

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

# **CytoSorbents**<sub>M</sub>

**WORKING TO SAVE LIVES** 

**NASDAQ: CTSO** 

Company Presentation
October 2023

#### 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 2022 Form 10-K filed with the Securities and Exchange Commission on March 9, 2023, and other reports and documents filed from time to time by us, which are available online at www.sec.gov.





# 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® blood purification cartridge in 75 countries worldwide
  - \$36.4M in total revenue\*
  - \$30.1M in product sales\*
  - 74% product gross margins (Q2 2023)
  - 198 employees
- Celebrated 11 years of CytoSorb commercialization with >212,000 cumulative CytoSorb devices utilized (Q2 2023)
  - 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:









- Now seeking U.S. FDA and Health Canada approval for DrugSorb-ATR, an equivalent polymer technology to CytoSorb, to reduce perioperative bleeding during cardiac surgery by removing a leading blood thinner, Brilinta®, under FDA Breakthrough Device Designation
  - Completed our pivotal STAR-T RCT in August and expect top-line data later this year, with submission to FDA and Health Canada to follow. Targets a \$650M TAM in the U.S. and Canada



## **Marketed Products and Product Pipeline**

Internal development supplemented by strong government support with ~\$48M in grants, contracts, other non-dilutive funds awarded to date for our technology from DARPA, NIH, NHLBI, U.S. Army, U.S. Air Force, HHS, and others



Sepsis,
Critical Care,
High Risk
Surgery
CE

ECOS-300CY®

Ex Vivo Organ
Perfusion
For Transplant

C€



Critical
Illnesses in
Animals

Marketed



Removal of Antithrombotic Drugs

**HemoDefend RBC** 

**Purification of pRBCs** 

**HemoDefend BGA** 

**Universal Plasma** 



**CytoSorb-XL** 

**Successor to CytoSorb** 



K\*ontrol

**Severe Hyperkalemia** 



**ContrastSorb** 

CT Imaging and Interventional Radiology

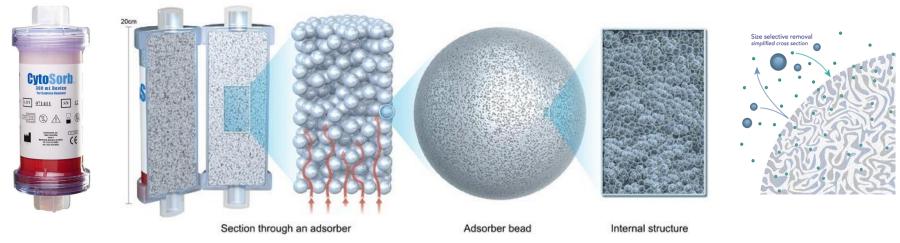
**Under Development** 



# 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



Massive surface area: 7 football fields in a single cartridge















- 19 issued U.S. patents and multiple patents issued and pending worldwide
- Manufactured at our ISO 13485 certified facility in New Jersey



## **Expanding the Dimension of Blood Purification**

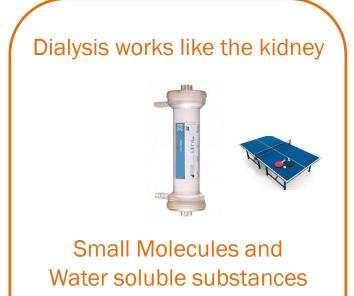
CytoSorb is fundamentally different from, but complementary to, dialysis technology, removing a broad range of dissimilar toxins that dialysis does not remove well

CytoSorb works like the liver with some kidney function



Large Molecules and Fat soluble substances

Cytokines
Inflammatory mediators
Bacterial toxins
Liver toxins
Proteins and peptides
Fat-soluble drugs



Urea, Ammonia

Electrolytes

Water

Water-soluble drugs

### 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



**Sepsis** 



Surgical Complications



Influenza



**Burn Injury** 



COVID-19



Cytokine Release Syndrome



**Lung Injury** 



**Liver Failure** 



Trauma



**Pancreatitis** 

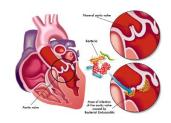
#### **Cardiothoracic Surgery**

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** 

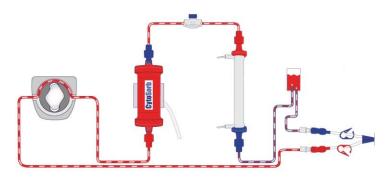


## CytoSorb is "Plug and Play" Compatible

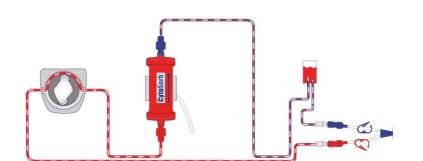
#### Compatible with Existing Blood Pump Infrastructure In Hospitals Today

#### **Dialysis or CRRT**

(Continuous Renal Replacement Therapy)

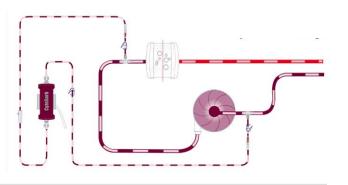


# Hemoperfusion (Standalone Treatment)



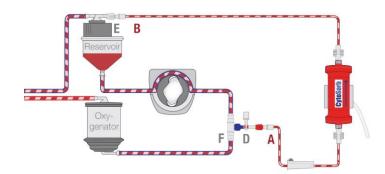
#### **ECMO**

(Extracorporeal Membrane Oxygenation)



#### **CPB**

(Cardiopulmonary Bypass)

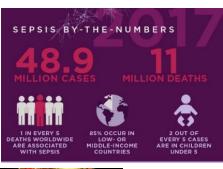




## Riding Many Macro Trends in Healthcare

#### 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 11 worldwide







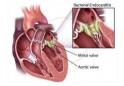
Cirrhotic liver



#### **Endocarditis**











# What is the Company's Business model and Financial performance?

# **CytoSorbents** Has a Strong Hybrid Sales Model

75 Countries Worldwide and >212,000 devices utilized

**Critical Care and Cardiac Surgery** 

#### **Direct Sales**



#### Distributor and Partner Sales



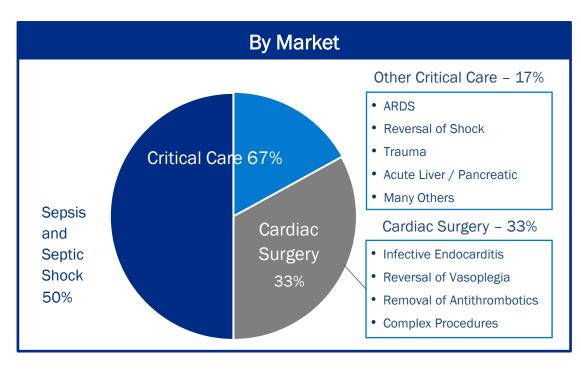
Direct sales in 15 countries: Germany, Austria, Switzerland, Belgium, Poland, Netherlands, Denmark, Norway, Sweden, Luxembourg, England, Wales, Scotland, Northern Ireland, Ireland

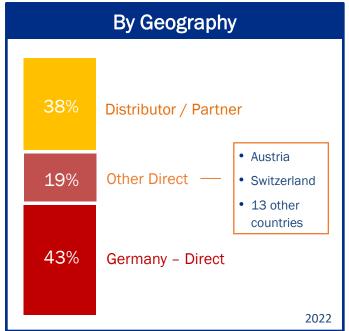


Distributor and Partner sales in >60 other countries Entered U.S. under FDA EUA, expanded to Latin America, the Middle East, South Korea, and many others



# **CytoSorb** Commercialization Focus



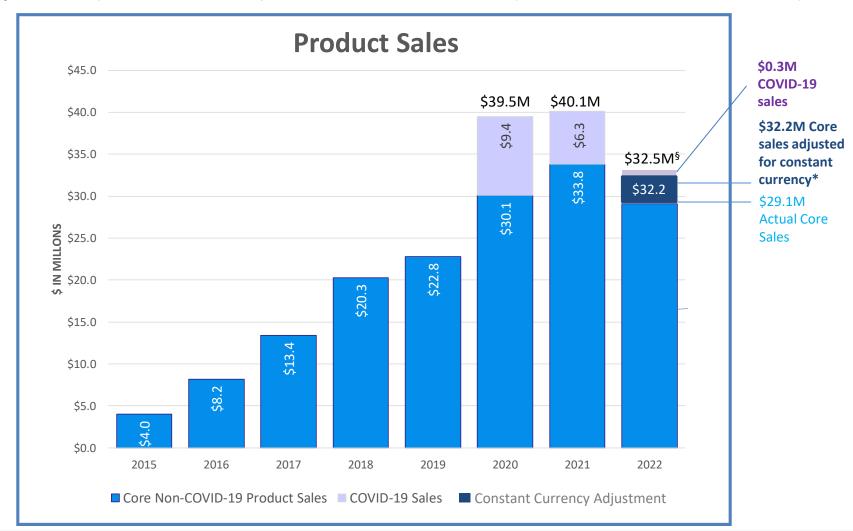


# CytoSorb Is a High Margin "Razorblade"

- High margin "razorblade" fully compatible with existing installed base of "razor" blood pumps: Dialysis, CRRT, and ECMO machines (ICU), and heart-lung machines (OR)
- Blended historic gross margins are 80+%, driven by volume production from our current manufacturing facility and manufacturing efficiencies
- Average Direct Selling Price is approximately \$1,000 per cartridge
- ~1 5 cartridges are typically used per patient depending on the course of treatment
  - Open heart surgery: 1-2 cartridges
  - Sepsis: 3-5 cartridges (or the cost of roughly 1 day in the ICU)
  - ARDS and ECMO: 5+ cartridges
- In Germany, 400 hospitals have >400 beds. Each hospital typically sees 300-600 sepsis patients per year. At 3-5 cartridges per patient:
  - Revenue per patient = ~\$3,000-5,000
  - Potential revenue per hospital = \$1-3M for sepsis alone
- Previously disclosed one German hospital with sales >\$1M, broadly adopting the use of CytoSorb in critical care and cardiac surgery, validating revenue model. Other hospitals are tracking along same path, giving us visibility on future growth

#### **Annual Product Sales**

2022 Core Product Sales were \$29.1M (excluding \$0.3M in COVID-19 related sales). On a constant currency basis, adjusted 2022 core product sales were \$32.2M (Within 5% of 2021,+30% 2019)



<sup>\*</sup> Avg Euro to Dollar exchange rate fell 11% from 1.18 in 2021 to 1.05 in 2022

§ Constant currency basis



## **Total Quarterly Product Sales**



Quarter over quarter sales have been steady over the past three quarters





# What are the key catalysts to create value?



Grow high margin CytoSorb sales



Get DrugSorb-ATR approved in U.S. and Canada – the second engine of growth

# Grow High Margin CytoSorb Sales

### New Manufacturing Facility Now Fully Operational

- Relocated to new Princeton, NJ headquarters with our new ISO 13485-certified manufacturing facility that increases manufacturing capacity by 5x to \$350-400M in annual sales
- CytoSorb and ECOS-300CY are currently being commercially manufactured on this line, while DrugSorb-ATR is expected to be added in the future
- Product gross margins have historically been ~80% but dropped in 2022 as we transitioned to the new facility. Product gross margins were 74% in Q2 2023 and are expected to return to 75-80% this year as we drive volume production from the new facility







#### Markets are Improving Post-COVID

 Seeing a firming of our markets worldwide, including the core Germany market, with sequential growth in Q2 2023 product sales and 10% quarterly growth year-over-year

Continued strong positive support from customers, where the feedback on the therapy

remains very enthusiastic



 Strong pipeline of positive data on CytoSorb across both critical care and cardiac surgery

Improved cross-functional synergy within our company,
 based on our new therapy area vertical strategy and leadership





# Global Marketing Agreement with



- In August 2022, we announced a new, expanded global marketing agreement with long-time partner, Fresenius Medical Care, the market leader in dialysis worldwide, with a massive installed base of blood purification machines in ICUs worldwide
- Fresenius is marketing CytoSorb as the "featured technology for cytokine, bilirubin, and myoglobin removal" on its critical care platforms worldwide (excluding the U.S.) through its sales force, website, conferences, marketing literature, social media, and other platforms
- The partnership "Expands the Dimension of Blood Purification" with excellent synergy between the two companies
  - Fresenius and competitor Baxter dominate kidney replacement blood purification technologies where 10-15% of patients in the ICU have failed kidneys
  - CytoSorbents strengthens and broadens the focus on the lucrative critical care segment, as CytoSorb acts as a liver replacement & helps to address deadly inflammation and toxin overload that afflicts ~40-50% of patients in the ICU
- CytoSorbents benefits from the global endorsement and push on Fresenius' sales and marketing platform and has agreed to subsidize this effort with a 0.9% royalty to FMC on ex-US CytoSorb sales

#### Preferred Supplier Agreements with Helios and Asklepios

- CytoSorbents has entered into preferred supplier agreements with the two largest private hospital chains in Germany: Helios and Asklepios
- Asklepios is one of the leading private hospitals operators in Germany with 170 healthcare facilities across 14 states, including 70 acute care hospitals
- Helios is a wholly-owned subsidiary of Fresenius, operating 87 acute care hospitals in Germany that treat
   1.1 million in-patients annually
- Is helping to open new sales opportunities of our products in these German hospitals
- Private hospital accounts grew by 50% in 2022 vs 2021











# Stand-Alone Hemoperfusion Pump Initiative

- The 2022 partnership with Nikkiso Medical, one of the world's leading manufacturers of products for acute and chronic care blood purification, to resell Nikkiso's PureAdjust® hemoperfusion machine in 14 countries, including Germany, Austria, Switzerland, and France, exemplifies our stand-alone pump strategy
- Hemoperfusion machines are a scaled down, simpler and cheaper blood pump compared to standard dialysis machines
- Our goal is to expand the installed base of machines on which CytoSorb can be used, expand well-beyond the 10-15% of patients on standard dialysis and CRRT, and importantly allow physicians to begin treatment earlier – a key to successful treatment
- Another major goal is to make CytoSorb available to centers that lack sufficient dialysis resources to implement our therapy, thereby opening up many new opportunities for growth



## **Driving Core Applications: Inflammation Control**

- Massive uncontrolled inflammation is a core problem in many critical illnesses leading to organ dysfunction and failure
- Inflammation is driven by cytokine storm and other inflammatory toxins
- This year, in a landmark well-controlled study, Jansen, et al. definitively demonstrated that CytoSorb can reduce the systemic inflammatory response and cytokine storm in healthy humans challenged with LPS endotoxin compared to controls

The ability to treat cytokine storm and reduce systemic inflammation by selecting the "Right patient at the right time with the right dose" is key to the ability of CytoSorb to treat conditions driven by inflammation such as septic shock, trauma, burn injury, pancreatitis, and many other critical illnesses

Jansen et al. Critical Care (2023) 27:117 https://doi.org/10.1186/s13054-023-04391-z Critical Care

**Open Access** 

#### RESEARCH

CytoSorb hemoperfusion markedly attenuates circulating cytokine concentrations during systemic inflammation in humans in vivo

Aron Jansen<sup>1,2\*</sup>, Nicole J. B. Waalders<sup>1,2†</sup>, Dirk P. T. van Lier<sup>1,2†</sup>, Matthijs Kox<sup>1,2</sup> and Peter Pickkers<sup>1,2\*</sup>

#### Abstract

**Background** The CytoSorb hemoadsorption device has been demonstrated to be capable of clearing inflammatory cytokines, but has not yet been shown to attenuate plasma cytokine concentrations. We investigated the effects of CytoSorb hemoperfusion on plasma levels of various cytokines using the repeated human experimental endotoxemia model, a highly standardized and reproducible human in vivo model of systemic inflammation and immunological tolerance induced by administration of bacterial lipopolysaccharide (LPS).

**Methods** Twenty-four healthy male volunteers (age 18–35) were intravenously challenged with LPS (a bolus of 1 ng/kg followed by continuous infusion of 0.5 ng/kg/hr for three hours) twice: on day 0 to quantify the initial cytokine response and on day 7 to quantify the degree of endotoxin tolerance. Subjects either received CytoSorb hemoperfusion during the first LPS challenge (CytoSorb group), or no intervention (control group). Plasma cytokine concentrations and clearance rates were determined serially. This study was registered at ClinicalTrials.gov (NCT04643639, date of registration November 24th 2020).

**Results** LPS administration led to a profound increase in plasma cytokine concentrations during both LPS challenge days. Compared to the control group, significantly lower plasma levels of tumor necrosis factor (TNF, -58%, p < 0.001), interleukin (IL)-6 (-71%, p = 0.003), IL-8 (-48%, p = 0.02) and IL-10 (-26%, p = 0.03) were observed in the CytoSorb group during the first LPS challenge. No differences in cytokine responses were observed during the second LPS challenge.

**Conclusions** CytoSorb hemoperfusion effectively attenuates circulating cytokine concentrations during systemic inflammation in humans in vivo, whereas it does not affect long-term immune function. Therefore, CytoSorb therapy may be of benefit in conditions characterized by excessive cytokine release.

Keywords Systemic inflammation, Hemoadsorption, CytoSorb, Extracorporeal therapy, Cytokines, Sepsis



#### **Expanding into New Markets: Liver Disease**

- 850 million people suffer from chronic liver disease due to viral hepatitis, alcoholism, and non-alcoholic fatty liver (NASH), and other causes leading to 1 million deaths from chronic liver disease each year
- Millions of patients are hospitalized each year for:
  - Acute-on-chronic liver failure
  - Acute liver failure
  - Severe alcoholic or other acute hepatitis
  - Post-hepatectomy liver failure
  - Other
- Inflammation often contributes to decompensation or severity of illness, with jaundice, organ failure, change in mental status, accumulation of fluid, and bleeding complications



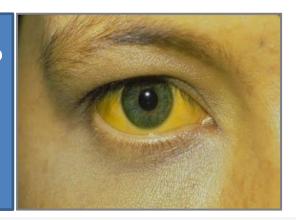


**Before** 

After

CytoSorb is E.U. approved to remove bilirubin in patients with liver disease and is being viewed by many as the next generation, easy to use, extracorporeal liver support therapy

CytoSorb reduces bilirubin and bile acids, but unlike other liver dialysis therapies, it also reduces cytokines that play a major role in acute exacerbations of chronic liver disease and alcoholic hepatitis, and has been used to reverse encephalopathy and pruritis (itching)

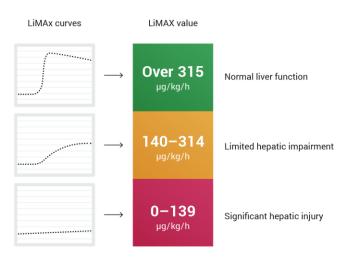


#### Theranostics Collaboration for Liver Disease

- In mid-2023, we partnered with Humedics, the pioneer of LiMAx®, an innovative breath analysis technology that quantitatively assesses liver function, without needing an invasive liver biopsy
- Meanwhile, CytoSorb works to improve liver health and function by reducing circulating cytokines and liver toxins such as bilirubin and bile acids that can compromise liver function
- By pairing the companion diagnostic, LiMAx, with CytoSorb, we intend to better define when and in which patients to intervene with CytoSorb, and importantly, assess their response to our therapy
- The overall goal of the partnership is to drive new business for both companies as our respective sales forces copromote this theranostics collaboration in Germany, U.K., France, Austria, Switzerland, Belgium, Netherlands, Luxembourg, Finland, Norway, Sweden, and Poland









## New Markets: Acute Respiratory Distress Syndrome

- Acute Respiratory Distress Syndrome (ARDS) is one of the most serious forms of lung injury, when both lungs are compromised by inflammation and fluid infiltration, severely compromising their ability to oxygenate the blood
- ARDS was the common cause in the vast majority of deaths during the COVID-19 pandemic, but is common in every day illnesses such as sepsis, pneumonia, pancreatitis, and other inflammatory conditions

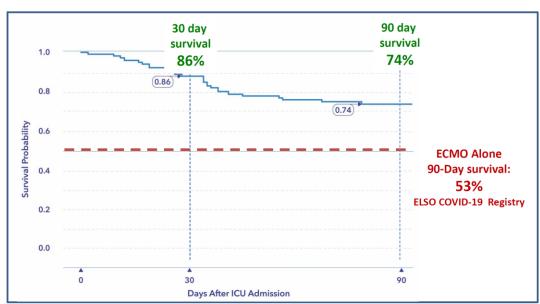


- In a typical year, there are more than 400,000 ARDS cases in the U.S. (250K) and Europe (150K)
- Pathology is driven by the underlying cause (e.g. sepsis, lung injury) & worsened by cytokine storm
- Steroids, proning (turning people over to redistribute fluid in the lungs), and low tidal volume ventilation are the current mainstays of treatment. Although mechanical ventilation helps keep patients alive, it can worsen lung injury through ventilator-induced lung injury, ventilator-acquired pneumonia, and lung fibrosis
- During COVID-19, despite the best standard of care treatment, ~30% of patients with severe
   ARDS on mechanical ventilation died. Mortality was 50% in patients who needed ECMO
- We believe "enhanced lung rest" with CytoSorb represents the new paradigm in which severe ARDS will be treated in the future, where CytoSorb actively removes circulating inflammatory toxins and treats cytokine storm

# **Enhanced Lung Rest: A New Way to Treat ARDS**

CytoSorb was granted FDA Emergency Use Authorization (EUA) to treat critically ill adult COVID-19 patients with imminent or confirmed respiratory failure. The U.S. CytoSorb Therapy in COVID-19 (CTC) registry documented 74% 90-day survival in 100 COVID patients with refractory lung failure (patients whose lung injury was so severe that they failed mechanical ventilation) from 5 major U.S. centers.

Early treatment with ECMO and CytoSorb led to the best clinical outcomes, including less time on mechanical ventilation, ECMO, and in the ICU and supports the concept of "enhanced lung rest" where ECMO reduces ventilator-induced lung injury while CytoSorb reduces circulating cytokines and other inflammatory toxins to reduce capillary leak syndrome, helping to reverse the key pathology in acute respiratory distress syndrome (ARDS), and allow the lungs to heal



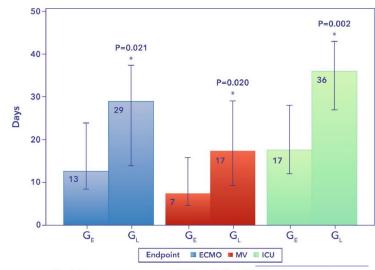


Fig. 1 Days on organ support and ICU stay in G<sub>E</sub> and G<sub>L</sub>. G<sub>E</sub>, early group; G<sub>L</sub>, late group; ECMO, extracorporeal membrane oxygenation; MV,

 Hayanga JWA, et al., "Extracorporeal hemoadsorption in critically ill COVID-19 patients on VV ECMO: The CytoSorb therapy in COVID-19 (CTC) registry." Crit Care 2023; 27:243



Get DrugSorb Approved in the U.S. and Canada – the Second Engine of Growth

#### **Blood Thinners Are Among the Most Prescribed Drugs**

"Blood thinners," also known as antithrombotic drugs, are used by millions of patients globally to prevent strokes and heart attacks cause by blood clots.



**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

#### Our Technology Removes the Drug to Stop the Bleeding

- CytoSorb and DrugSorb-ATR (uses an equivalent polymer technology to CytoSorb) installs easily into a heart-lung machine or cardiopulmonary bypass machine and as blood flows through the cartridge, removes these drugs rapidly during surgery from whole blood to reverse their anticoagulant effect.
- CytoSorb is already approved in the E.U. for this indication
- DrugSorb-ATR is focused on the U.S. and Canadian market and has completed the first of two independent pivotal trials:
  - STAR-T (removal of Brilinta) completed
  - STAR-D (removal of Eliquis and Xarelto)



#### Brilinta is the Antiplatelet Drug of Choice in the U.S.

- Antiplatelets are widely used: heart attacks, strokes, stents, heart valves
  - Brilinta® (ticagrelor), Plavix® (clopidogrel), or Effient® (prasugrel)
- Brilinta has superior antithrombotic efficacy, but Plavix is generic and inexpensive
- Brilinta is expected to go generic in 2024 (ticagrelor). The price of ticagrelor is expected to fall, potentially enabling market share gains against clopidogrel (Plavix) and branded Effient





2023 publication highlights U.S. prescribing physician preference for ticagrelor vs other antiplatelet agents following acute coronary syndrome and percutaneous coronary intervention (PCI; e.g. stent) in >62,000 patients between 2010-2019

Figure 1. Initial Platelet ADP P2Y12 Receptor (P2Y12) Inhibitor Choice After Percutaneous Coronary Intervention, 2010-2019

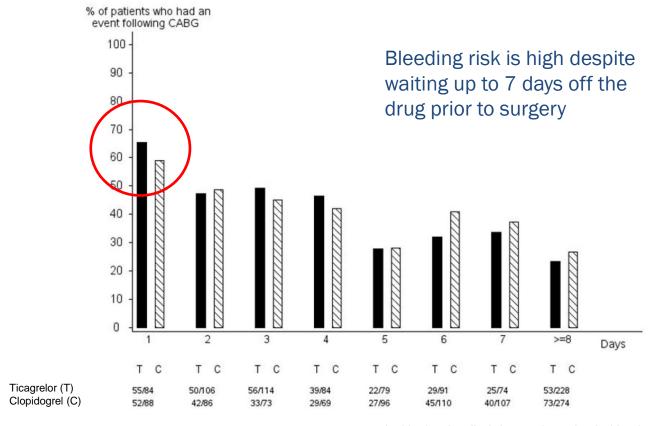




#### Risk of Bleeding Is High in CABG Patients on Brilinta

In the Brilinta (ticagrelor) registration PLATO (PLAeleT inhibition and patient Outcomes) trial, 1584 patients underwent CABG surgery, randomized between those who received either ticagrelor or clopidogrel. Those patients (%) with life-threatening bleeding are shown.

Figure 1 - 'Major fatal/life-threatening' CABG-related bleeding by days from last dose of study drug to CABG procedure (PLATO)



**PLATO Major bleed, fatal/life-threatening:** any major bleed as described above and associated with a decrease in Hb of more than 5 g/dL (or a fall in hematocrit (Hct) of at least 15%); transfusion of 4 or more units. **Fatal:** A bleeding event that directly led to death within 7 days.

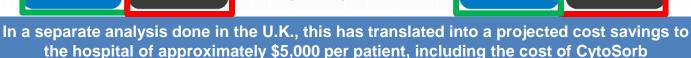


<sup>\*</sup> Astra Zeneca Prescribing Information for Ticagrelor PLATO Trial: Wallentin, L. et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes, NEJM 2009 Sep 10; 361(11):1045-57.

#### By Removing Drug, CytoSorb Reduces Bleeding Complications



	43 patients emergency surgery with ticagrelor		55 patients	12 patients emergency surgery with rivaroxaban	
ATO KEO COV	32 patients with intra- operative CytoSorb	11 patients control without CytoSorb	A	7 patients with intra- operative CytoSorb	5 patients control without CytoSorb
	CPB + CytoSorb (n=32)	CPB alone (n=11)	9	CPB + CytoSorb (n=7)	CPB alone (n=5)
	288 ± 63	353 ± 84	Procedure duration** (min; mean ± SD)	184 ± 97	309 ± 50
	21.9% (n=7)	45.5% (n=5)	Red blood cell transfusion	14.3% (n=1)	100% (n=5)
	34.4% (n=11)	100% (n=11)	Platelet transfusion	28.6% (n=2)	100% (n=5)
	350 [300 - 450]	890 [630 - 1025]	Chest tube drainage remove volume/24hrs (ml; median [IQR])	390 [310 - 430]	600 [590 - 1000]
	0% (n=0)	36.4% (n=4)	Re-thoracotomy	0% (n=0)	40% (n=2)
	2 [1 - 3]	3 [2 - 4]	Days in intensive care (median [IQR])	2 [2 - 3]	6 [5 - 6]
	11 [9 - 12]	14 [10 - 16]	Total length of stay (days; median [IQR])	11 [10 - 13]	18 [18 - 20]



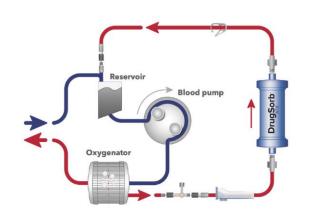
Hassan K, et al. Ann Thor Surg. 2019; 1:45-51.



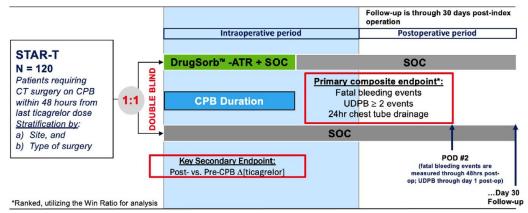
#### **STAR-T Pivotal Trial**



- We were awarded two FDA Breakthrough Device
   Designations for this application –one for Brilinta,
   one for Eliquis/Xarelto, a "fast track" path for
   devices addressing major unmet clinical needs







Design Overview: STAR-T U.S Pivotal Trial: SOC = standard of care. One-to-one randomization is to the investigational treatment (SOC + ticagrelor removal with DrugSorb during CPB) vs control (SOC alone). The primary effectiveness endpoint is a hierarchical composite of a full spectrum of bleeding events through 48 hours post-operation. Ticagrelor resumption is recommended after this time. The key secondary endpoint is a drug removal endpoint, as less circulating ticagrelor is presumed to be the mechanism for reduced bleeding.

#### **STAR-T Timeline**



- STAR-T completed in August 2023, with 140 patients enrolled at 30 sites in the U.S. and Canada
- The trial remains blinded, with data monitoring in process and database lock upcoming
- No safety issues raised as of the last independent Data and Safety Monitoring Board (DSMB) analysis at 80 patients enrolled, recommending the study continue to completion without modification. Final DSMB review will occur after database lock
- Expecting topline data on primary endpoint (reduction in perioperative bleeding) by year-end
- If the trial data are positive, submission to U.S. FDA and Health Canada for regulatory approval
  is expected in early-2024. Targeting potential approval by late-2024 or early 2025, based on
  time of submission, potential acceleration of review due to FDA Breakthrough Designation, and
  other factors
- Presentation and publication of the full data set is expected thereafter at a major conference
- With positive data, plan to initiate commercial buildout and to start sales with potential approval
- STAR-D (for Xarelto and Eliquis removal) trial to follow STAR-T to establish DrugSorb as a "onestop shop" for ATR



#### **United States TAM for Brilinta Removal**

50,000 patients on Brilinta needing emergent/urgent open heart surgery annually in US

X

\$5,000 per device

#### \$250M Initial U.S. Total Addressable Market



#### Brinlinta market share expected to grow

- DrugSorb-ATR would make Brilinta the only reversible platelet inhibitor
- Brilinta goes off patent in 2024 leading to a likely drop in prices



\$500M U.S. Total Addressable Market



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



#### **Competition and Comparables**

- CytoSorb is the only approved reversal agent in the E.U. for Xarelto and Brilinta/Brilique during cardiothoracic surgery. DrugSorb-ATR uses an equivalent polymer technology to CytoSorb and has received 2 FDA Breakthrough Device Designations for the removal of Brilinta, as well as the DOACs Eliquis and Xarelto. DrugSorb-ATR removes all three major classes of blood thinners and seeks to become the "one-stop shop" for blood thinner removal during surgery
- Andexxa® was developed by Portola Pharmaceuticals and is the only U.S. approved reversal agent for the Factor Xa inhibitors, such as Xarelto and Eliquis. It is used mainly in catastrophic bleeding events. However, it is not a direct competitor to DrugSorb-ATR as it cannot be used in cardiothoracic surgery, is expensive, and has a black box warning for being prothrombotic (causing heart attacks and strokes)

#### Alexion acquired Portola in May 2020 for \$1.4 billion, more than 12x sales of ~\$112 million.

- Praxbind® (Boehringer Ingelheim) is a specific MAb reversal agent for the direct thrombin inhibitor, Pradaxa® (Boehringer Ingelheim). It also carries a risk of being prothrombotic.
- Bentracimab was being developed by PhaseBio as a reversal agent for Brilinta. Bentracimab also carries a risk of being prothrombotic. PhaseBio filed for bankruptcy in October 2022. The bentracimab asset was seized by PhaseBio's co-development partner, SJF Pharmaceuticals, who licensed U.S. rights to SERB Pharma in May 2023

#### **Today: CytoSorb Drives our Growth**

- CytoSorb forms the Company's foundation
  - E.U. approved and sold around the world
  - Generated ~\$200M in sales since launch
  - High margin razorblade business model with industry top-tier 80+% blended product gross margins
  - Strong validation by customers, partners, and government agencies



 Current sales supports near-breakeven, less clinical trial costs, which we believe helps to derisk the Company and the investment opportunity

We believe CytoSorb represents the fuel for future strong anticipated growth targeting the \$20-30B worldwide TAM of major unmet medical needs in critical care, cardiac surgery, as well as liver and kidney disease

We believe this gives CytoSorbents the potential upside of a biotechnology company, with the lower risk profile of a high margin medical device company with sales

# Soon: CytoSorh & DrugSorb = Dual Growth Engines

- STAR-T has now completed and is heading to database lock with top-line data expected later this year. International usage and trial safety to date gives us confidence.
- Should STAR-T be successful and DrugSorb-ATR achieves U.S. FDA and Health Canada regulatory approval, we intend to commercialize DrugSorb-ATR in both the U.S. and Canada – a potentially <u>major second engine of growth</u>, working in tandem with CytoSorb to drive sales
- DrugSorb-ATR would open an expected U.S. and Canadian TAM of \$600-650M for Brilinta® alone, where we expect significant penetration, given the major unmet need indicated by our FDA Breakthrough Designation
- If successful, this could transform CytoSorbents into a dual U.S. and international growth company that current and prospective institutional and retail shareholders, are excited



about and have been waiting for, and that can create significant value.



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

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