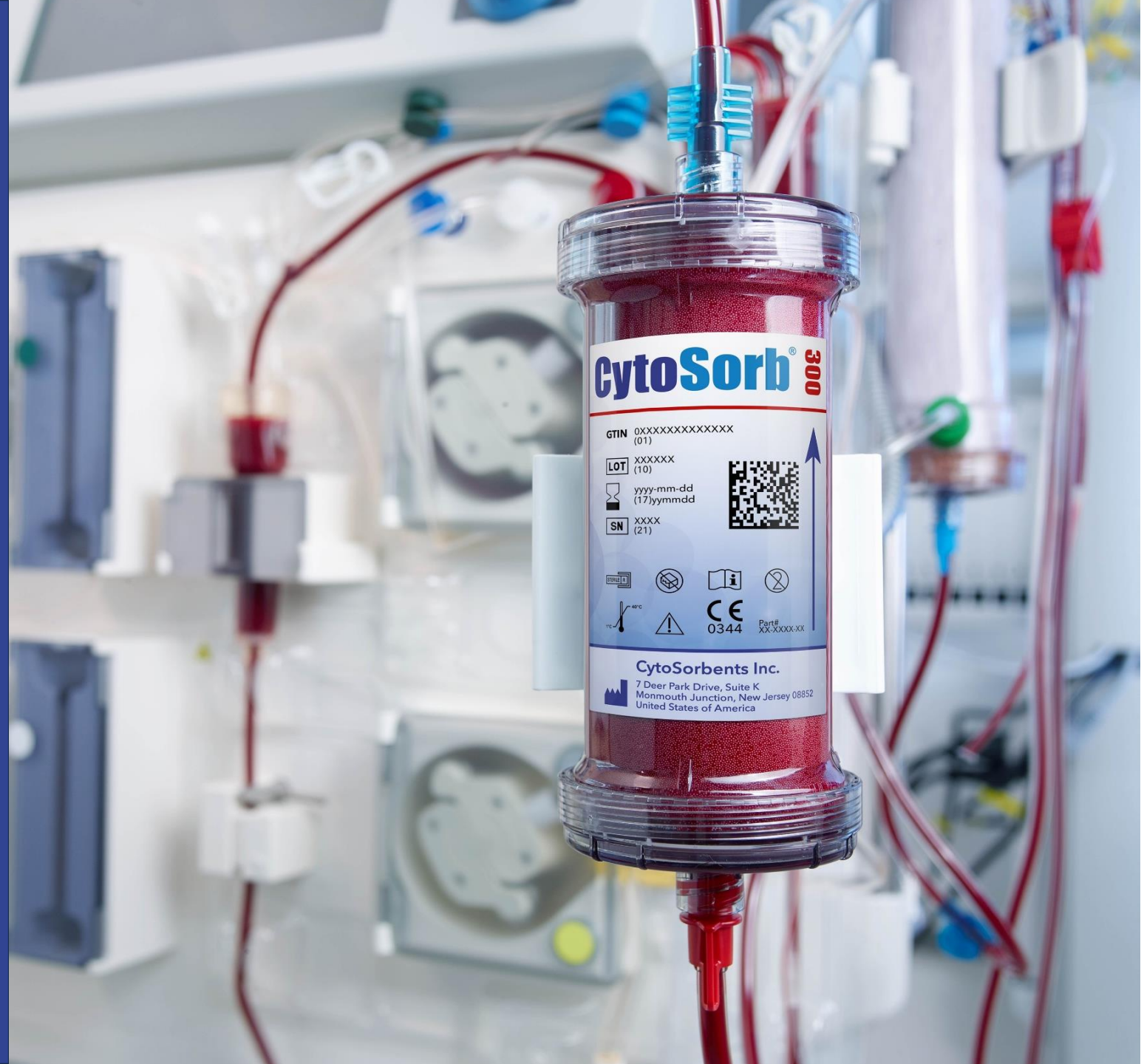

CytoSorbents™

Working to save lives **together.**

NASDAQ: CTSO

Jefferies Global Healthcare Conference

June 5, 2025

CytoSorbents™

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.

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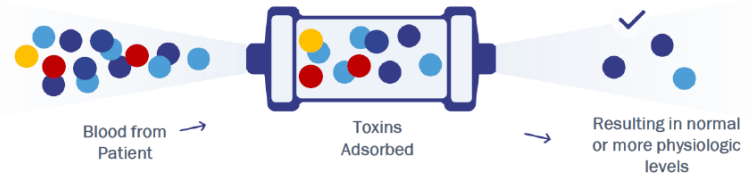
CytoSorbents at a Glance



- **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

- 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

DrugSorb ATR

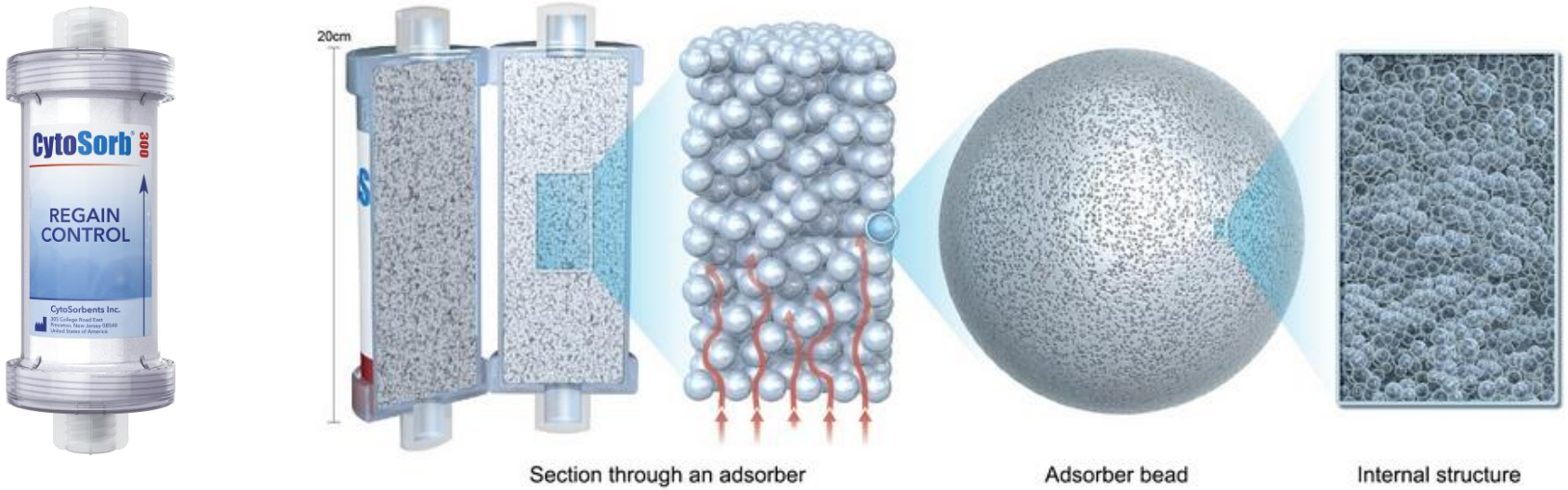
- Investigational device to reduce the severity of perioperative bleeding during CABG surgery due to blood thinners
- **Two FDA Breakthrough Device Designations**
- **Submitted to FDA (9/2024)** and **Health Canada (11/2024)** with **final regulatory decisions expected in 2025**
- If approved/cleared, we expect to begin commercialization rapidly, targeting a significant unmet need in large U.S. and Canada addressable markets

* CytoSorb and DrugSorb-ATR are not yet cleared or approved in the U.S. or Canada

CytoSorbents™

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



- 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

CytoSorbents™

Expanding the Dimension of Blood Purification

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

CytoSorb works like the liver

Large Molecules and
Fat soluble substances

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

Dialysis works like the kidney

Small Molecules and
Water soluble substances

Urea, Ammonia
Electrolytes
Water
Water-soluble drugs

CytoSorb has 7 football fields of surface area to bind toxins compared to ¾ of a ping pong table for a dialyzer

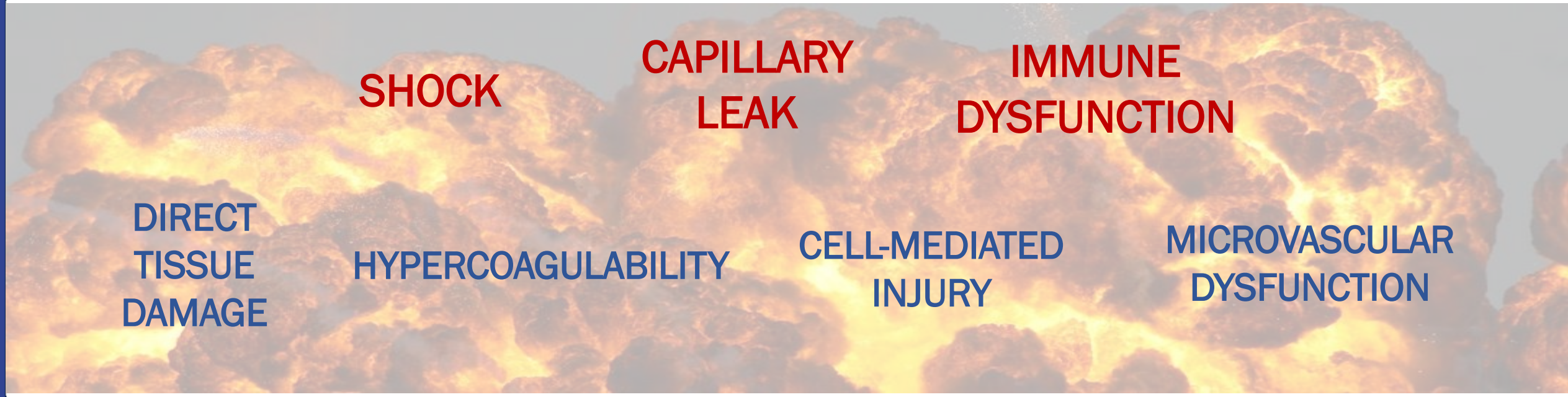
CytoSorbents™

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

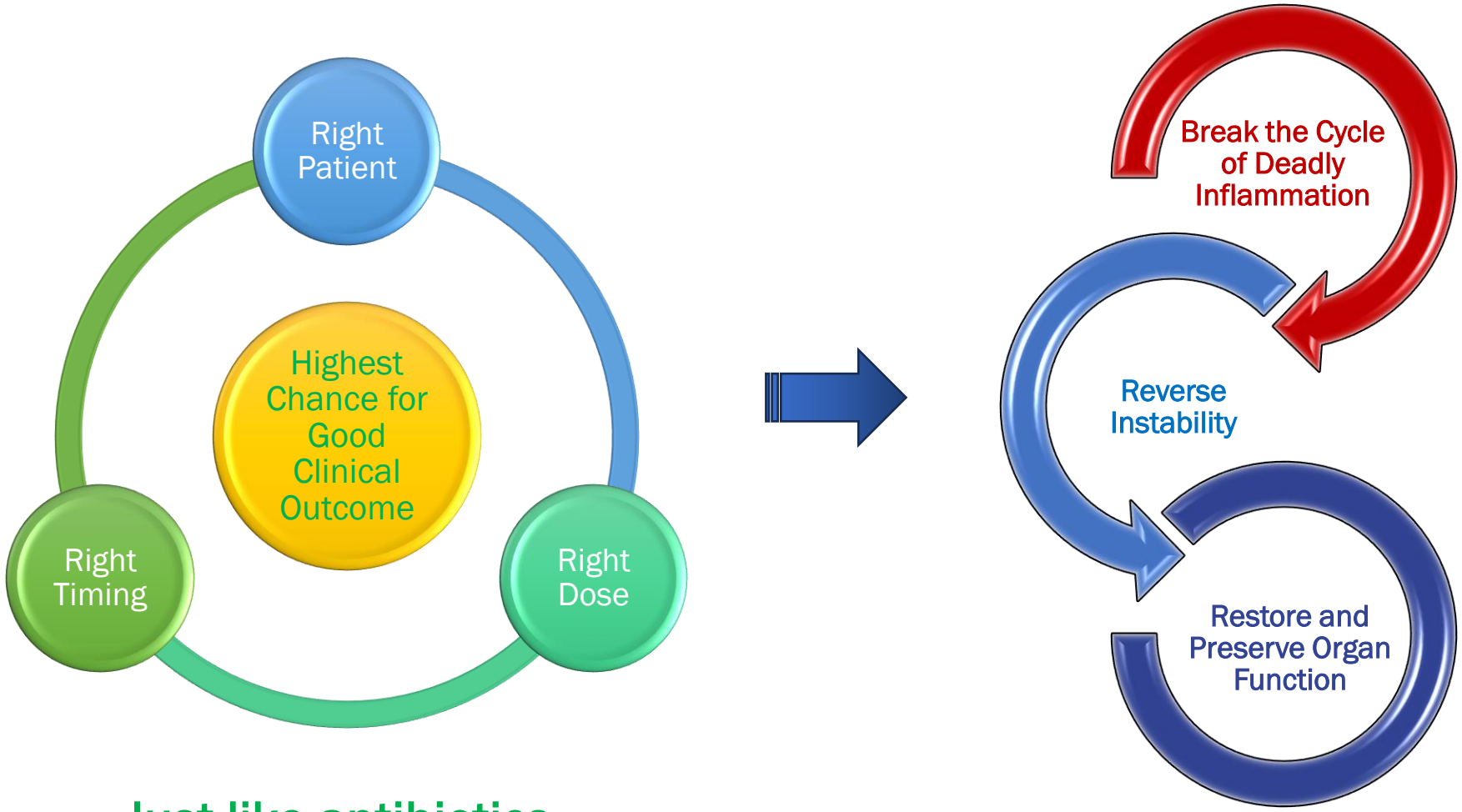


- Severe inflammation is the common thread amongst most critical illnesses and impacts up to 60% of patients in the ICU. Is directly correlated to increased severity of illness, organ failure, and mortality

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

CytoSorbents™

CytoSorb Integrated Approach for Critical Care



Just like antibiotics…

Treat early, treat aggressively, & complete the full course of treatment to have a good outcome

CytoSorbents™

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, MD[1], Paolo Carocci, MD[1], Valentina Votrico, MD[2], Barbara Iacoviello, MD[1], Nicolò Taverna, MD[1], Ugo Gerini, MD[3], Vittorio di Maso, MD[4], and Ariella Tomasini, MD[1]

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

High intensity
Patients underwent ≥3 procedures

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

Low intensity
Patients underwent ≤ 2 sessions

Amount of Blood Purified (ABP) positively affects survival

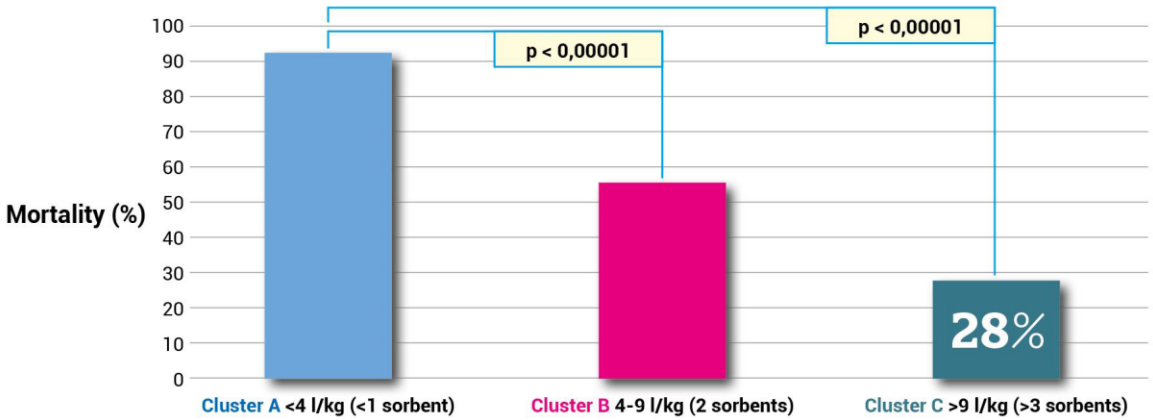


Table 3. Observed Versus Expected Mortality (%).

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

Journal of Clinical Medicine

MDPI

Systematic Review

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

David Steindl [1,†], Tim Schroeder [2,†], Alexander Krannich [3,*] and Jens Nee [2]

- 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)

CytoSorbents™

The Opportunity of

DrugSorb™ ATR

CytoSorbents™

* 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

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

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

Xarelto® (rivaroxaban)
(Bayer, Jansenn/J&J)
Atrial Fibrillation (lifelong therapy)

Anti-platelets (P2Y12 platelet inhibitor)

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
  - 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

CytoSorbents™

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

FDA BREAKTHROUGH DEVICE DESIGNATION

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

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Brilinta® and the Use Case for DrugSorb™ ATR

DrugSorb™ ATR

weekly plan						
monday	tuesday	wednesday	thursday	friday	saturday	sunday
	X	X	X	X	X	

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

CytoSorbents™

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 ≥ 3 event, or >1L 24-hour CTD bleed)
  - Overall favorable benefit-to-risk profile

* 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

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

journal homepage: www.sciencedirect.com/journal/cardiovascular-revascularization-medicine

Early CABG with intraoperative hemoadsorption in patients on ticagrelor: Real world data from the international Safe and Timely Antithrombotic Removal (STAR) registry

Robert F. Storey, Kambiz Hassan, Anna L. Meyer, Thomas Eberle, Nikolaas deNeve, Matthias Thielmann, Martin H. Bernardi, Nandor Marczin, Ulf Guenther, Bernd Panholzer, Heinrich Maechler, Steven Hunte, Michael Schmoeckel

Schmoeckel et al. Journal of Cardiothoracic Surgery (2025) 20:74 https://doi.org/10.1186/s13019-024-03326-1

Journal of Cardiothoracic Surgery

RESEARCH Open Access

Direct-acting oral anticoagulant removal by intraoperative hemoadsorption in CABG and/or single valve surgery: interim analysis of the International Safe and Timely Antithrombotic Removal (STAR) registry

Michael Schmoeckel, Matthias Thielmann, Keti Vitanova, Thomas Eberle, Nandor Marczin, Kambiz Hassan, Andreas Liebold, Sandra Lindstedt, Georg Mächler, Marijana Matejic-Spasic, Daniel Wendt, Efthymios N. Deliargyris and Robert F. Storey

Abstract

Objective Patients on direct-acting oral anticoagulants (DOACs) are at high risk of perioperative bleeding complications. Intraoperative hemoadsorption is a novel strategy to reduce perioperative bleeding in patients on DOACs undergoing non-deferable cardiac surgery. The international STAR-registry reports real-world clinical outcomes 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 DOACs undergoing CABG and/or single valve surgery before completing the recommended washout were included. Outcome measurements included bleeding events according to standardized definitions and 24-hour chest-tube-drainage (CTD).

Results A total of 62 patients were included from 7 institutions in Austria, Germany, Sweden, and the UK (mean age 69.9 ± 7.5years, 71% male). Approximately half were on apixaban and the other half was split between rivaroxaban and edoxaban with 21% of patients also on aspirin. Surgery occurred at a median time of 28.9 h since the last DOAC dose with single valve surgery accounting for 2/3 of cases. Mean CPB duration was 118.6 ± 46.4 min. Severe bleeding (UDPB ≥ 3) occurred in 4.8%, and BARC-4 bleeding occurred in 3.2% 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 38th EACTS Annual Meeting in Lisbon, Portugal, Oct 9–12, 2024.

*Correspondence: Michael Schmoeckel michael.schmoeckel@med.uni-muenchen.de

Full list of author information is available at the end of the article

BMC

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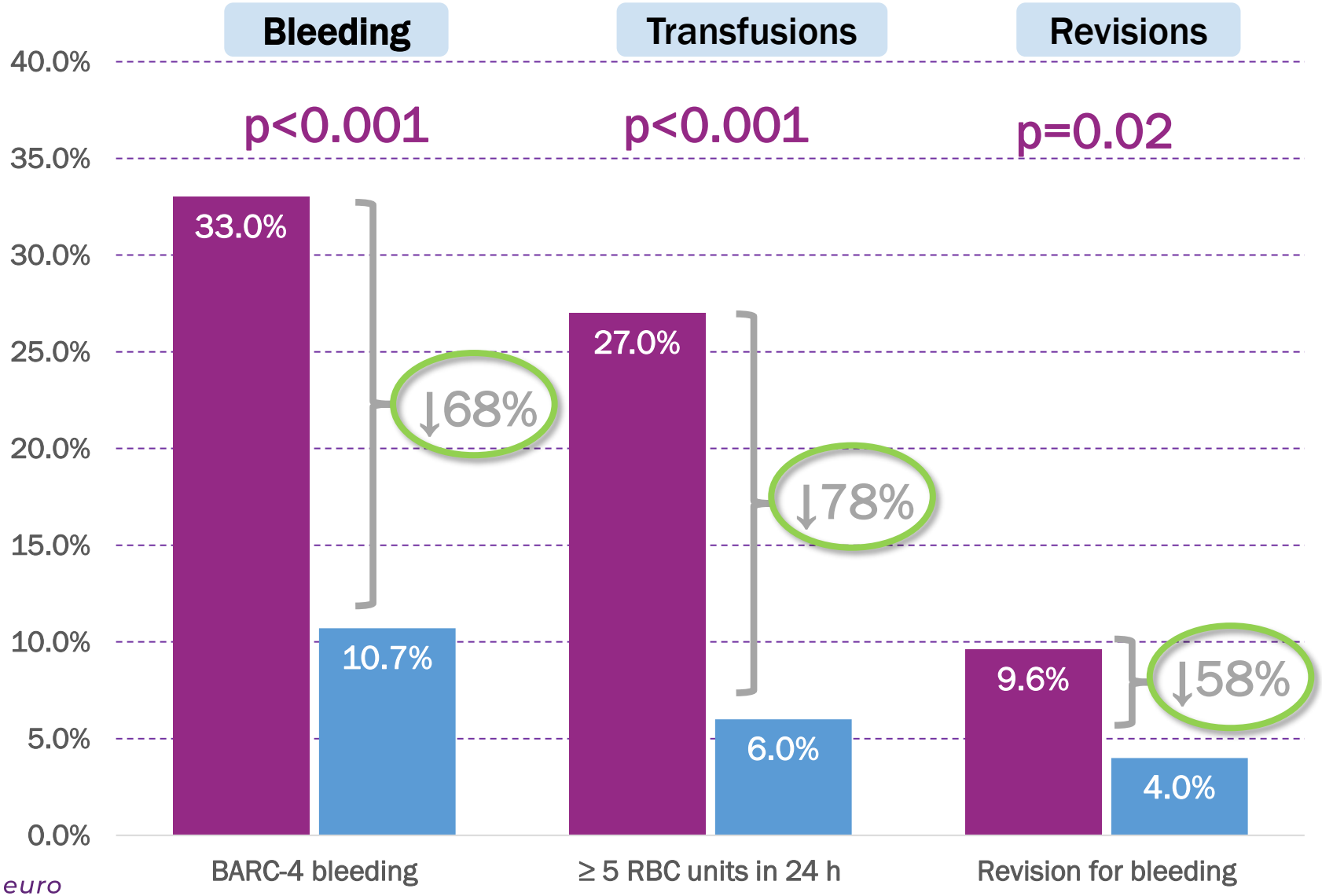
 DrugSorb-ATR and CytoSorb are investigational medical devices in the U.S. and Canada and are not yet cleared or approved.

Statistically and Clinically Significant Impact on Bleeding



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

- **Control (n=644)#**
- **Device (n=150)****

#Schoerghuber, M., et al. Eur J Cardiothorac Surg, 2024
*STAR Registry

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
- We continue to expect final regulatory decisions in U.S. and Canada in 2025

 DrugSorb-ATR is an investigational medical device in the U.S. and Canada and is not yet cleared or approved.

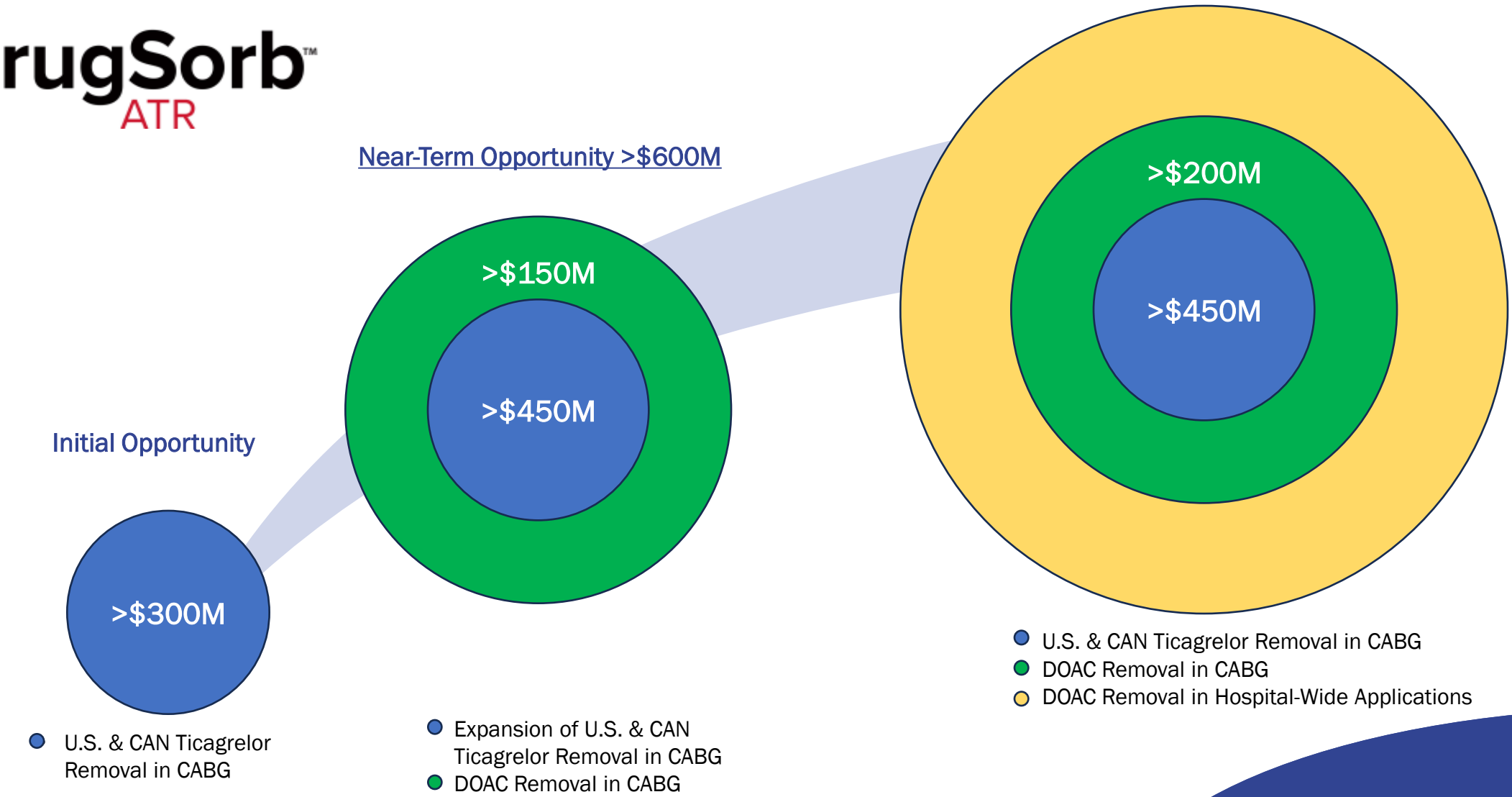
Large Total Addressable Market

DrugSorb™ ATR

Initial Opportunity

Near-Term Opportunity >$600M

Future Opportunity
$1+ Billion



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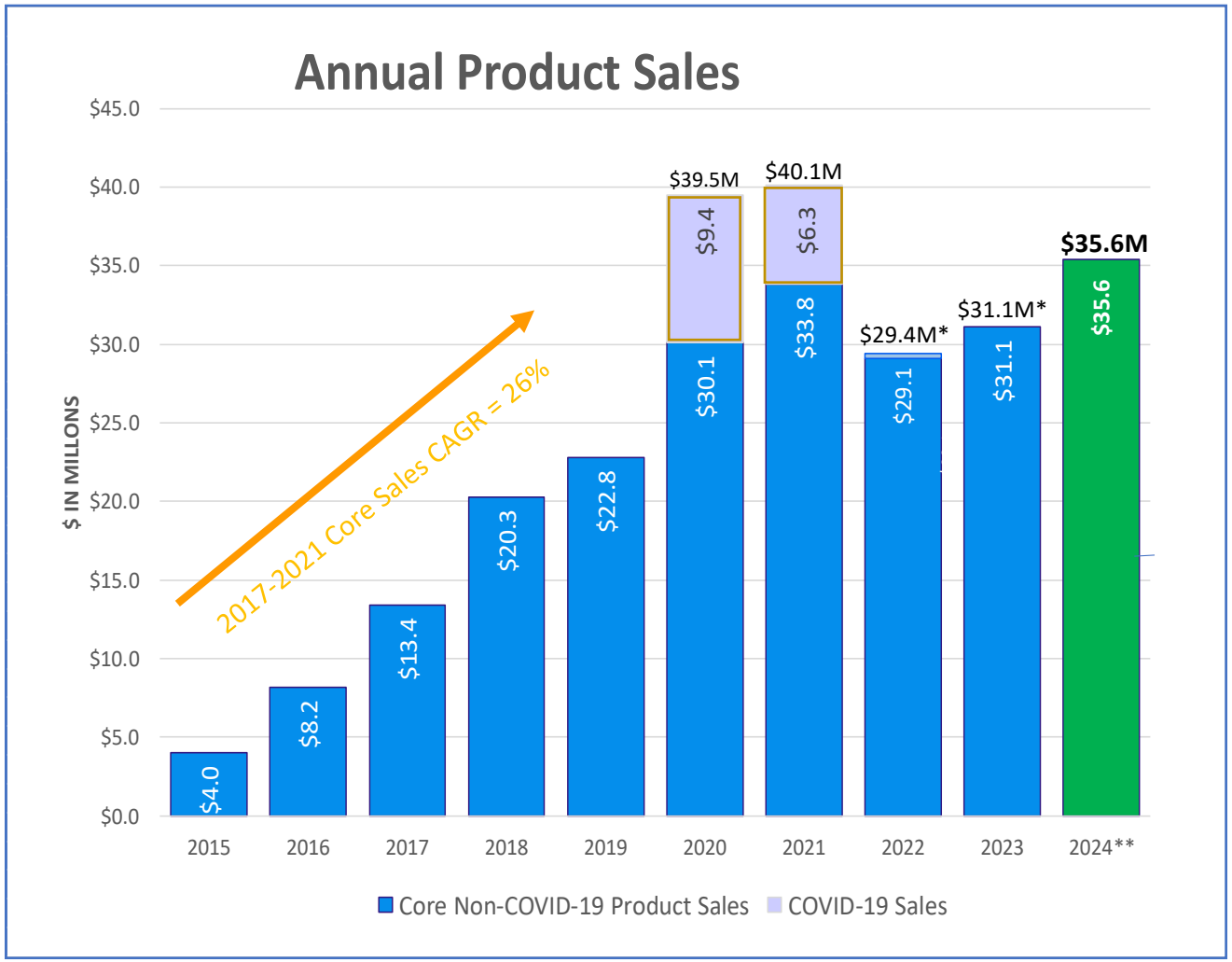
Financial Performance

CytoSorbents™

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%

** Constant currency revenue growth

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

- $7.85 million received from successful Rights Offering in Q1 2025 that unlocked $5.0M in restricted cash on our balance sheet
- $13.1 million in cash, cash equivalents and restricted cash at March 31, 2025
- $1.7 million received in April 2025 from Sale of NJ NOL and R&D tax credits
- $5.0 million second tranche available at our option on our debt agreement with FDA marketing authorization

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™

CytoSorbents Corporation

NASDAQ: CTSO

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