deterring or preventing a change in control of our company.

Our board of directors will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of each series that we sell under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends; whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period and the conversion price or how the conversion price will be calculated, and under what circumstances it may be adjusted;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period and the exchange price or how the exchange price will be calculated, and under what circumstances it may be adjusted;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;

TABLE OF CONTENTS

a discussion of any material or special U.S. federal income tax considerations applicable to the preferred stock; the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock. When we issue shares of our preferred stock under the terms of the Underwriting Agreement and this prospectus, the shares will be fully paid and nonassessable and, unless specified in the applicable prospectus supplement, will not have or be subject to any rights of first refusal or similar rights.

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Registration Rights

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

Under the New Purchase Agreement, the Company had the right, but not the obligation, to direct LPC to purchase up to \$8,500,000 of its Common Stock in amounts up to \$50,000 as often as every two business days under certain conditions. The Company could also accelerate the amount of its Common Stock to be purchased under certain circumstances. No sales of Common Stock could occur at a purchase price below \$0.10 per share or without a registration statement having been declared effective. The purchase price of the Common Stock was based on the market prices of the Company's Common Stock at the time of sale as computed under the New Purchase Agreement without any fixed discount. The Company had the right at any time at its sole discretion to terminate the New Purchase Agreement without fee, penalty or cost upon one business days' notice.

There was no up-front commitment fee paid to LPC for entering into the New Purchase Agreement. In the event the Company directs LPC to purchase up to \$8,500,000 of its Common Stock, the Company would have been obligated to issue up to an additional 1,634,615 commitment fee shares of Common Stock on a pro rata basis. LPC could not assign any of its rights or obligations under the New Purchase Agreement.

During the three months ended March 31, 2014, the Company received approximately \$300,000 as proceeds from the sale of 2,425,709 shares of Common Stock per the terms of the New Purchase Agreement with LPC at an average price of approximately \$0.124 per share of Common Stock. Per the terms of the New Purchase Agreement, the Company also issued an additional 57,690 shares of Common Stock as additional commitment fee shares.

The Company has not sold any shares of its Common Stock under the New Purchase Agreement since January 17, 2014. The New Purchase Agreement expired in August 2014.

Certain Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval. We may issue these additional shares for a variety of corporate purposes, including future public offerings to raise additional capital or facilitate corporate acquisitions or for payment as a dividend on our capital stock. The existence of unissued and unreserved common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with

TABLE OF CONTENTS

terms that could render more difficult or discourage a third-party attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise, thereby protecting the continuity of our management. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Delaware Law and Amended and Restated Certificate of Incorporation and Bylaws Provisions

Board of Directors. Our bylaws provide that:

subject to the rights of the holders of any series of preferred stock then outstanding, any directors, or the entire Board of Directors, may be removed from office at any time, but only for cause, by the affirmative vote of the holders of sixty-six and two-thirds percent (66 2/3%) of the voting power of all of the outstanding shares of capital stock entitled to vote generally in the election of directors, voting together as a single class; and vacancies in the Board of Directors resulting from such removal may be filled by a majority of the directors then in office, though less than a quorum, or by the sole remaining director. Directors so chosen shall hold office until the next annual meeting of stockholders at which the term of office of the class to which they have been elected expires.

These provisions could discourage, delay or prevent a change in control of our company or an acquisition of our company at a price which many stockholders may find attractive. The existence of these provisions could limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions may also have the effect of discouraging a third party from initiating a proxy contest, making a tender offer or attempting to change the composition or policies of our board of directors.

Stockholder Action; Special Meeting of Stockholders. Our amended and restated certificate of incorporation and by-laws also provide that:

stockholder action may be taken only at a duly called and convened annual or special meeting of stockholders and then only if properly brought before the meeting;

stockholder action may not be taken by written action in lieu of a meeting;

special meetings of stockholders may be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of directors; and

in order for any matter to be considered properly brought before a meeting, a stockholder must comply with requirements regarding specified information and advance notice to us.

These provisions could delay, until the next stockholders meeting, actions which are favored by the holders of a majority of our outstanding voting securities. These provisions may also discourage another person or entity from making a tender offer for our common stock, because a person or entity, even if it acquired a majority of our outstanding voting securities, would be able to take action as a stockholder only at a duly called stockholders meeting, and not by written consent.

Indemnification. Our amended and restated certificate of incorporation provides that we shall, to the fullest extent permitted by, and in accordance with the provisions of, the Delaware General Corporation Law, indemnify each of our directors or officers or employees against expenses (including attorneys fees), judgments, taxes, fines and amounts paid in settlement, incurred by him in connection with, and shall advance expenses (including attorneys fees) incurred by him in defending, any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) to which he is, or is threatened to be made, a party by reason of the fact that he is or was a director or officer or employee of ours, or is or was serving at the request of us as a director, officer, partner, employee or agent of another domestic or foreign corporation, partnership, joint venture, trust or other enterprise.

Advancement of expenses shall be made upon receipt of an undertaking, with such security, if any, as the Board of Directors or stockholders may reasonably require, by or on behalf of the person seeking indemnification to repay amounts advanced if it shall ultimately be determined that he is not entitled to be indemnified as authorized therein.

TABLE OF CONTENTS

DESCRIPTION OF DEBT SECURITIES

We may issue from time to time, in one or more offerings, senior or subordinated debt securities covered by this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus.

The debt securities will be issued under an indenture between us and a trustee, as it may be amended and supplemented from time to time. The form of the indenture is filed as an exhibit to the registration statement of which this prospectus is a part. You should read the indenture for provisions that may be important to you.

WARRANTS

Please note that in this section references to holders mean those who own warrants registered in their own names, on the books that we or our agent maintain for this purpose, and not those who own beneficial interests in warrants registered in street name or in warrants issued in book-entry form through one or more depositaries. Owners of beneficial interests in the warrants should read the section below entitled "Book-Entry Procedures and Settlement .

General

We may offer warrants separately or together with our debt or equity securities.

We may issue warrants in such amounts or in as many distinct series as we wish. This section summarizes terms of the warrants that apply generally to all series. Most of the financial and other specific terms of your warrant will be described in the prospectus supplement. Those terms may vary from the terms described here.

The warrants of a series will be issued under a separate warrant agreement to be entered into between us and one or more banks or trust companies, as warrant agent, as set forth in the prospectus supplement. A form of each warrant agreement, including a form of warrant certificate representing each warrant, reflecting the particular terms and provisions of a series of offered warrants, will be filed with the SEC at the time of the offering and incorporated by reference in the registration statement of which this prospectus forms a part. You can obtain a copy of any form of warrant agreement when it has been filed by following the directions outlined in "Where You Can Find More Information; Incorporation of Documents by Reference" or by contacting the applicable warrant agent.

The following briefly summarizes the material provisions of the warrant agreements and the warrants. As you read this section, please remember that the specific terms of your warrant as described in the prospectus supplement will supplement and, if applicable, may modify or replace the general terms described in this section. You should read carefully the prospectus supplement and the more detailed provisions of the warrant agreement and the warrant certificate, including the defined terms, for provisions that may be important to you. If there are differences between the prospectus supplement and this prospectus, the prospectus supplement will control. Thus, the statements made in this section may not apply to your warrant.

Types of Warrants

We may issue debt warrants or equity warrants. A debt warrant is a warrant for the purchase of our debt securities on terms to be determined at the time of sale. An equity warrant is a warrant for the purchase or sale of our equity securities. We may also issue warrants for the purchase or sale of, or whose cash value is determined by reference to

the performance, level or value of, one or more of the following: securities of one or more issuers, including those issued by us and described in this prospectus or debt or equity securities issued by third parties; a currency or currencies; a commodity or commodities; and other financial, economic or other measure or instrument, including the occurrence or non-occurrence of any event or circumstances, or one or more indices or baskets of these items.

TABLE OF CONTENTS

Information in the Prospectus Supplement

The prospectus supplement will contain, where applicable, the following information about the warrants:

the specific designation and aggregate number of, and the price at which we will issue, the warrants;
the currency or currency unit with which the warrants may be purchased and in which any payments due to or from the holder upon exercise must be made;

the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;

whether the exercise price may be paid in cash, by the exchange of warrants or other securities or both, and the method of exercising the warrants;

whether the warrants will be settled by delivery of the underlying securities or other property or in cash;
whether and under what circumstances we may cancel the warrants prior to their expiration date, in which case the holders will be entitled to receive only the applicable cancellation amount, which may be either a fixed amount or an amount that varies during the term of the warrants in accordance with a schedule or formula;

whether the warrants will be issued in global or non-global form;
the identities of the warrant agent, any depositaries and any paying, transfer, calculation or other agents for the warrants;
any securities exchange or quotation system on which the warrants or any securities deliverable upon exercise of the warrants may be listed;

whether the warrants are to be sold separately or with other securities, and if the warrants are to be sold with the securities of another company or other companies, certain information regarding such company or companies; and
any other terms of the warrants.

No holder of a warrant will, as such, have any rights of a holder of the debt securities, equity securities or other warrant property purchasable under or in the warrant, including any right to receive payment thereunder.

Additional Information in the Prospectus Supplement for Debt Warrants

In the case of debt warrants, the prospectus supplement will contain, where appropriate, the following additional information:

the designation, aggregate principal amount, currency and terms of the debt securities that may be purchased upon exercise of the debt warrants; and

the designation, terms and amount of debt securities, if any, to be issued together with each of the debt warrants and the date, if any, after which the debt warrants and debt securities will be separately transferable.

No Limit on Issuance of Warrants

The warrant agreements will not limit the number of warrants or other securities that we may issue, except for the limitation of the number of shares authorized.

TABLE OF CONTENTS

Modifications

We and the relevant warrant agent may, without the consent of the holders, amend each warrant agreement and the terms of each issue of warrants, for the purpose of curing any ambiguity or of correcting or supplementing any defective or inconsistent provision, or in any other manner that we may deem necessary or desirable and that will not adversely affect the interests of the holders of the outstanding unexercised warrants in any material respect.

We and the relevant warrant agent also may, with the consent of the holders of at least a majority in number of the outstanding unexercised warrants affected, modify or amend the warrant agreement and the terms of the warrants. No such modification or amendment may, without the consent of each holder of an affected warrant:

- reduce the amount receivable upon exercise, cancellation or expiration;
- shorten the period of time during which the warrants may be exercised;
- otherwise materially and adversely affect the exercise rights of the beneficial owners of the warrants; or

reduce the percentage of outstanding warrants whose holders must consent to modification or amendment of the applicable warrant agreement or the terms of the warrants.

Merger and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The warrant agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another firm or to engage in any other transactions. If at any time there is a merger or consolidation involving us or a sale or other disposition of all or substantially all of our assets, the successor or assuming company will be substituted for us, with the same effect as if it had been named in the warrant agreement and in the warrants. We will be relieved of any further obligation under the warrant agreement or warrants, and, in the event of any such merger, consolidation, sale or other disposition, we as the predecessor corporation may at any time thereafter be dissolved, wound up or liquidated.

The warrant agreements will not include any restrictions on our ability to put liens on our assets, including our interests in our subsidiaries, nor will they provide for any events of default or remedies upon the occurrence of any events of default.

Warrant Agreements Will Not Be Qualified under Trust Indenture Act

No warrant agreement will be qualified as an indenture, and no warrant agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of warrants issued under a warrant agreement will not have the protection of the Trust Indenture Act with respect to their warrants.

Enforceability of Rights by Beneficial Owner

Each warrant agent will act solely as our agent in connection with the issuance and exercise of the applicable warrants and will not assume any obligation or relationship of agency or trust for or with any registered holder of or owner of a beneficial interest in any warrant. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant certificate, including any duty or responsibility to initiate any proceedings at law or otherwise or to make any demand upon us.

Holders may, without the consent of the applicable warrant agent, enforce by appropriate legal action, on their own

behalf, their right to exercise their warrants, to receive debt securities, in the case of debt warrants, and to receive payment, if any, for their warrants, in the case of universal warrants.

Governing Law

Unless otherwise stated in the prospectus supplement, the warrants and each warrant agreement will be governed by Delaware law.

TABLE OF CONTENTS

UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions of the governing unit agreement;

the price or prices at which such units will be issued;

the applicable United States federal income tax considerations relating to the units;

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and

any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under Description of Capital Stock, Description of Debt Securities and Description of Warrants will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of your series will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

to cure any ambiguity; any provisions of the governing unit agreement that differ from those described below;

TABLE OF CONTENTS

to correct or supplement any defective or inconsistent provision; or to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or

reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or

If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document. In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by Delaware law.

TABLE OF CONTENTS

Form, Exchange and Transfer

We will issue each unit in global i.e., book-entry form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.

Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.

If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

TABLE OF CONTENTS

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its nominee. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event,

TABLE OF CONTENTS

we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;
whether it imposes fees or charges;
how it would handle a request for the holders' consent, if ever required;
whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
if the securities are in book entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security held by a depositary that represents one or any other number of individual securities. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under **Special Situations When a Global Security Will Be Terminated**. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated.

If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non global certificates for his or her interest in the securities, except in the special situations we describe below;

33

TABLE OF CONTENTS

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe under **Legal Holders** above; an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book entry form; an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective; the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security. We and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security. We and the trustee also do not supervise the depositary in any way; the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book entry system use immediately available funds, and your broker or bank may require you to do so as well; and financial institutions that participate in the depositary's book entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When A Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
if we notify any applicable trustee that we wish to terminate that global security; or
if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

TABLE OF CONTENTS**SELLING STOCKHOLDER**

We are registering an aggregate of 2,500,000 shares of common stock to permit NJTC Investment Fund, LP, which we otherwise refer to herein as NJTC or the selling stockholder, and their permitted assigns that receive their shares after the date of this prospectus, to resell the shares in the manner contemplated under Plan of Distribution. NJTC became a stockholder of the Company in 2008 as part of the Company's then-Series B Convertible Preferred Stock financing. In connection with such investment, NJTC received certain registration rights which were never exercised and were ultimately waived by NJTC in 2014.

The table below presents information regarding the beneficial ownership of outstanding shares of common stock by the selling stockholder and the shares that they may sell or otherwise dispose of from time to time under this prospectus. Information concerning the selling stockholder may change from time to time, and any changed information will be presented in a prospectus supplement if and when necessary and required. The shares set forth below may also be sold by certain transferees or successors-in-interest of the selling stockholder.

The number of shares of common stock in the column Number of Shares Offered Hereby represents all of the shares of common stock that the selling stockholder may offer under this prospectus. In addition, the table assumes that the selling stockholder will sell all of such shares. However, because the selling stockholder may offer from time to time all or some of their shares under this prospectus, or in another permitted manner, we cannot assure you as to the actual number of shares that will be sold or otherwise disposed of by the selling stockholder or that will be held by the selling stockholder after completion of such sales. We do not know how long the selling stockholder will hold the shares before selling them.

We have determined beneficial ownership in accordance with the rules of the SEC. Except as indicated in the footnotes to the following table, the selling stockholder has sole voting and investment power with respect to the shares set forth below. The percentage of beneficial ownership is based on 28,356,906 fully-diluted shares of common stock and common stock equivalents as of June 15, 2015, shares of common stock subject to options, and warrants expected to be exercisable with the passage of time, are deemed outstanding for purposes of computing the percentage of the person holding such options or warrants.

Name of Stockholder	Shares Beneficially Owned		Number of Shares Offered Hereby	Shares Beneficially Owned After Sale of Shares Offered Hereby	
	Number ⁽¹⁾	Percentage		Number ⁽²⁾	Percentage ⁽²⁾
NJTC Investment Fund, LP	4,901,779	17.3%	2,500,000	2,401,779	8.5%
Total	4,901,779	17.3%	2,500,000	2,401,779	8.5%

- (1) Includes 4,870,219 shares of common stock and 31,560 shares of common stock issuable pursuant to stock options exercisable within 60 days of the date of this prospectus.

TABLE OF CONTENTS

PLAN OF DISTRIBUTION

We or the selling stockholder may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

at a fixed price or prices, which may be changed;
at market prices prevailing at the time of sale;
at prices related to such prevailing market prices; or
at negotiated prices.

Each time that securities covered by this prospectus are sold, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We or the selling stockholder may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

The securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their

over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

TABLE OF CONTENTS

If indicated in the applicable prospectus supplement, underwriters or other persons acting as agents may be authorized to solicit offers by institutions or other suitable purchasers to purchase the securities at the public offering price set forth in the prospectus supplement, pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in the prospectus supplement. These purchasers may include, among others, commercial and savings banks, insurance companies, pension funds, investment companies and educational and charitable institutions. Delayed delivery contracts will be subject to the condition that the purchase of the securities covered by the delayed delivery contracts will not at the time of delivery be prohibited under the laws of any jurisdiction in the United States to which the purchaser is subject. The underwriters and agents will not have any responsibility with respect to the validity or performance of these contracts.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate proceeds of the offering.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The selling stockholder may also use any one or more of the following methods when selling shares of common stock:

- on The NASDAQ National Market (or any other exchange on which the shares may be listed);
- on the over-the-counter market;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

TABLE OF CONTENTS

a combination of any such methods of sale; and
any other method permitted pursuant to applicable law.

In connection with the sale of our common stock or interests therein, the selling stockholder may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, the selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholder may also sell shares of our common stock short and deliver these securities to close out its short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholder may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities that require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholder from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. The selling stockholder reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from the offering by the selling stockholder.

The selling stockholder also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that such transactions meet the criteria and conform to the requirements of that rule.

The selling stockholder and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be underwriters within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. If the selling stockholder is an underwriter within the meaning of Section 2(11) of the Securities Act, it will be subject to the prospectus delivery requirements of the Securities Act.

General Information

Underwriters, dealers and agents that participate in the distribution of our securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive and any profit they make on the resale of the offered securities may be treated as underwriting discounts and commissions under the Securities Act. Any underwriters or agents will be identified and their compensation described in a prospectus supplement. We may indemnify agents, underwriters, and dealers against certain civil liabilities, including liabilities under the Securities Act, or make contributions to payments they may be required to make relating to those liabilities. Our agents, underwriters, and dealers, or their affiliates, may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

Each series of securities offered by this prospectus may be a new issue of securities with no established trading market. Any underwriters to whom securities offered by this prospectus are sold by us for public offering and sale may make a market in the securities offered by this prospectus, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. No assurance can be given as to the liquidity of the trading market for any securities offered by this prospectus.

Representatives of the underwriters through whom our securities are sold for public offering and sale may engage in over-allotment, stabilizing transactions, syndicate short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves syndicate sales in excess of the offering size, which creates a syndicate short position. Stabilizing transactions permit bids to purchase the offered securities so long as the stabilizing bids do not exceed a specified maximum.

TABLE OF CONTENTS

Syndicate covering transactions involve purchases of the offered securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the representative of the underwriters to reclaim a selling concession from a syndicate member when the offered securities originally sold by such syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Such stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the offered securities to be higher than it would otherwise be in the absence of such transactions. These transactions may be effected on a national securities exchange and, if commenced, may be discontinued at any time.

Underwriters, dealers and agents may be customers of, engage in transactions with or perform services for, us and our subsidiaries in the ordinary course of business.

We will bear all costs, expenses and fees in connection with the registration of the securities as well as the expense of all commissions and discounts, if any, attributable to the sales of any of our securities by us.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the United States Securities and Exchange Commission (the "SEC"). You may read and copy any document we file with the SEC at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The SEC maintains a website at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. In addition, we maintain a website at <http://www.cytosorbents.com> and make available free of charge on this website our annual reports on Form 10-K, quarterly reports on Form 10-Q, 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 with, or furnish it to, the SEC.

TABLE OF CONTENTS

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with them under Commission File No. 000-31719, which means that we can disclose important information to you by referring you to those publicly available documents. All of the information that we incorporate by reference is considered to be part of this prospectus, and any of our subsequent filings with the SEC will automatically update and supersede this information. This prospectus incorporates by reference the documents listed below and any future filings made by CytoSorbents Corporation with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information furnished under Items 2.02 or 7.01 of Current Report on Form 8-K, or exhibits related thereto, until the filing of a post-effective amendment to this prospectus which indicates that all securities registered have been sold or which deregisters all securities then remaining unsold:

our annual report on Form 10-K for the fiscal year ended December 31, 2014, filed on March 31, 2015, pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act), in which there is set forth the audited financial statements for the Registrant's fiscal year ended December 31, 2014;

our proxy statement for our annual meeting of stockholders, filed on April 22, 2015;

our quarterly report on Form 10-Q for the quarter ended March 31, 2015, filed on May 11, 2015;

our current reports on Form 8-K, filed on January 14, 2015, April 3, 2015, April 8, 2015, April 14, 2015, May 11, 2015, June 4, 2015, and July 15, 2014;

our description of our common stock contained in the Registration Statement on Form 8-A12B filed with the Securities and Exchange Commission on December 17, 2014; and

all other reports filed pursuant to Section 13(a) or 15(d) of the Exchange Act after the date of this registration statement and prior to the effectiveness of the registration statement.

We will provide, upon written or oral request, to each person to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus.

You may request a copy of these filings, at no cost, by writing us at CytoSorbents Corporation, 7 Deer Park Drive, Suite K, Monmouth Junction, New Jersey 08852. Our telephone number is (732) 329-8885.

You should rely only on the information incorporated by reference or provided in this prospectus or any supplement. We have not authorized anyone else to provide you with different information. The selling stockholder will not make an offer of these shares in any jurisdiction where the offer is not permitted. You should not assume that information in this prospectus or any supplement is accurate as of any date other than the date on the front of these documents.

TABLE OF CONTENTS

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by DLA Piper LLP (US), Short Hills, New Jersey. Any underwriters will be advised about other issues relating to any offering by their own legal counsel.

EXPERTS

The consolidated financial statements of CytoSorbents Corporation appearing in CytoSorbents Corporation's Annual Report (Form 10-K) for the year ended December 31, 2014, and the effectiveness of CytoSorbents Corporation's internal control over financial reporting as of December 31, 2014 have been audited by WithumSmith+Brown, PC, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

TABLE OF CONTENTS

68,791 Shares of Common Stock

PROSPECTUS
