

CytoSorbents_M

Working to save lives **together.**

NASDAQ: CTSO

CytoSorbents_{...}

Investor Presentation June 2025

Safe Harbor Statement

Statements in this presentation regarding CytoSorbents Corporation and its operating subsidiaries CytoSorbents Medical, Inc. and CytoSorbents Europe GmbH that are not historical facts are forward-looking statements and are subject to risks and uncertainties that could cause actual future events or results to differ materially from such statements. Any such forward-looking statements are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. It is routine for our internal projections and expectations to change. Although these expectations may change, we are under no obligation to inform you if they do. Actual events or results may differ materially from those contained in the projections or forward-looking statements. The following factors, among others, could cause our actual results to differ materially from those described in a forward-looking statement: our history of losses; potential fluctuations in our quarterly and annual results, the restructuring of our direct sales team and strategy in Germany, our ability to resolve deficiencies in the FDA denial letter through a successfully appeal the FDA's decision, competition, inability to achieve regulatory approval for our devices, technology systems beyond our control and technology-related defects that could affect the companies' products or reputation, risks related to adverse business conditions, our dependence on key employees, competition for qualified personnel, the possible unavailability of financing as and if needed, and risks related to protecting our intellectual property rights or potential infringement of the intellectual property rights of third parties. This list is intended to identify only certain of the principal factors that could cause actual results to differ from those discussed in the forward-looking statements. Readers are referred to a discussion of important risk factors detailed in the Company's 2024 Form 10-K filed with the Securities and Exchange Commission on March 31, 2025, and other reports and documents filed from time to time by us, which are available online at www.sec.gov.



CytoSorbents at a Glance



CytoSorbents

- Platform blood purification technology for removing toxins and harmful substances from the blood
- High margin "razorblade" disposables that are "plug and play" into existing hospital blood pumps
- Two main products leveraging the underlying polymer technology

CytoSorb

REGAIN

- Treatment of life-threatening conditions in the ICU and cardiac surgery
- Record core, non-COVID product sales of **\$35.6 million** in 2024, that grew 15% year over year
- E.U. Approved with > 270,000 CytoSorb devices utilized cumulatively to date in 70+ countries

- Investigational device to reduce the severity of perioperative bleeding during CABG surgery due to blood thinners
- Two FDA Breakthrough Device Designations
- Submitted to FDA (9/2024) and Health Canada (11/2024) with final regulatory decisions expected in 2025
- If approved/cleared, we expect to begin commercialization rapidly, targeting a significant
 - unmet need in large U.S. and Canada addressable markets
- 3 * CytoSorb and DrugSorb-ATR are not yet cleared or approved in the U.S. or Canada

The Power of the Bead

Hemocompatible, highly porous polymer bead platform technology that act like tiny sponges to remove harmful substances from blood by pore capture, adsorption, and concentration



Section through an adsorber

Adsorber bead

Internal structure

- Excellent removal of a broad range of substances from whole blood and plasma
- Solid state porous polymer chemistry that does not use ligands, antibodies, cells, or biologics
- 22 issued U.S. patents and multiple patents issued and pending worldwide
- Beneficiary of ~\$50M in grants and non-dilutive funding from NIH, DARPA, DOD



Expanding the Dimension of Blood Purification

CytoSorb removes a broad range of harmful substances that dialysis does not





CytoSorb has 7 football fields of surface area to bind toxins compared to 34 of a ping pong table for a dialyzer

Products are "Plug and Play" Compatible

<u>Compatible with Existing Blood Pump Infrastructure In Hospitals Today</u>

Dialysis or CRRT (Continuous Renal Replacement Therapy)



ECMO (Extracorporeal Membrane Oxygenation)



Hemoperfusion (Standalone Treatment)



CPB (Cardiopulmonary Bypass)



<u>CytoSorbents</u> <u>PuriFi Pump</u> <u>Launched Q2 2024</u>

CytoSorbents launched its PuriFi pump, an easy-to-use hemoperfusion pump, to excellent reviews in June 2024



PuriFi gives hospitals the ability to administer CytoSorb therapy earlier and without the need for dialysis. This is particularly important in countries that do not have a well-established dialysis infrastructure

CytoSorb Our Core Business



CytoSorb Targets Massive Inflammation - the Heart of Critical Illness

- Acute inflammation is the body's mechanism to fight injury and infection
- However, severe inflammation, driven by cytokine storm, can cause a chain reaction of problems that can end in organ failure and death



 Severe inflammation is the common thread amongst most critical illnesses and is directly correlated to increased severity of illness, organ failure, and mortality

CytoSorb controls deadly inflammation and has demonstrated the ⁸ | reversal or prevention of many of these complications

CytoSorbents...

Inflammation Affects Up to 60% of ICU Patients



Sepsis, Septic Shock, Other Shock



Infectious diseases (flu, COVID-19, other)

Acute Respiratory

(ARDS)

Distress Syndrome



Burn injury

Trauma,

Rhabdomyolysis

Liver

failure



Cytokine storm/ Cytokine release syndrome



High risk surgical procedures, aortic surgery, Infective endocarditis



Pancreatitis







Drug overdose Blood thinner toxicity



CytoSorb helps to treat critical illnesses where massive inflammation plays a dangerous role in up to 60% of patients in the ICU. Compare this to the only 10-15% of patients who require dialysis in the ICU

CytoSorbents

Percentage of Applicable Patients in the ICU



CytoSorb Is An Integrated Approach to Critical Care



2025: COSMOS Registry Highlights Treatment Strategy Success

COSMOS registry, patient characteristics

- Data from 150 patients analyzed
- Critical care indications:
 - Septic shock (57.6%)
 - Cardiogenic shock (12.9%)
 - Rhabdomyolysis (10.6%)
 - Acute/acute-on-chronic liver failure (10.6%)
 - Acute respiratory distress syndrome (6.8%)
 - Others (9.1%)

When added to standard therapy, CytoSorb treatment:

- Led to significant improvements in fundamental problems in critical illness: Shock, capillary leak, and lung function
- Observed mortality rates in Registry participants were lower compared with the predicted mortality rates according to standardized and established critical care risk scores



CvtoSorbents

2025: Early and Intensive Treatment with More Blood Treated Works Best



Original Research

Real-World Outcomes of Hemoadsorption with CytoSorb[®] in Patients with Septic Shock: Insights from a Single-Center Study

Giorgio Berlot, MD¹, Paolo Carocci, MD¹, Valentina Votrico, MD², Barbara Iacoviello, MD¹, Nicolò Taverna, MD¹, Ugo Gerini, MD³, Vittorio di Maso, MD⁴, and Ariella Tomasini, MD¹

Amount of Blood Purified (ABP) positively affects survival





Early starters CytoSorb® was initiated within 24 hours from the onset of septic shock.





Late starters CvtoSorb® was initiated from 25 to 48 hours from the onset of septic shock



Patients underwent ≤ 2

Table 3. Observed Versus Expected Mortality (%).

Categories	Expected mortality (%)	Observed mortality (%)	p-value
All $(n = 175)$	66	49	0.048
Early starters $(n = 102)$	66	48	n.s.
Late starters $(n = 73)$	70	51	n.s.
High intensity $(n = 90)$	63	30	0.002
Low intensity $(n = 85)$	71	69	n.s.
Early starters-high intensity (n = 56)	63	30	0.02
Late starters-low intensity $(n = 38)$	74	68	n.s.

Abbreviations: n.s., nonsignificant.

2025: First Meta-Analysis in Septic Shock

Septic shock is a dreaded complication of sepsis resulting in a potentially lethal drop in blood pressure with a high expected mortality. CytoSorb can reverse shock and reduce mortality



∕		
Μ	DP	
	\searrow	

Systematic Review

Hemoadsorption in the Management of Septic Shock: A Systematic Review and Meta-Analysis

David Steindl ^{1,†}^(b), Tim Schroeder ^{2,†}^(b), Alexander Krannich ^{3,*} and Jens Nee ²^(b)

- 2025 Meta-analysis is the first to specifically investigate the use of CytoSorb in critically-ill patients with septic shock (1 RCT and 8 observational studies between 2019-2024).
 CytoSorb was associated with a statistically significant:
 - Reversal of shock with significant hemodynamic improvement and reductions in vasopressor need in CytoSorb patients
 - Reduction of in-hospital mortality (OR 0.64 [0.42-0.97], p=0.04, N=462)
 - Reduction in 28-30-day mortality by half (OR 0.49 [0.28;0.83], p=0.003, N=250)











* The DrugSorb-ATR system is an investigational device that is not yet cleared/approved by FDA, Health Canada, or by any other Global Regulatory Agency and is not commercially available for sale

14

Large Unmet Need for Blood Thinner Reversal

Millions of people worldwide are on Anti-thrombotic blood thinners to reduce risk of heart attack and stroke



Brilinta® (ticagrelor) (AstraZeneca) Acute Coronary Syndrome, Stents, Prosthetic Heart Valves

Anti-platelets (P2Y12 platelet inhibitor)

Eliquis[®] (apixaban) (Pfizer, BMS) A-Fib, Peripheral Vascular Disease, DVT/PE, Others



Atrial Fibrillation (lifelong therapy)

Direct Oral Anticoagulants (DOAC)

- Cardiac surgeons are frequently faced with **patients on antithrombotics needing urgent surgery**
- Guidelines recommend that such patients wait for 3-5 days for these drugs to "washout" to avoid bleeding complications
- Frequently the surgery cannot wait, and patients are operated at a very high risk for major bleeding complications
- Delaying surgery for washout is also not optimal
 - Exposes patients to risk for complications while waiting
 - o Hospital efficiency is reduced when beds are occupied with patients waiting

There is no approved reversal agent for these specific drugs in the U.S. or Canada for cardiac surgery. CytoSorb is approved for this indication in the E.U. and is the only option for cardiac surgery ROW



Cardiac Surgery and Bleeding Risk

Bleeding at baseline varies according to type of cardiothoracic surgery without the use of antithrombotic drugs



In-hospital bleeding complications and reoperation rates in:

7,774 cardiac surgery patients (3,963 CABG; 2,363 valve replacement/ repair; 160 aortic procedures; 1,288 multiple procedures, primarily CABG + valve).

16

Factors associated with bleeding:

- Type of Surgery
- Surgical duration
- Duration of cardiopulmonary bypass (CPB)
- Body temperature
- Use of cardiac assist devices
- Intraoperative complications

What happens when blood thinners are added to the mix?

CytoSorbents

Brilinta Increases Bleeding Risk in Isolated CABG Surgery

The European Multicenter Study on CABG (E-CABG) Registry is one of the largest real-world data registries evaluating outcomes in CABG patients – the most common cardiac surgery



- In this E-CABG registry study, the incidence of severe or massive bleeding in patients on Plavix[®] (clopidogrel) or Brilinta[®] (ticagrelor) was assessed based on last dose of the drug and timing of CABG surgery
- Used the Universal Definition of Perioperative Bleeding (UDPB) – a bleeding scale developed specifically for cardiac surgery – where UDPB ≥ 3 represents severe, massive, or fatal bleeding

The rate of severe or massive bleeding is >3X higher in patients undergoing CABG within 2 days of last dose of Brilinta[®], compared with a 4-5 day washout

CvtoSorbents



DrugSorb-ATR is an FDA Breakthrough Device

- DrugSorb-ATR is an investigational device that uses an equivalent polymer technology to CytoSorb and installs easily into a cardiopulmonary bypass machine *
- As whole blood is pumped through the cartridge, it is designed to remove free drug during surgery from blood to reverse its antithrombotic effect
- FDA has granted 2 Breakthrough Device Designations (BDD) for DrugSorb-ATR highlighting the major unmet medical need and lack of effective therapies, and provides for priority review of marketing submissions



18

2020: Removal of Brilinta[®] in emergent or urgent cardiothoracic surgery 2021: Removal of DOACs, Eliquis[®] and Xarelto[®] for same

Brilinta is our initial focus for the U.S. and Canadian market





* The DrugSorb-ATR system is an investigational device that is not yet cleared/approved by FDA, Health Canada, or by any other Global Regulatory Agency and is not commercially available for sale

Brilinta[®] and the Use Case for DrugSorb







The ultimate goal of DrugSorb-ATR is to allow patients to get the critical surgery they need without delay, while reducing or preventing bleeding complications

////

DETOUR

CytoSorbents

DrugSorb⁻

The Pivotal STAR-T RCT

In the U.S. & Canadian 140-patient pivotal STAR-T RCT evaluating the safety and efficacy of DrugSorb-ATR to reduce the severity of perioperative bleeding in cardiac surgery patients when used within 2 days of Brilinta (ticagrelor, AstraZeneca) discontinuation, the Principal Investigators of the study concluded:

- Primary safety endpoint was met
- Primary efficacy endpoint was not met in the all-comer surgery population
- However, the severe bleeding efficacy endpoint was met in the isolated CABG PP population (>90%)
- In isolated CABG patients, the intraoperative use of DrugSorb-ATR was also associated with:
 - Reduced bleeding severity by either Universal Definition of Perioperative bleeding (UDPB) grade or 24-hour Chest Tube Drainage (CTD) volume
 - NNT (Number Needed to Treat) of 6 to prevent a major bleed (UDPB \geq 3 event, or >1L 24-hour CTD bleed)
 - Overall favorable benefit-to-risk profile

20 * The DrugSorb-ATR system is an investigational device that is not yet cleared/approved by FDA, Health Canada, or by any other Global Regulatory Agency and is not commercially available for sale

STAR Registry: Real World Evidence

- STAR Registry now in 6 countries (GER, UK, BEL, AUT, SWE, CH) with 600+ subjects enrolled in different cardiac surgeries
- Ticagrelor removal in 102 CABG patients now published
- Ticagrelor removal in an updated cohort of 150 CABG patients presented in Paris at EuroPCR 2025
- First report on DOAC removal in 62 CABG patients now published
- Results consistently show significant reductions in severe bleeding
- Excellent safety: Zero device-related adverse events reported to date
- Device is increasingly used in the routine care of patients on blood thinners undergoing cardiac surgery at heart centers around the world
- Based on our experience, we believe our technology represents a compelling value to patients, surgeons, and hospitals in this application

Real world d		tive hemoadsorption in patients on ticagrelor: ternational Safe and Timely Antithrombotic
		all and all many and and any and all and a
lobert F. Storey Matthias Thielm	ann ^{g,1} , Martin H. B	an ^{c,1} , Anna L. Meyer ^{d,1} , Thomas Eberle ^{e,1} , Nikolaas deNeve ^{f,1} , ernardi ^{h,1} , Nandor Marczin ^{i,j} , Ulf Guenther ^{k,1} , Bernd Panholzer ^{1,1} ,
Ieinrich Maechl ⁄Iichael Schmoe	er ^{m, 1} , Steven Hunte ckel ^{r,1}	Schmoeckel et al. Journal of Cardiothoracic Surgery (2025) 20:74 Journal of Cardiothoracic fittps://doi.org/10.1186/s13019-024-03326-1 Surgery
Division of Clinical Medicin NIHR Sheffield Biamedical	e, University of Sheffield, Sheffield, Research Centre, Sheffield Teachin	
Department of Cardia: Surg	gery, Asklepios Kilnik St. Georg, Ha gery, University Haspital Heidelberg	RESEARCH Open Access
Department of Anesthesia a Department of Anesthesiolog Department of Thoracic- an	nd Intensive Care Medicine, MediCi gy, Intensive Care and Emergency N d Cardiovascular Surgery, Westger Anest hesia and Intensive Care Med	Direct-acting oral anticoagulant removal
Division of Anaesthesia, Pai	in Medicine and Intensive Care, Imp and Intensive Care, Semmelweis Un	
University Clinic of Anaesth	iesiology, Klinkum Oldenburg, Old Henburg, Oldenburg, Germany	of the International Safe and Timely
Department of Cardiac Surg	ery, UKSH, Kiel, Germany y, Medical University of Gras, 8086	
Department of Cardiothora	cic surgery, The Northern General F	Antithrombotic Removal (STAR) registry
CotoSorbenia GmbH, Borlin, Gormany ¹ Bsen, Medical School, University Cihite of Bsen, Essen, Gorma ¹ CytoSorbenia Inc., Princeton, NJ, USA Department of Cardiac Surgey, Klinkum Grosshadern, Ludskj		Michael Schmoeckel ^{1,15°} , Matthias Thielmann ⁷ , Keti Vitanova ³ , Thomas Eberle ⁴ , Nandor Marczin ³ , Kambiz Hassan ⁶ , Andreas Liebold ⁷ , Sandra Lindstedt ⁸ , Georg Mächler ⁹ , Marijana Matejic-Spasic ¹⁰ , Daniel Wendt ^{10,11} , Efthymios N. Dellargyris ¹² and Robert F. Storey ^{13,14}
		Abstract Objective Patients on direct-acting oral anticoagulants (DOACs) are at high risk of perioperative bleeding in patients or DDACs undergoing non-deferable cardiac surgery. The international STAR-registry reports real-world clinical outcome associated with this application. Methods The hemoadsorption device was incorporated into the cardiopulmonary bypass (CPB) circuit and active for the duration of the pump run. Patients on DDACs undergoing CABG and/or single valve surgery before completing the recommended washout were included. Obucome measurements included bleeding events according to standardzed definitions and 24-hour chest-tube-drainage (CTD). Results. A total of 62 patients were included. Oncome measurements included bleeding events according to standardzed definitions and 24-hour chest-tube-drainage (CTD). Results. A total of 62 patients were included. Oncome measurements included bleeding events according to standardzed definitions and 24-hour chest-tube-drainage (CTD). Results. A total of 62 patients were included. Oncome measurement in cluded bleeding events according to a standardzed definitions and 24-hour chest-tube-drainage (CTD). Results. A total of 62 patients also on aspiring. Surgery occurred at a mediant ince 728 h since the last DOAC dose with single valve surgery accounting for 73 of cases. Mean CPB duration was 118.6 ± 464 min. Severe bleeding (UDPB as) occurred in 4.8% and BAR-4 bleeding occurred in 4.8% of the patients. Only one patient (1.6%) required reoperation for bleeding control. The mean 24-hour CTD was 771.3 ± 482.79mL. No device-related adverse events were reported.
		Presented at the 38h EACTS Annual Meeting in Liabon, Portugal, Oct 9-12, 2004. "Correspondence Michael Schmoeskelligmenturis in warechendie Michael Schmoeskelligmenturis in waldebie at the end of the article
		BRANCE BRA

Contents lists available at ScienceDirect

CRM



Two real-world cohorts of patients on ticagrelor undergoing **isolated on-pump CABG** <u>before completing the</u> <u>recommended washout</u> were compared:

- > No intraoperative ticagrelor removal Control (n=644)#
- Intraoperative ticagrelor removal Device (n=150)*

Primary outcome:

• BARC – 4 Bleeding

Additional outcomes:

- Revision for bleeding
- Blood product transfusions
- 24-h chest tube drainage (CTD)
- Mortality at 30 days

Device Integration on CPB



Statistically and Clinically Significant Impact on Bleeding





BARC – Bleeding Academic Research Consortium; **RBC** – red blood cells; **CTD** – chest tube drainage

FDA and Health Canada Regulatory Update

- FDA De Novo submission and Medical Device License application to Health Canada included STAR-T RCT data and STAR registry real world evidence (RWE)
- Interactive review with FDA resolved many issues, however, a denial letter was issued April 25, 2025
- Subsequent meeting with FDA provided clarity on remaining issues
- We continue to believe that our submission package is strong and that remaining issues can be resolved
- We plan to file a formal appeal within 60 days from the FDA letter as the most expedited path forward
 - Prescribed process includes a formal hearing with the Company, our regulatory counsel DuVal & Associates, the FDA review team, FDA senior officials, and testimony from external clinical experts (e.g. cardiac surgeons)
 - Appeal decision estimated at ~ 60 days after filing
 - Three potential outcomes: Decision can be upheld, reversed, or reversed with conditions
- Meanwhile, our Health Canada submission is in advanced review
 - While Health Canada has indicated that application reviews are currently delayed beyond target deadlines, they reaffirmed their commitment to issue a decision as soon as possible

CvtoSorbents

- We continue to expect final regulatory decisions in U.S. and Canada in 2025
 - 24 DrugSorb-ATR is an investigational medical device in the U.S. and Canada and is not yet cleared or approved.

Pre-Launch Activities are Underway



DrugSorb-ATR is a Potential Win for All Stakeholders



Patients

- Minimize delays to definitive surgery
- Reduce serious bleeding risk, which is associated with longer hospital stays and increased morbidity and mortality

Surgeons

- No change in workflow, seamless integration into heart-lung machine
- Reduce serious perioperative bleeding
- Protect surgeon's reputation and quality rating
- Faster disposition of patients, increased throughput of new patients, reduces expensive and time-consuming re-exploratory surgery

Hospital Administrators

- Reduces hospital resource utilization
- Avoiding costs of 3 5 day washout: ~\$18-30K in the ICU, ~\$6-10K in a cardiac bed
- Reduced adverse events protects hospital's CMS STAR rating

CytoSorbents

Cleveland Clinic 2023 Patient Price Information List

26

** The DrugSorb-ATR system is an investigational device that is not yet cleared/approved by FDA, Health Canada, or by any other Global Regulatory Agency and is not commercially available for sale

Strong Value Proposition for Hospitals

Waiting in the hospital for multiple days for the drug to "washout" is highly problematic:

- Exposes patients to added risk due to the delay of having the needed operation
- Increases hospital costs and reduces efficiency by blocking beds and reducing throughput

Survey of Select STAR-T US Pivotal Trial Sites*

Average Washout Duration:

US: 4 days CAN: 3.7 days

Washout Location			
	ICU	Stepdown ICU	General Ward
US	13%	79%	8%
CANADA	24%	26%	50%

Guidelines recommend Ticagrelor washout for 3-5 days

Illustrative Hospital Savings with DrugSorb-ATR



Surgery at 1.6 days with DrugSorb-ATR

Cost savings calculated based on washout duration and hospital location. Hospital bed costs as reported in literature.

CvtoSorbents

* CytoSorbents data on file

** The DrugSorb-ATR system is an investigational device that is not yet cleared/approved by FDA, Health Canada, or by any other Global Regulatory Agency and is not commercially available for sale



Global Regulatory Agency and is not commercially available for sale

Financial Performance



Annual Product Sales

CytoSorbents sells through Direct Sales in 9 countries and Distributors in 63+ others



2022 and 2023 Core Product Sales were impacted by fall of the Euro to dollar compared to 2021.

Recent Financial Performance			
	FY2024	1Q25	
Revenue	\$35.6M	\$8.7M	
Growth %	15%	(3%)/0%**	
Gross Margin	71%	71%	
Adj EBITDA loss	\$11.5M	\$2.7M	
Improvement %	56%	17%	

CytoSorbents

** Constant currency growth rate

Strengthened Balance Sheet with Goal to Drive Core Business to Near Cash-Flow Breakeven in 2H 2025

- \$7.85 million in aggregate proceeds received from successful Rights Offering in Q1 2025
 - Provided \$6.8 million, net of fees, to date
 - Released \$5.0 million of restricted cash on the balance sheet
 - Together increased net liquidity of \$11.8 million
 - 60-day extension of the Series B Right Warrant to June 10, 2025
- \$13.1 million in cash, cash equivalents and restricted cash at March 31, 2025
 - \$3.7 million cash used in Q1 2025, inclusive of \$0.9 million of disbursements unique to Q1 2025
- \$1.7 million received in April 2025 from Sale of NOL and R&D credits
- \$5.0 million second tranche available at our option on our debt agreement
 - Requires FDA approval of DrugSorb-ATR prior to December 31, 2025

We are currently well-capitalized. Through a combination of sales growth, improved product gross margins, and tight cost controls, we expect to drive the core business to near cash-flow breakeven in 2H 2025

A Clear and Compelling Value Proposition

- CytoSorb is the basis of our established, international core business in critical care and cardiac surgery with \$35M+ in high margin product sales with expectations for growth due to:
 - Significant market opportunity, targeting major unmet medical needs
 - "Right patient at the Right Time with the Right Dose of CytoSorb"
 - Strong growth from Direct sales outside Germany and Distributor/Partner sales
 - Active measures to restore Germany back to growth
- ✓ Goal is to drive towards near breakeven in this core business and achieve financial independence
- We remain committed to bringing DrugSorb-ATR to the North American market, and continue to believe that we can successfully work through remaining questions on our application with the FDA and Canada and expect to have final regulatory decisions in 2025
 - Actively preparing as we wait for regulatory decisions from FDA and Health Canada



CytoSorbents Corporation NASDAQ: CTSO

Company Contact: Peter J. Mariani Chief Financial Officer <u>pmariani@cytosorbents.com</u> www.cytosorbents.com

