

# CytoSorbents™



HELPING REDUCE DEADLY UNCONTROLLED INFLAMMATION IN HOSPITALIZED PATIENTS WORLDWIDE

NASDAQ: CTSO

Canaccord Genuity Medical Technologies & Diagnostics Forum

November 15, 2018

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# CytoSorbents is a Leader in Critical Care Immunotherapy



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

# CytoSorbents **At a Glance**

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- NASDAQ-traded (CTSO): ~\$10.00 per share. ADTV ~230K shares per day, ~\$2.3M value
- CytoSorb<sup>®</sup>, is E.U. approved, with 51,000+ treatments; distributed in 53 countries
- \$19.1M in trailing 12-month product sales (from \$11.7M). 72% blended product gross margins. Healthy cash balance of \$24.9M (9/30/18)
  - 2017 Deloitte Technology Fast 500 and Frost & Sullivan Global Blood Purification award
- 110 employees with international footprint across two wholly-owned subsidiaries
  - CytoSorbents Medical, Inc - New Jersey, USA
    - Headquarters, ISO 13485 manufacturing, QA/QC, R&D
  - CytoSorbents Europe GmbH: International sales office - Berlin, Germany
- Strategic Partnerships with Fresenius Medical Care, Terumo, Biocon, and Dr. Reddy's
- Strong government support with ~\$25M in grants, contracts, other non-dilutive funding
- Russell 2000 & 3000 listed with coverage by Cowen, B Riley, HCW, Aegis, Maxim, Zacks
- ✓ **Expecting rapid growth and quarterly operating profitability in Q4 2018**
- ✓ **On path to potential U.S. approval with U.S. REFRESH 2 pivotal trial in cardiac surgery**

# Uncontrolled Inflammation is Deadly



# Massive Inflammation Causes Organ Failure

Organ failure occurs when vital organs stop working,  
**causing nearly half of all deaths in the ICU.**



Little can be done to prevent or treat organ failure today

# No Ideal Options to Treat Severe Inflammation

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## **Anti-Inflammatory (too weak)**

**NSAIDs**

**Aspirin**

**Anti-cytokine  
antibodies**

**Anti-integrin  
antibodies**

**Anti-oxidants**

## **Immunosuppressive (too strong)**

**Corticosteroids**

**Chemotherapy**

**Organ transplant  
Anti-rejection drugs**

**Radiation**

**Immune system  
ablation**

**Anti-leukocyte Abs**

# CytoSorb Bridges the Gap

## Anti-Inflammatory (too weak)

NSAIDs

Aspirin

Anti-cytokine  
antibodies

Anti-integrin  
antibodies

Anti-oxidants



## Immunosuppressive (too strong)

Corticosteroids

Chemotherapy

Organ transplant  
Anti-rejection drugs

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Immune system  
ablation

Anti-leukocyte Abs

# CytoSorb® Reduces the Fuel to the Fire

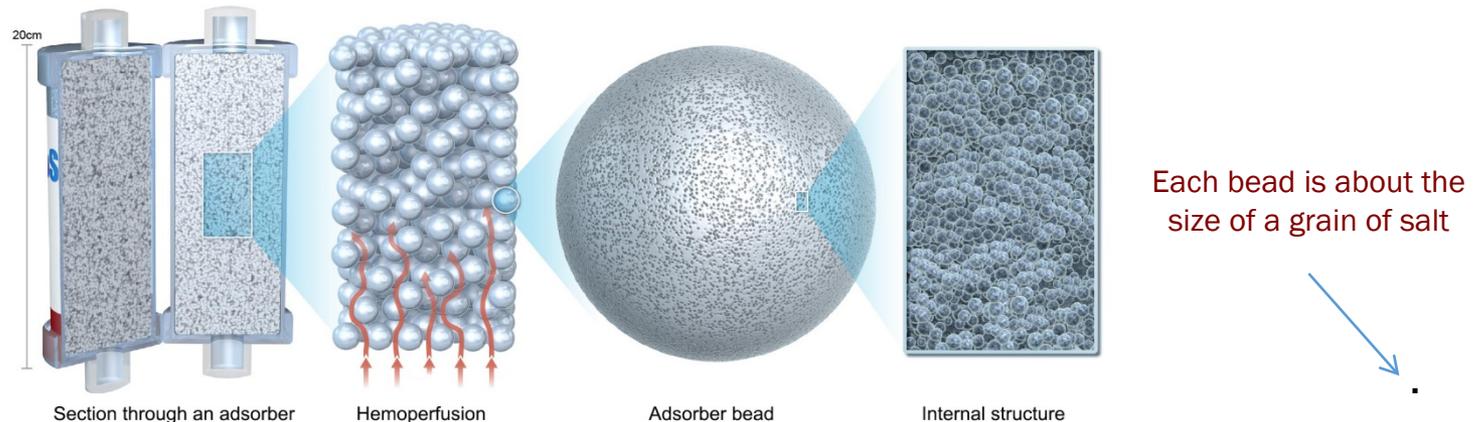
- CytoSorb® targets the \$20+ billion opportunity in critical care and cardiac surgery
- Approved in the European Union as the first specifically approved extracorporeal cytokine adsorber
- Broad indication for use where cytokines are elevated
- Removes cytokines and many other inflammatory mediators such as free hemoglobin, bacterial toxins, myoglobin, and activated complement
- Safe and well-tolerated: 51,000+ cumulative treatments delivered, up from 31,000 a year ago



\*CytoSorb is not yet approved in the U.S.

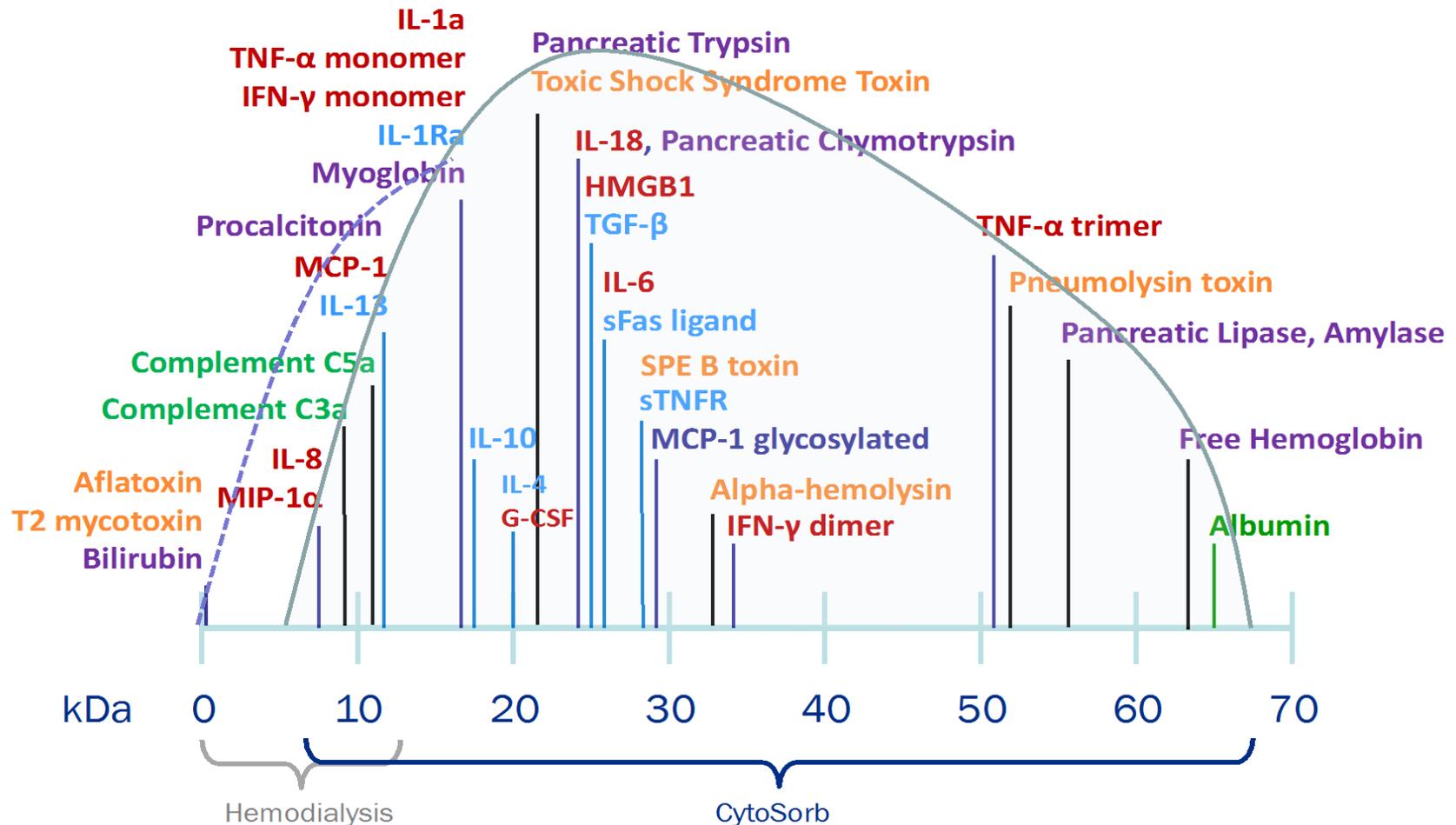
# Patented Blood Purification Technology

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



- Proprietary patented technology with multiple patents pending worldwide
- Manufactured at our ISO 13485 certified facility in New Jersey
- One of the highest grade medical sorbents on medical market today

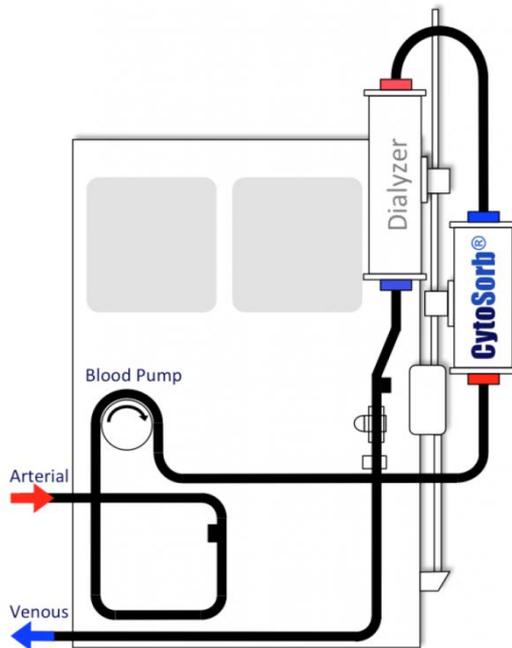
# CytoSorb® Is Active in Cytokine Sweet Spot



CytoSorb has been shown to adsorb a wide range of inflammatory mediators, including bilirubin, free hemoglobin, bacterial toxins, and other PAMPs and DAMPs. Dotted line shows removal primarily based on adsorption

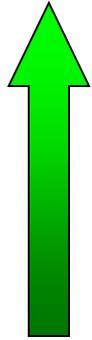
# CytoSorb is “Plug and Play”

## Compatible with Existing Dialysis and Heart-Lung Machines

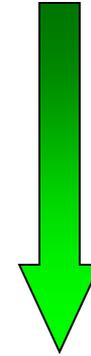


- Place a temporary dialysis catheter in a major vein
- Connect the device to a standard dialysis, ECMO, or heart-lung machine found in hospitals worldwide
- Pump blood out of the body and through the cartridge
- The polymer beads directly contact blood and remove unwanted or toxic substances
- “Purified” blood is pumped back into the patient
- Can treat 70+ total blood volumes per 24 hour treatment
- Each treatment uses a new cartridge

# Goal: To Prevent or Treat Organ Failure

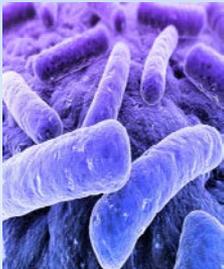


Improve  
Patient  
Outcome  
and  
Survival

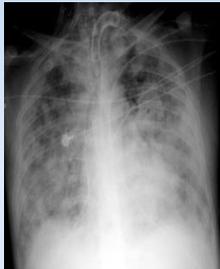


Decrease  
Costs Of  
ICU and  
Patient  
Care

Sepsis



ARDS



Burn Injury



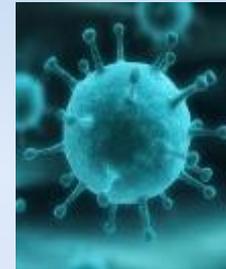
Trauma



Pancreatitis



Influenza



Surgical



The Potential to Revolutionize Critical Care Medicine

# Refractory Septic Shock

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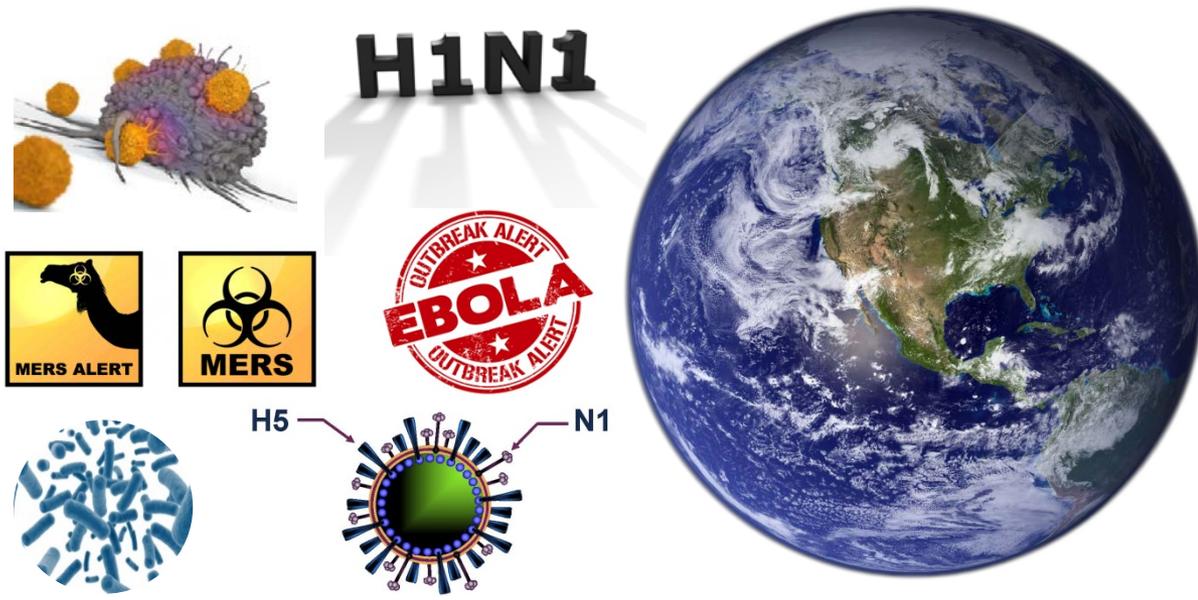
Prospective, single arm study in 20 patients with refractory late-stage septic shock using CytoSorb aggressively every 12 hours with a new cartridge

- Patients had refractory shock despite high doses of vasopressors, respiratory failure requiring mechanical ventilation, oligo-anuric kidney failure requiring dialysis, and lactate > 8 mmol/L
- Results from the CytoSorb Greifswald Study
  - Resolution of shock in 65% of patients treated with CytoSorb
  - 28-day survival was 45%, a 30-40% absolute improvement over expected (0-10%)
  - Reduction of IL-6 from an initial average of 87,000 pg/mL to below 10,000 pg/mL after 24 hours of treatment
- A similar population (n=16) receiving standard of care but no CytoSorb therapy, where shock could not be reversed, also on mechanical ventilation with an initial lactate level of  $6.1 \pm 4$  mmol/L, and 75% requiring renal replacement therapy had a mortality of 100% at 28 days.\*

- Conrad, M., et. al., "Early prediction of norepinephrine dependency and refractory septic shock with a multimodal approach of vascular failure", J Crit Care, 2015; 30:739-743.
- Friesecke, S, et.al., "Extracorporeal cytokine elimination as rescue therapy in refractory septic shock: a prospective single center study", J Artif Organs 2017 Sep; 20(3):252-259.



# The World Needs CytoSorb®



**Hospital Stays for Sepsis Appear to Be Rising Dramatically**  
Experts say cases of sepsis may have been undercounted for years

**Recognizing Sepsis as a Global Health Priority — A WHO Resolution**  
Konrad Reinhart, M.D., Ron Daniels, M.D., Niranjan Kissoon, M.D., Flavia R. Machado, M.D., Ph.D., Raymond D. Schachar, L.L.B., and Simon Finfer, M.D.

"Some very impressive digital... the world have died prematurely... code" in the Global Burden of Disease statistics, where more deaths due to sepsis are classified as being caused by the underlying infection, improving the coding

WHO Healthcare Cost and Utilization Project

**Bloomberg**

**America Has a \$27 Billion Sepsis Crisis**



# CytoSorb

51,000+ Treatments

53 Countries Worldwide with E.U.

Critical Care

Cardiac Surgery

United States

Cardiac Surgery



60+ Investigator Initiated Studies



# CytoSorb® Is Like a High Margin Razorblade

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- High margin “razorblade” fully compatible with existing installed base of “razor” blood pumps: Dialysis/CRRT, ECMO machines (ICU), heart-lung machines (OR)
- Blended gross margins are 72%, expected to rise with volume production from new plant that came on-line June 2018
- Average Direct Selling Price is approximately \$1,000 per cartridge
- Approximately 1 - 10 cartridges are typically used per patient
  - Open heart surgery: 1-2 cartridges
  - Sepsis: 3-5 cartridges or roughly 1 day in the ICU
- 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
- In 2016, one German hospital achieved sales >\$1M, validating revenue model

# Direct Sales: Focused on 5 Countries

CytoSorbents' direct sales force focused on most major university and public hospitals in Germany, Austria, Switzerland, Belgium and Luxembourg. German market alone is \$1.0-1.5 billion



**Dr. Christian Steiner, MD**  
Vice President – Sales and Marketing and General Manager  
CytoSorbents Europe GmbH



**Stefan M. Baudis**  
International Sales Director



**Dr. Joerg Scheier, MD**  
Senior Medical Director Europe



**Dr. Volker Humbert, MD**  
Senior Manager - Clinical Affairs



**Franziska Preissing**  
Senior Manager – Reimbursement & Health Economics



**Patrick Waltrich**  
Senior Manager – Finance/Operations



**Kristin von Hammerstein**  
Marketing Manager



**Dominik Gutzler**  
Head of Product Management



**Dr. Rainer Kosanke, PhD**  
Director Scientific Affairs Europe



**Alexandru Bojan**  
Regional Sales Director



**Bettina Sabisch**  
Regional Sales Director



**Christian Tembaak**  
Regional Sales Director



**Winfried Dramburg**  
Regional Sales Director



**Uwe Gerks**  
Sales Director  
Central Europe



**Hans-Juergen Kraus**  
Regional Sales Manager  
Southern Germany



**Matthias Hoeldtke**  
Regional Sales Manager  
Southeast Germany



**Andreas Gassmann**  
Sales Representative  
Southern Germany



**Christian Koptik**  
Regional Sales Manager  
Austria



**Daniel Gadke**  
Regional Sales Manager  
Northern Germany



**Martin Heinzinger**  
Regional Sales Manager  
Central Germany



**Christin Preiss**  
Executive Admin



**Martin Scherer**  
Regional Sales Manager  
Southwest Germany



**Andreas Pendleder**  
Regional Sales Manager  
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**Marco Dietrich**  
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Northeast Germany



**Oliver Lupoli**  
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**Harriet Adamson**  
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**Eva Wechsler**  
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**Anke Applehoff**  
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**Pamela Leckie**  
Application Specialist  
International



**Paolo Balboni**  
Application Specialist  
International



**Petra Hoffman**  
Sales Assistant/Customer Support



**Fernanda Goncalves Zawieja**  
Sales Assistant/Customer Support



**Jaqueline Bloch**  
Sales Assistant  
Customer Support

# Dedicated Reimbursement In Germany

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- CytoSorb achieved a permanent, dedicated reimbursement code in Germany
  - Most important market and the largest medical device market in Europe and third largest in the world
- Was achieved rapidly through the initiative and strong support of several major medical societies across different medical specialties, helping to demonstrate the broad support of our therapy by physicians in the country
- Reimbursement rate was negotiated by individual hospitals in 2017, resulting in significantly higher reimbursement in most many hospitals
- We expect direct sales momentum to accelerate as the impact of this higher reimbursement is being felt
- Meanwhile, CytoSorb has now been awarded a specific procedural code in Switzerland, that awaits payment negotiations

# CytoSorb® Distributed in 53 Countries



Dr.Reddy's



HOANG LONG PHARMA

IntensivMed

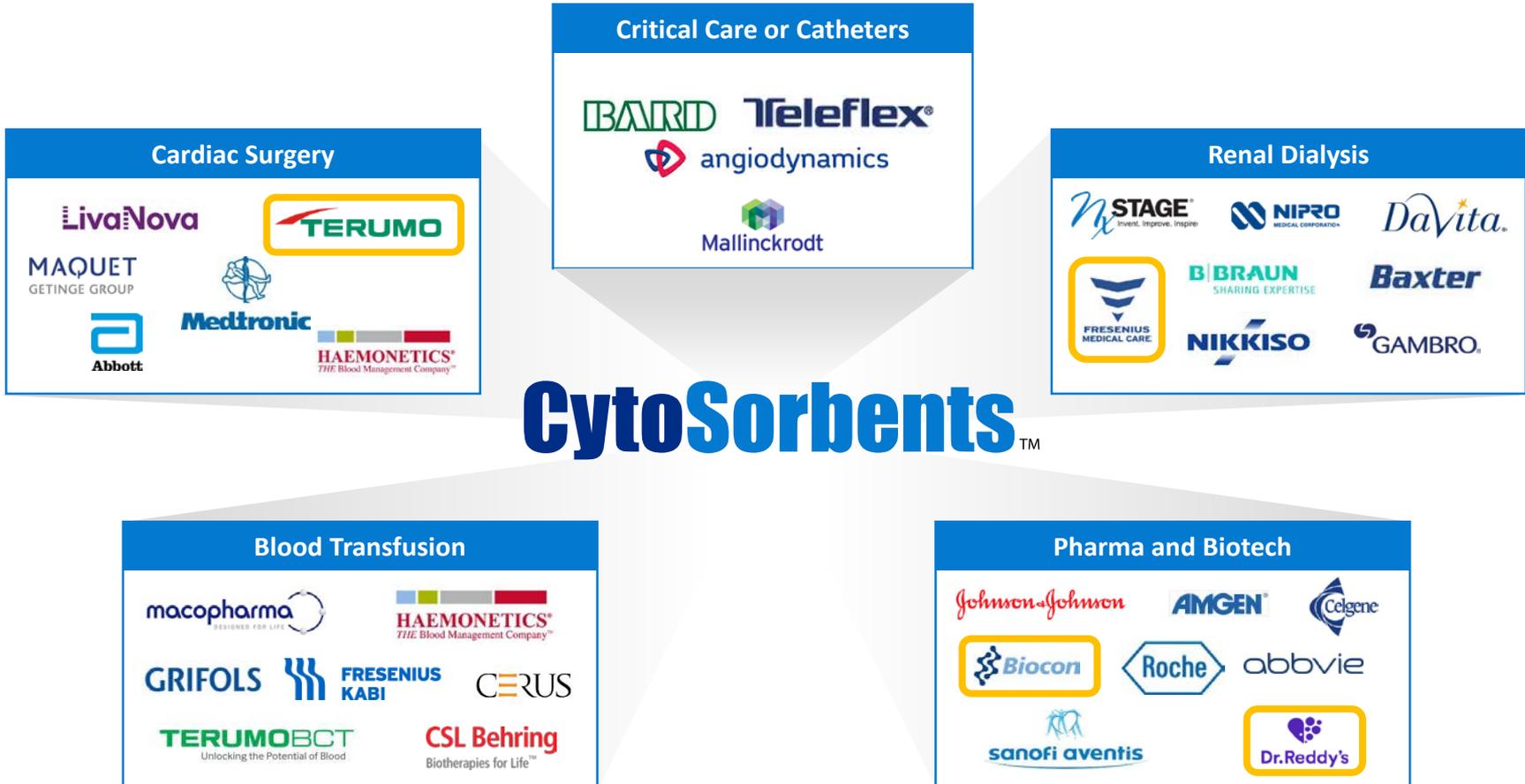


TekMed



WMC

# Four Major Partnerships, Potential for More



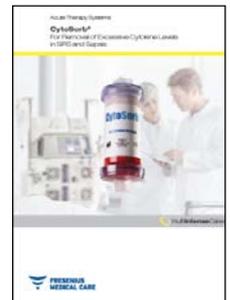
Partnered with leading multinational corporations:

Fresenius Medical Care, Terumo Cardiovascular, Biocon Ltd, and Dr. Reddy's Laboratories

\* Companies listed here are used simply as examples of companies in these respective verticals. We make no other representations as to our relationship with any of these companies.

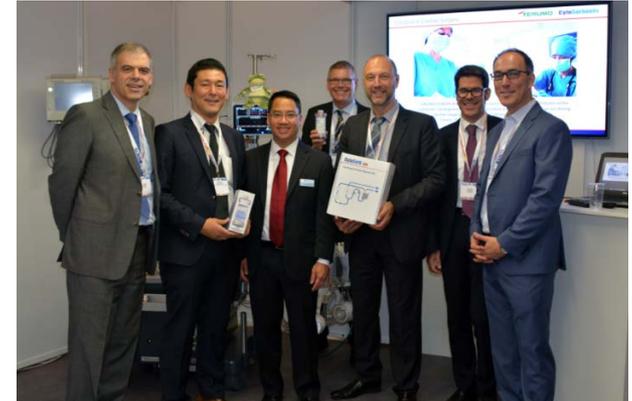
# Fresenius Co-Marketing Critical Care Partnership

- CytoSorbents renewed and expanded its partnership with Fresenius Medical Care in January 2017
- Extension on exclusive distribution of CytoSorb for critical care applications in France, Poland, Denmark, Norway, Sweden, and Finland through 2019
- Guaranteed minimum quarterly orders and payments of CytoSorb evaluable every 1.5 years
- Co-marketing agreement across all of the countries where CytoSorb is sold, where possible
  - Adds to the “effective” sales force in each country
  - Fresenius has provided written endorsement of CytoSorb for the multiFiltrate platform



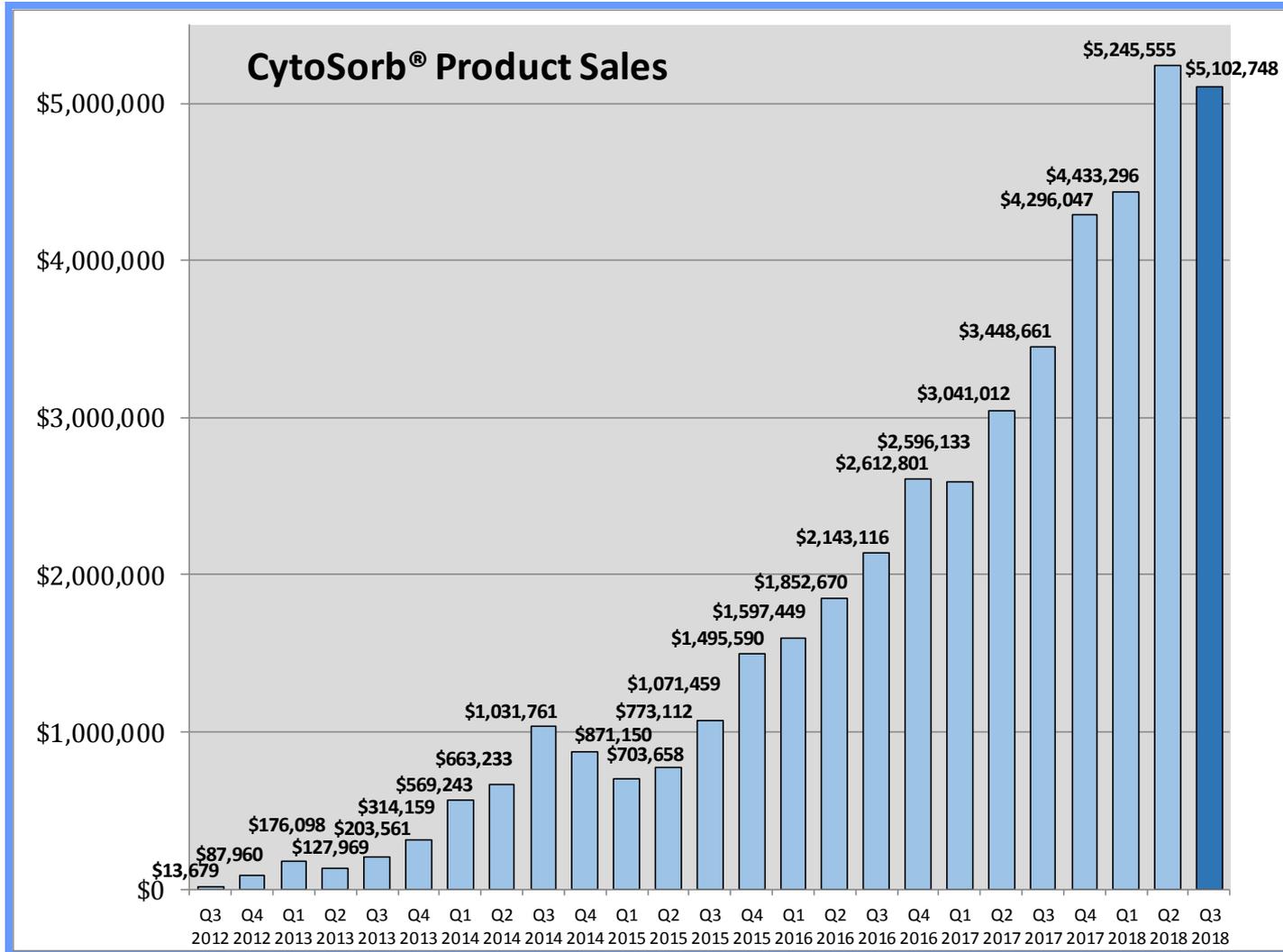
**We are working with Fresenius in 11 countries and plan to ramp up to other countries soon**

- Entered into a multi-country strategic partnership with Terumo Cardiovascular Group, a global leader in medical devices for cardiac and vascular surgery
- Initial exclusive distribution of CytoSorb® CPB Procedure Pack for intra-operative use during cardiac surgery in France, Denmark, Norway, Sweden, Finland, and Iceland
- Launched December 2016
- We believe this strategic partnership opens the door to potential expansion to other countries, such as Japan – the second largest medical device market in the world



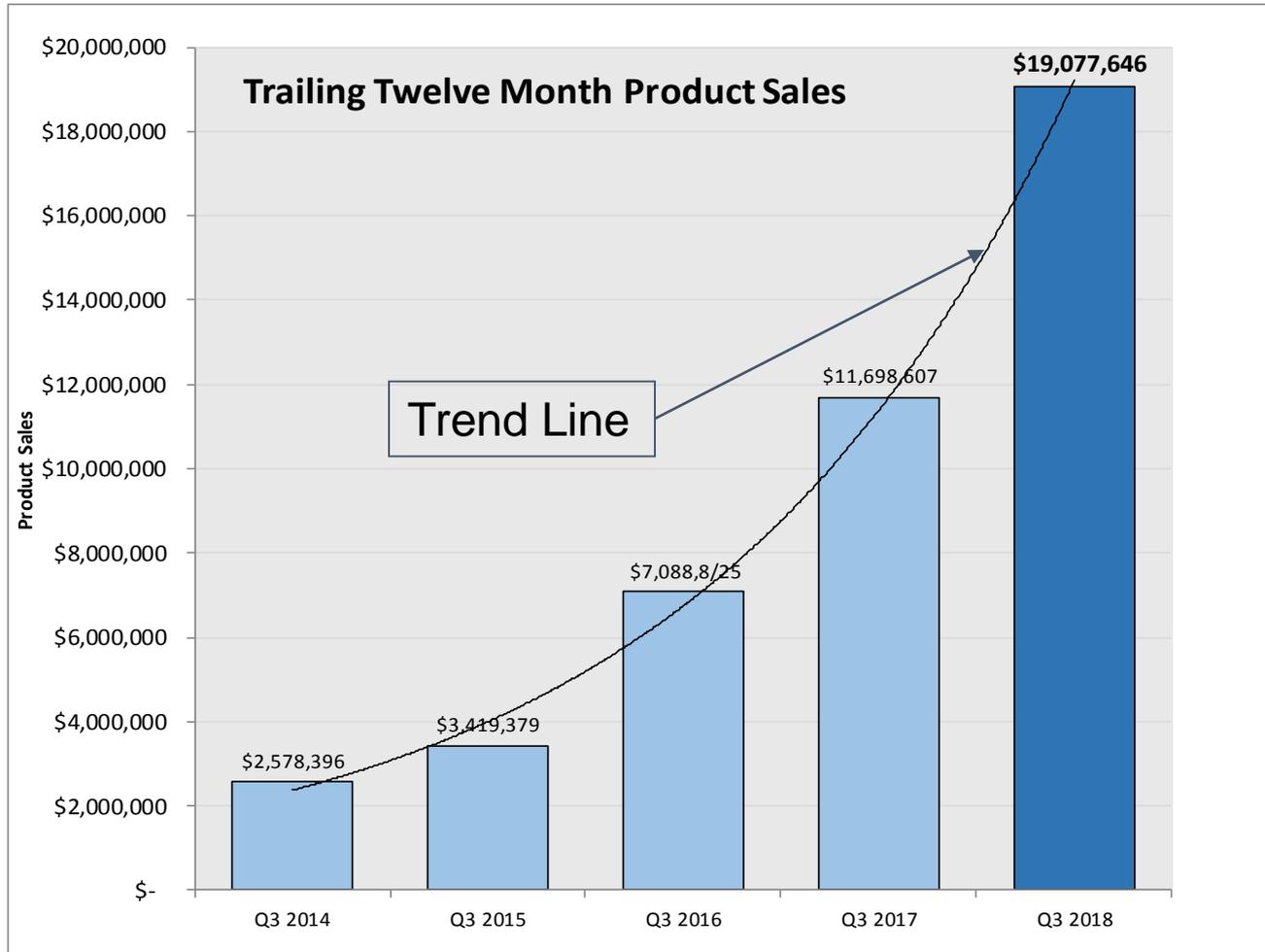
# Quarterly Product Sales

25 Consecutive Quarters of Year-over-Year Sales Growth



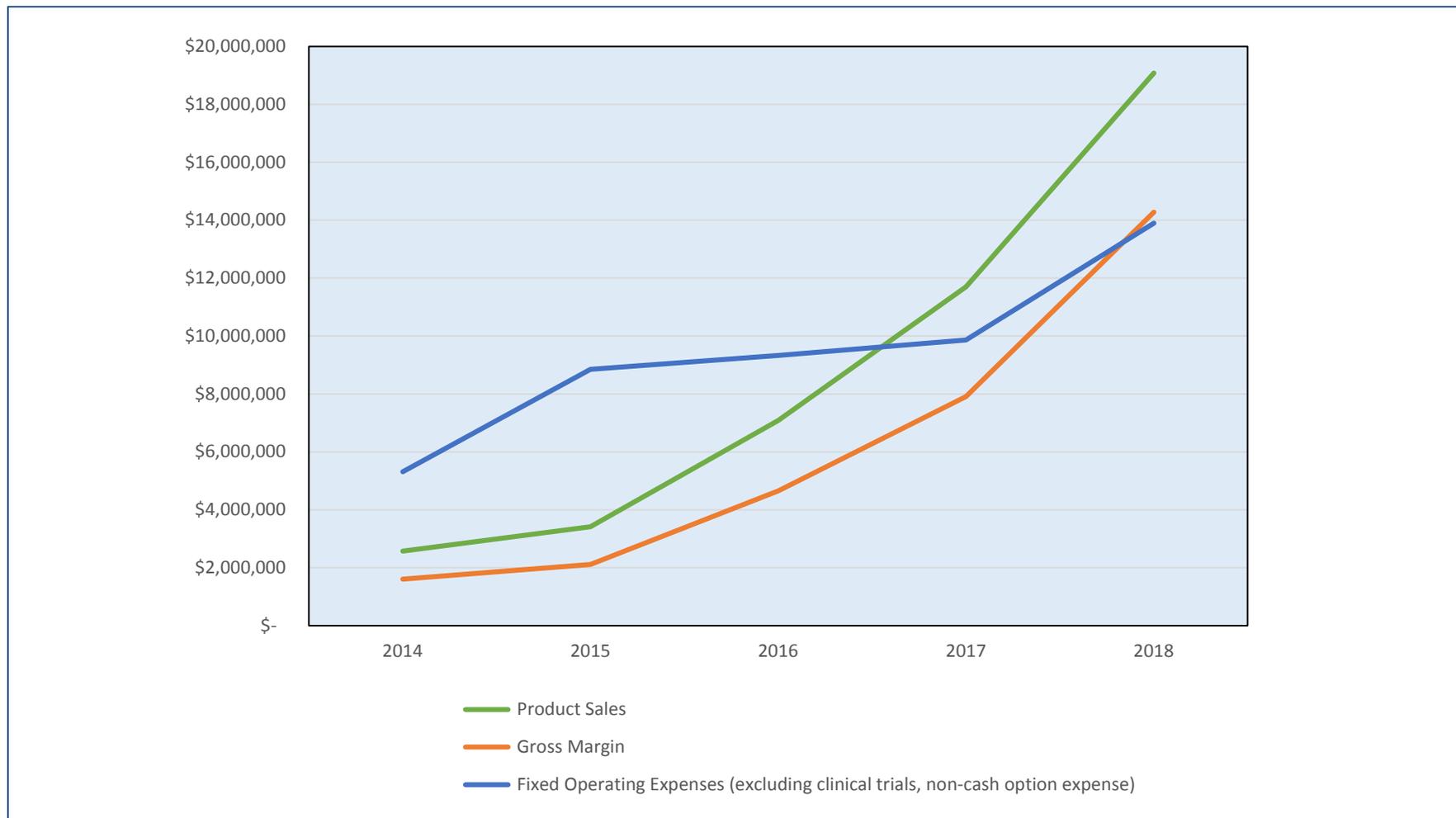
# Trailing Twelve Months Product Sales

Over the past three years, the compound growth rate of return (“CAGR”) on product sales was 77%



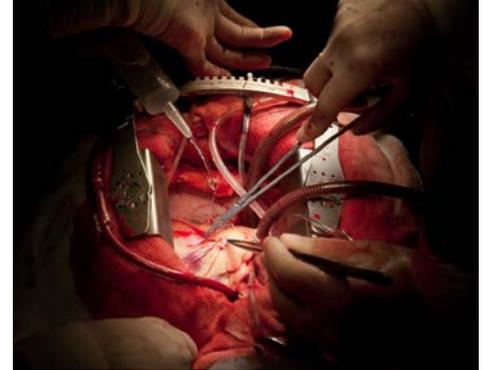
# Driving Toward Operating Breakeven

## Trailing Twelve Months Key Performance Indicators



# U.S. Approval Targets Cardiac Surgery

- Heart disease is the leading cause of death worldwide driven by smoking, unhealthy lifestyles, and an aging baby boomer population
- ~1M cardiac surgeries performed annually in U.S. and E.U.
  - Coronary artery bypass graft surgery
  - Valve repair or replacement
  - Heart or lung transplantation
  - Congenital defect repair
  - Aortic reconstruction
- Complex cardiac surgeries require long heart-lung machine pump times, causing:
  - ↑ Hemolysis and free hemoglobin
  - ↑ Inflammatory mediators, cytokines, and activated complement



**Severe inflammation, nitric oxide scavenging, and reduced blood flow can lead to kidney, lung, and/or heart failure in many patients following surgery**

# U.S. REFRESH 1 Trial

## REduction in FREe Hemoglobin



- 46-patient, eight-center trial evaluating the safety and efficacy of intra-operative use of CytoSorb® in a heart-lung machine during elective, non-emergent complex cardiac surgery with heart-lung machine time  $\geq 3$  hours

- Working with major cardiac surgery centers

- Baylor and Texas Heart Institute
- Baystate Medical Center
- Columbia University
- Cooper University Hospital
- University of Kentucky
- University of Maryland
- University of Pennsylvania
- University of Pittsburgh

CPB Length	Mean Reduction of pfHb (mg/dL)	P-value
3.0	35 mg/dL	0.09
3.5	48 mg/dL	0.05
4.0	61 mg/dL	0.05
4.5	74 mg/dL	0.07

- First RCT using CytoSorb in high risk cardiac surgery

- Demonstrated safety
- Identified valve replacement patients who are the highest levels of peak pfHb
- Demonstrated that CytoSorb significantly reduces pfHb by 35-40% and activated complement during treatment in this population

- Data from the REFRESH 1 Trial was selected for podium presentation at the American Association of Thoracic Surgery (AATS) conference in May 2017 and was submitted for publication

# REFRESH 2 - AKI Targets US Approval



Pivotal, multi-center RCT using CytoSorb intraoperatively to reduce the incidence or severity of acute kidney injury (AKI) in high risk cardiac surgery

- The development of even mild AKI after surgery predicts 1 and 5 year mortality and progression to chronic kidney disease
- Trial design approved by FDA:
  - Up to 400 patient, 20-25 center 1:1 randomized, controlled PMA trial in elective, valve replacement or aortic reconstruction with hypothermic cardiac arrest, enriched for risk of kidney injury
  - Intervention: Standard of care (control) or Standard of care + CytoSorb intraoperatively
  - Primary endpoint: Postoperative acute kidney injury (AKI)
  - Secondary clinical and cost-effectiveness endpoints: Reduction in other organ injury (incidence of stroke, time on mechanical ventilation, hemodynamic stability), days in the ICU
  - Expected study completion: 2020 with potential 2021 FDA approval
  - Cost: Approximately \$12M spread out over 3 years
- Recent protocol amendment approved by FDA and trial site ethics committees
  - 14 active sites, with six additional sites to be added soon – targeting 25 total trial sites
  - 20 patients already enrolled, target enrollment 1 patient per site per month

# German Govt Funding REMOVE Endocarditis Trial

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- Infective endocarditis (heart valve infection) occurs when bacteria seeds a heart valve from IV drug abuse and dirty needles, or from dental procedures
- The incidence of endocarditis is rising due to the opiate crisis
- Patients often require open heart surgery valve replacement but are very hemodynamically unstable before, during, and after surgery due to a combination of sepsis and heart valve destruction
- Intraoperative CytoSorb has been used to help stabilize such patients peri-operatively with good success
- The German Federal Ministry of Education and Research is funding a 250 patient, multi-center, randomized, controlled study (REMOVE) using CytoSorb during valve replacement open heart surgery in patients with infective endocarditis
- Primary endpoint is improvement of SOFA score
- Enrolled 62 patients to date. Interim analysis on reduction of inflammatory mediators planned on first 50 patients

# Expanded Label Targets Liver Failure and Trauma

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Recently received European approval to expand the use of CytoSorb in liver disease to reduce bilirubin, and in trauma to reduce myoglobin – both very large 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, and another 1 million from hepatic cancer
- CytoSorb has been used as a liver dialysis therapy in numerous acute exacerbations of liver disease including acute-on-chronic liver failure, alcoholic hepatitis and others showing both bilirubin and bile acid reduction, and important clinical benefits such as hepatic coma reversal

- **Trauma**

- 56 million hospitalizations in trauma worldwide each year with approximately 5 million deaths. Severe crush injury of muscle releases myoglobin, called rhabdomyolysis, which can precipitate kidney failure, and increase the risk of death

# CAR-T Cell Immunotherapy and CRS

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- CAR-T cell cancer immunotherapy is a blood cancer treatment breakthrough.
- However, ~40-50% of patients can develop severe, high grade cytokine release syndrome (CRS), a cytokine storm that can lead to rapid organ failure and potentially death
- CytoSorb® was specifically designed to control cytokine storm and CRS and has already successfully treated a dozen cases of the closely related disease hemophagocytic lymphohistiocytosis (HLH)
- With FDA and E.U. approvals of Kymriah (Novartis) and Yescarta (Gilead), we are positioning CytoSorb® to be used as an alternative to, or in conjunction with, tocilizumab and steroids
- In 2017, the pioneer of CAR T-cell immunotherapy, Dr. Carl June at University of Pennsylvania, joined our Scientific Advisory Board



# HemoDefend Nearing U.S. Pivotal Trial

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- 100M pRBC units transfused each year worldwide, each carrying a risk of transfusion reactions on the order of 1-3%
- HemoDefend pRBC is a point-of-transfusion in-line filter designed to improve the safety and quality of the blood supply by reducing non-infectious contaminants like antibodies, cytokines, bioactive lipids, free hemoglobin, and others that can cause transfusion reactions
  - Ranges from fever and allergic reactions, to transfusion related acute lung injury (TRALI) – the leading reported cause of transfusion related death that occurs in 1 to 5,000 transfusions
- The development of HemoDefend pRBC has been generously supported with nearly \$5M in funding by National Heart, Lung, and Blood Institute (NHLBI – a division of NIH), and U.S. Special Operations Command (USSOCOM)
- On track to initiate a pivotal study in early 2019 that is designed to support U.S. approval

# Upcoming Milestones

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- Ongoing progress in international sales
- Operating profitability targeted in Q4 2018 with blended product gross margin expansion to 80% in 2019
- Potential new partnerships and expansion of existing partnerships
- Ramping of pivotal REFRESH 2-AKI study
- Early 2019 start to HemoDefend pivotal US Trial
- Publications of clinical and research data
- Greater institutional ownership (currently at 25%) and expanded analyst coverage



# CytoSorbents Investment Summary

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CytoSorbents is strongly positioned and on track to have strong growth in 2018

- Established, well-run U.S. medtech but with a biotech profile, nearing critical mass
- Strategically positioned to address some of the largest, most visible, unmet medical needs worldwide in critical care, cardiac surgery, cancer immunotherapy, and others
- Highly profitable “razorblade” in someone else’s “razor” business model
- Significant CytoSorb® sales growth and expected gross margin expansion and near-term operating profitability
- Excellent validation by customers, partners, and government agencies
- Gaining momentum in institutional ownership and poised for greater awareness
- Creating optionality on multiple potential exits for investors



***Providing Hope  
in a helpless situation***



HELPING PATIENTS SURVIVE CRITICAL ILLNESSES WORLDWIDE



**CytoSorbents™**

Working to Save Lives Through Blood Purification

NASDAQ: CTSO

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