

HELPING TO TREAT LIFE-THREATENING CONDITIONS IN THE ICU AND CARDIAC SURGERY AROUND THE WORLD



#### WORKING TO SAVE LIVES

### NASDAQ: CTSO

Investor Presentation October 2024

# 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 forwardlooking 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; competition, inability to achieve regulatory approval for our device, 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 2023 Form 10-K filed with the Securities and Exchange Commission on March 14, 2024, and other reports and documents filed from time to time by us, which are available online at <u>www.sec.gov</u>.





# **CytoSorbents**

Leading the Prevention or Treatment of Life-Threatening Inflammation and other Deadly Conditions in the ICU and Cardiac Surgery using CytoSorb® Blood Purification



# **CytoSorbents** At a Glance (NASDAQ: CTSO)

- U.S.-based international medical device company commercializing our E.U. approved CytoSorb<sup>®</sup> blood purification cartridge in 76 countries worldwide
  - \$37.2M in total revenue\*
  - \$32.9M in product sales\*
  - 75% product gross margins\*\*
- More than 250,000 CytoSorb devices utilized cumulatively to date, ~1,000 publications, and ~\$50M in grant and contract support from U.S. agencies like NIH, DOD, and DARPA
  - Treating cytokine storm and massive uncontrolled inflammation (e.g. sepsis, ARDS)
  - Reducing other toxins such as bilirubin (liver disease), myoglobin (trauma)
  - Removing "blood thinners" or antithrombotic drugs during cardiac surgery that cause bleeding
- Partnered with leading multi-national corporations:







- Pursuing U.S. FDA and Health Canada approval for DrugSorb-ATR, an investigational FDA Breakthrough Device, to reduce the severity of perioperative bleeding in patients undergoing coronary artery bypass graft (CABG) surgery by reducing the leading blood thinner, Brilinta<sup>®</sup> - a major unmet medical need
- On 9/27/24, submitted DrugSorb-ATR FDA De Novo marketing application. If accepted, FDA review process begins for clearance/approval, eligible for priority review. Health Canada submission pending





<sup>•</sup> Trailing twelve months as of 6/30/24

Publications include published peer-reviewed journal articles, abstracts, and posters where CytoSorb is used or discussed

# **CytoSorbents** Business Update (as of 10.1.2024)

- As discussed, the DrugSorb ATR De Novo marketing application was submitted to FDA on September 17, 2024 to reduce the severity of perioperative bleeding in patients on ticagrelor undergoing CABG surgery
- Completed our DrugSorb-ATR Health Canada Medical Device License application which will be submitted with the expected near-term receipt of the Medical Device Single Audit Program (MDSAP) certification
- We expect FDA and Health Canada decisions in 2025
- We estimate that our Q3 2024 Product Sales (excluding grant income) will be in the range of approximately \$8.3 million to \$8.5 million, representing growth of 7% to 10%, versus \$7.8 million in Q3 2023
- A planned temporary slowdown in production to rebalance inventory levels coupled with a short-term manufacturing issue resulted in a significantly lower number of CytoSorb devices produced in the quarter. Because of this, we estimate that our product gross margins for Q3 2024 will be in the range of approximately 50% 60%, compared to 71% in Q3 2023. The Company believes the short-term manufacturing issue has been resolved and expects a return to more normalized production levels and product gross margins in Q4 2024. The Company continues to have sufficient inventory to meet demand.

\*Disclosed in press release and SEC 8-k filed 10/1/24



## What does CytoSorb do and How does it work??



## The CytoSorb adsorber

The underlying blood purification technology is based on biocompatible, highly porous polymer beads that act like tiny sponges to remove harmful substances from blood



Section through an adsorber

Adsorber bead

Internal structure

**CytoSorbents**...

Massive surface area: 7 football fields in a single cartridge



- 22 issued U.S. patents and multiple patents issued and pending worldwide
- Manufactured at our state-of-the-art ISO 13485 certified facility in New Jersey
- \* Since inception

# CytoSorb Is "Plug and Play" Compatible

#### Compatible with Existing Blood Pump Infrastructure In Hospitals Today

#### Dialysis or CRRT (Continuous Renal Replacement Therapy)



Hemoperfusion (Standalone Treatment)



ECMO

(Extracorporeal Membrane Oxygenation)



**CPB** (Cardiopulmonary Bypass)





# Expanding the Dimension of Blood Purification®

CytoSorb is fundamentally different from, but complementary to, dialysis technology, removing a broad range of dissimilar toxins that dialysis does not remove well





### **Targets Deadly Conditions That Afflict Millions of People**

#### **Critical Care**

Removes the "fuel to the fire" of massive uncontrolled <u>inflammation</u> that is often associated with organ failure and death



#### **Cardiothoracic Surgery**

Reduces <u>inflammation and blood thinners</u>, targeting reduction in complications of cardiac surgery like sepsis, bleeding, shock, and others



Life-threatening bleeding due to anti-thrombotic "blood thinners"



#### Infective Endocarditis



#### **High Risk Procedures**

# **Riding Many Macro Trends in Healthcare**

#### Aging Population is Getting Older



The Use of Blood Thinners Millions worldwide are on blood thinners to reduce risk of stroke and heart attack







Chronic Liver Disease Afflicts 1 in 5 worldwide







Cirrhotic liver

#### Endocarditis







### **Reversal of Shock and Fluid Removal**





Reversal of shock is a key feature of CytoSorb usage, resulting in the ability to wean vasopressors, restore both macro and microcirculation, reduce lactate, promote capillary leak reversal, and enable fluid removal



Figure 2. Norepinephrine requirements before and after treatment with Cytosorb. Data are summarized as boxplots. The "x" in the box represents the mean value. There is a significant decline in median norepinephrine requirements before and after hemoadsorption with Cytosorb (from 0.55 (0.39–0.9) ug/kg/min to 0.09 (0.0–0.25) ug/kg/min p < 0.001).



**CvtoSorbents**...

Hawchar, F., et al. Biomedicines 2021. 9(7):768 Siddall, E, et al. Kidney Intl 2017. 92(1):37-46 Kogelmann, K., et al. J Clin Med 2024. 13-294

### **Enhanced Lung Rest: A New Paradigm for Severe ARDS**



Dr. Robert Bartlett (ECMO Pioneer & Former CytoSorbents CMO for 10 years)

- Rest lungs and prevent VILI with ECMO
- Stop ongoing injury and capillary leak by cytokine removal with CytoSorb

Hayanga et al. Critical Care (2023) 27:243 https://doi.org/10.1186/s13054-023-04517-3

#### RESEARCH

Critical Care

#### Open Access

Extracorporeal hemoadsorption in critically ill COVID-19 patients on VV ECMO: the CytoSorb therapy in COVID-19 (CTC) registry

J. W. Awori Hayanga<sup>1\*</sup>, Tae Song<sup>2</sup>, Lucian Durham<sup>3</sup>, Lawrence Garrison<sup>4</sup>, Deane Smith<sup>8</sup>, Zsolt Molnar<sup>56</sup>, Joerg Scheier<sup>5</sup>, Efthymios N. Deliargyris<sup>7</sup> and Nader Moazami<sup>8</sup>

"Enhanced Lung Rest" with CytoSorb and ECMO under FDA EUA achieved 74% 90-day survival in 100 COVID patients with refractory lung failure from 5 major U.S. centers (CTC Registry). In comparison, 90-day survival was only 53% with ECMO alone per the ELSO COVID Registry



Kaplan Meyer Survival Curve with 30-day and 90-day survival. ELSO (Extracorporeal Life Support Organization) North American cohort with ECMO alone results provided for comparison

# The Future of Extracorporeal Liver Support

Roughly one in 5 people worldwide have chronic liver disease with millions admitted to hospitals each year with acute exacerbations of liver disease







After

Before



# **CytoSorb** Commercialization Focus



\* U.S., Switzerland, Austria, Belgium, Luxembourg, Poland, Netherlands, Sweden, Denmark, Norway, England, Wales, North Ireland, Scotland, Ireland



### **Annual Product Sales**

CytoSorbents sells through Direct Sales in 15 countries and Distributors in 60+

#### 2023 Core CytoSorb sales grew 10% over 2022...



\*2022 and 2023 Core Product Sales were impacted by fall of the Euro to dollar compared to 2021. \*\*Estimated range of TTM sales as of 9/30/24

#### 2024: Continued Growth **Q1-Q3 2024 Results** \$26.1-26.3M product • sales\*\* +10-11% year over year \$33.4-33.6M Trailing 12-٠ month sales\*\* Historic blended (mixing ٠ higher margin direct sales with lower margin distributor sales) product gross margins in the 70-80% range

## **Bigger Critical Care Opportunity than Dialysis**



Sepsis, Septic Shock, Other Shock



FRESENIUS MEDICAL CARE

Asahi KASEI

Infectious diseases (flu, COVID-19, other)



Trauma, Rhabdomyolysis



Cytokine storm/ Cytokine release syndrome

Post-surgical complications Organ transplant

High risk surgical procedures aortic, Infective endocarditis



Pancreatitis



Neuroinflammation



Acute Respiratory Distress Syndrome (ARDS)

> Dialysis/CRRT for Kidney Failure

> > **B BRAUN**

JMS

Baxter

NIKKISO



Liver failure





Drug overdose Blood thinner toxicity



Percentage of Applicable Patients in the ICU



# Targeting the U.S. and Canadian Market: DrugSorb-ATR for Blood Thinner Removal



### Millions of People are on Blood Thinners

"Blood thinners," also known as antithrombotic drugs, are used by millions of patients globally to prevent stroke and heart attack



**Brilinta® (ticagrelor, aka Brilique®** - **AstraZeneca)** is a blockbuster P2Y<sub>12</sub> anti-platelet agent ("blood thinner") with more than \$1.6 billion in 2022 global sales, used in patients with acute coronary syndrome, stents, prosthetic heart valves



Xarelto® (rivaroxaban – Bayer, Jansenn/J&J) is a blockbuster Factor Xa inhibitor anticoagulant (DOAC) with \$7.5 billion in 2022 global sales used as lifelong therapy in patients with atrial fibrillation



**Eliquis®** (apixaban – Pfizer, BMS) is a Factor Xa inhibitor (DOAC) and the #3 non-COVID pharmaceutical in the world with \$18.4 billion in 2022 global sales, for afib, peripheral vascular disease, DVT, and others

# Problem: Patients that require urgent or emergent cardiothoracic surgery on these blood thinners can develop serious bleeding complications.

There is no approved reversal agent in the U.S. or Canada for cardiac surgery



#### \* 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

#### 20

### 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
  - 2020: Removal of Brilinta<sup>®</sup> in emergent or urgent cardiothoracic surgery
    - 2021: Removal of DOACs, Eliquis<sup>®</sup> and Xarelto<sup>®</sup> for same



**CvtoSorbents** 



# 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





A Pivotal Randomized, Sham-Controlled Trial Examining the Safety and Efficacy of Intraoperative Removal of Ticagrelor in Patients Undergoing Urgent Cardiac Surgery

# Topline Results of the STAR-T Trial

Michael Mack, MD Richard Whitlock, MD C. Michael Gibson, MD for the STAR-T Investigators April 28, 2024



### **STAR-T RCT:** Safe & Timely Antithrombotic Removal of Ticagrelor

Randomized, controlled, double blinded pivotal trial with 140 patients from ~30 trial sites in U.S. and Canada



## **STAR-T Results Presented by Dr. Michael Mack**



https://lifescievents.com/event/cytosorbents/

**CytoSorbents**<sub>m</sub>

# **STAR-T Key Takeaways & Next Steps**

- No safety concerns Primary safety endpoint met
- Imbalances in the number of high-risk non-CABG surgeries and other factors in the treatment arm led to missing the primary efficacy endpoint in overall surgery population (92% CABG + 8% other)
- However, the severe bleeding endpoint was met in the CABG per protocol population
- Overall, in patients undergoing CABG, DrugSorb-ATR was associated with:
  - Reduced bleeding severity by either UDPB grade or CTD volume
  - NNT (Number Needed to Treat) of 6 to prevent a major bleed (UDPB 3 event or CTD >1 Liter)
  - Favorable benefit-to-risk profile
- U.S. FDA De Novo FDA marketing application submitted 9/27/24. With acceptance + FDA Breakthrough Device = priority review (6-12 months)
- Health Canada Medical Device License application completed, and will be submitted with expected MDSAP certification in the near term
- FDA and Health Canada decisions expected in 2025

\* 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



### A Potential Win-Win-Win "Market Pull" Proposition

#### CytoSorb and DrugSorb-ATR have the potential to:

#### • Patients

• Minimize delays to definitive surgery while reducing serious bleeding risk that is associated with longer hospital stays and increased morbidity and mortality

#### • Surgeons

- Not change workflow with seamless integration into CPB machine
- Reduce excessive intraoperative bleeding that can significantly complicate surgeries and extend operating times
- Reduce serious postoperative bleeding: Protect surgeon's quality rating, faster disposition of patients, increased throughput of new patients, reduces expensive and time-consuming re-exploratory surgery

#### Hospital Administrators

- Reduce hospital resource utilization:
  - Avoid a 3 5 day washout: ~\$18-30K in the ICU, ~\$6-10K in a cardiac bed
  - Decrease operative times due to faster hemostasis: Every 30 min = \$4-4.5K in cost\*
  - Decrease use of blood products, need for reoperations, ICU, hospital stay = \$5K savings\*\*
- Reduce adverse events and protect a hospital's CMS STAR rating
- Increase surgical revenue by enabling more surgeries by reducing bleeding complications

\* Cleveland Clinic 2023 Patient Price Information List

\*\* Javanbakht, M, et al. Pharmacoecon Open. 2020 Jun; 4(2):307-319.

### U.S. and Canadian TAM For Current and Potential Future Indications for Antithrombotic Removal by DrugSorb-ATR



# **The Path Forward**

- We see tremendous opportunity in critical care and cardiac surgery fueled by important demographic trends
- We are at the forefront of innovation in critical care because of our ability to treat deadly inflammation that is core to so many diseases and can remove other toxins as well
- We are excited by our near-term operational progress with sales
- Submitted for regulatory approval of DrugSorb-ATR to U.S. FDA on September 27th and expect to file with Health Canada upon near-term receipt of the Medical Device Single Audit Program certification
- By continually pushing boundaries and driving innovation, we are committed to "Expanding the Dimension of Blood Purification<sup>®</sup>", setting the stage to truly transform medicine and create value for shareholders





HELPING TO TREAT LIFE-THREATENING CONDITIONS IN THE ICU AND CARDIAC SURGERY AROUND THE WORLD

Phillip Chan, MD, PhD Chief Executive Officer pchan@cytosorbents.com

# **CytoSorbents**<sub>TM</sub>

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