

# CytoSorbents Corporation

OTCBB: CTSO

An Emerging Leader in  
Critical Care Immunotherapy

Q2 2014 Review – August 12, 2014



# Safe Harbor Statement

Statements in this presentation regarding CytoSorbents Corporation and its operating subsidiary CytoSorbents, Inc 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; 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 Form 10-K filed with the Securities and Exchange Commission on March 31, 2014 and other reports and documents filed from time to time by us, which are available online at [www.sec.gov](http://www.sec.gov).



**CytoSorbents**

Working to Save Lives Through Blood Purification

# Conference Call Participants

Dr. Phillip Chan, MD, PhD

Chief Executive Officer and President

Vincent Capponi, MS

Chief Operating Officer

Kathleen Bloch, MBA, CPA

Chief Financial Officer

Dr. Christian Steiner, MD

Vice President of Sales and Marketing

Christopher Cramer, MS, MBA

Vice President of Business Development  
(Absent)

**Moderator: Amy Vogel – CytoSorbents Corporation**

# **CytoSorbents** is an Emerging Leader in the \$20B Critical Care Immunotherapy Space



Leading the Prevention or Treatment of Life-Threatening Inflammation in the ICU



**CytoSorbents**

Working to Save Lives Through Blood Purification

# Inflammation Plays a Major Role in Nearly Every Known Disease

- Life threatening conditions like sepsis & trauma
- Autoimmune diseases like rheumatoid arthritis, inflammatory bowel, psoriasis, and lupus
- Heart disease, peripheral artery disease
- Cancer, cancer cachexia, graft vs host disease
- Neurodegenerative diseases such as Alzheimer's, multiple sclerosis (MS), Parkinson's
- Many, many others

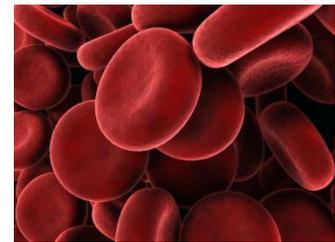


Uncontrolled inflammation wreaks havoc on the body and can be deadly



# Severe Inflammation Drives Organ Failure

Organ failure occurs when vital organs stop working, causing nearly half of all deaths in the ICU, but little can be done to treat or prevent it today



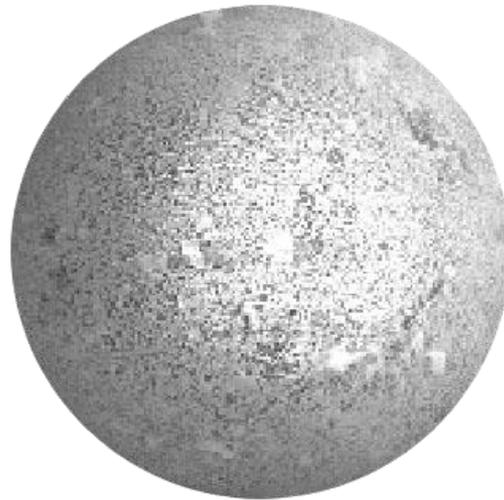
# CytoSorb® Removes the Fuel to the Fire

- CytoSorb® represents a powerful immunotherapy to control inflammation
- Approved in the European Union as the only specifically approved extracorporeal cytokine filter
- Clinically proven to reduce key cytokines in blood in critically-ill patients
- Approved for use in any situation where cytokines are elevated
- Safe: More than 3,000 human treatments, with no serious device related adverse events reported

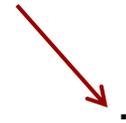


# The Heart of the Technology

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



Each bead is about the size of a grain of salt



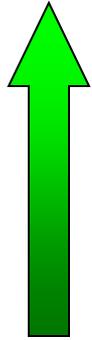
- Protected by 32 issued US patents and multiple applications pending
- Manufactured at our ISO 13485 certified facility in New Jersey
- One of the highest grade medical sorbents on the medical market today



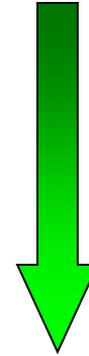
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# Goal: To Prevent or Treat Organ Failure

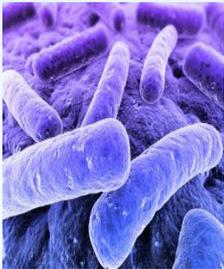


Improve  
Patient  
Outcome  
and  
Survival

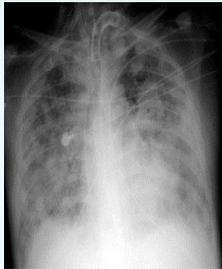


Decrease  
Costs Of  
ICU and  
Patient  
Care

Sepsis



ARDS



Burn Injury



Trauma



Pancreatitis



Influenza



Surgical



The Potential to Revolutionize Critical Care Medicine



**CytoSorbents**

Working to Save Lives Through Blood Purification

# CytoSorb® Marketed in 19 Countries

Available for sale in all 28 countries in the EU. Sold direct in Germany, Austria, and Switzerland. Established distribution in the UK, Ireland, Netherlands, Turkey, Russia, India, Taiwan, and Middle East covering ~1.7 billion lives.

Expanding to other EU countries and countries outside the EU that accept the CE Mark



# \$15+ Million in US Government Support

- DARPA awarded \$3.8M five year (2012-present) contract as part of “Dialysis-Like Therapeutics” program to treat sepsis by removing cytokines and pathogen-derived toxins
- U.S. Army awarded \$1.15M SBIR contracts for trauma and burn injury research (2011-present)
- U.S. Air Force is funding a 30-patient human pilot study in trauma valued at \$3M (2013-present). FDA approved trial that has begun enrollment
- US Dept of Health and Human Services awarded \$0.5M grant (2010) for therapies that can save lives and reduce costs under the QTDP Program
- NIH grant awarded \$7M five year (2006-2010) to University of Pittsburgh and Dr. John Kellum to research CytoSorb bead for treatment of sepsis
- NIH/NHLBI awarded \$0.2M Phase I SBIR to advance the HemoDefend purification technology intended to improve the quality and safety of blood transfusions (2013-present)



# Q2 2014 Operating and Financial Highlights



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# First Half Comparative Revenue Results

|                        | Six Months Ended June 30, 2014 | Six Months Ended June 30, 2013 | % Incr. |
|------------------------|--------------------------------|--------------------------------|---------|
| Product revenue        | \$ 1,232,476                   | \$ 304,067                     | 305%    |
| Grant and other income | 854,351                        | 358,746                        | 138%    |
| Total revenue          | \$ 2,086,827                   | \$ 662,813                     | 215%    |

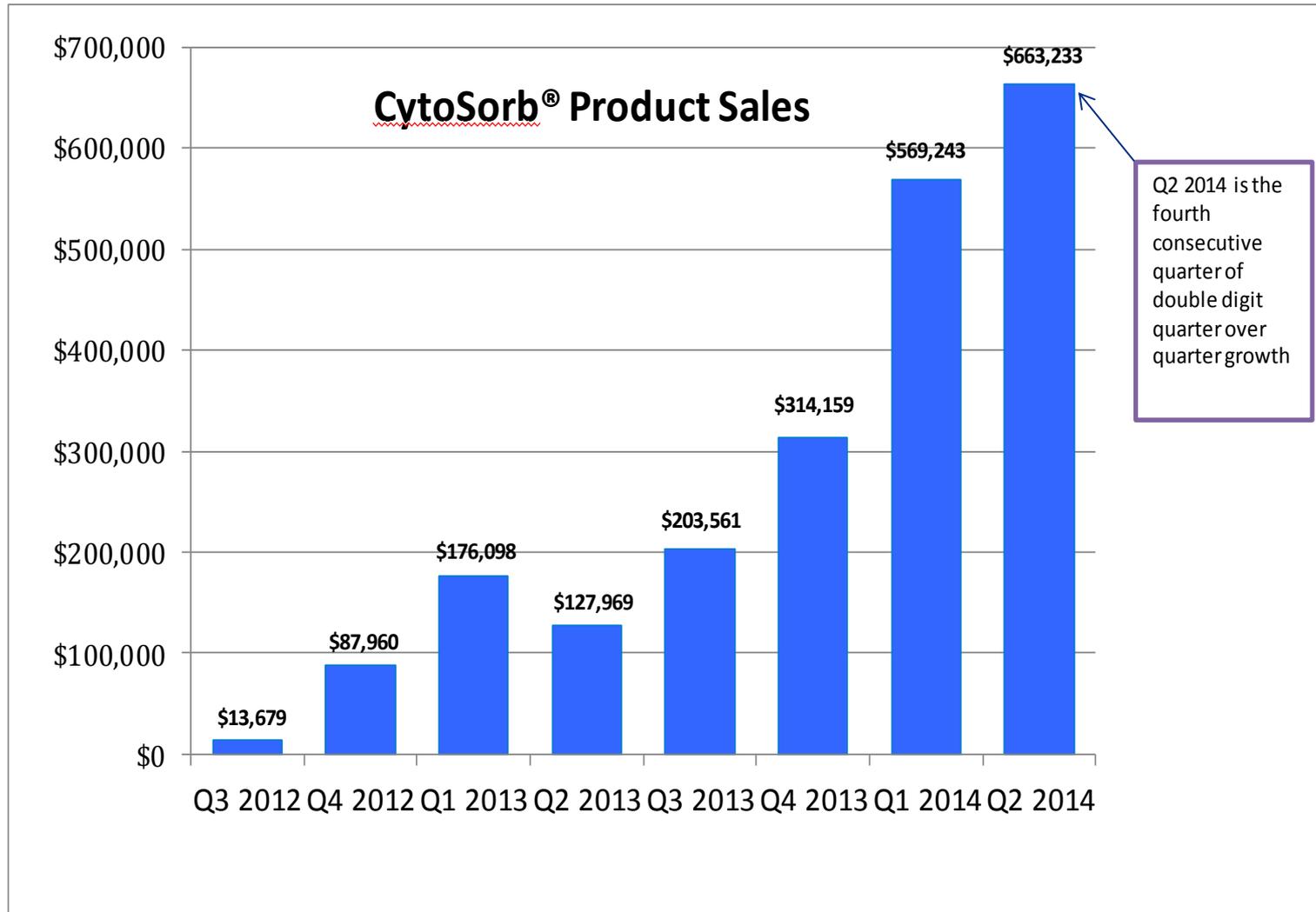
- First half 2014 total revenue of approximately \$2.1M, an increase of 215% compared to total revenues of approximately \$663K for the first half of 2013.
- First half 2014 product sales were approximately \$1.2M, an increase of 305% over first half 2013 product sales of approximately \$304K.
- Grant income for the first half of 2014 was approximately \$854K, an increase of \$495K or 138% as compared to grant income of approximately \$359K for the first half of 2013.
- First half 2014 blended gross margins were approximately 36%, with product gross margins of approximately 63%.

# Q2 2014 Comparative Revenue Results

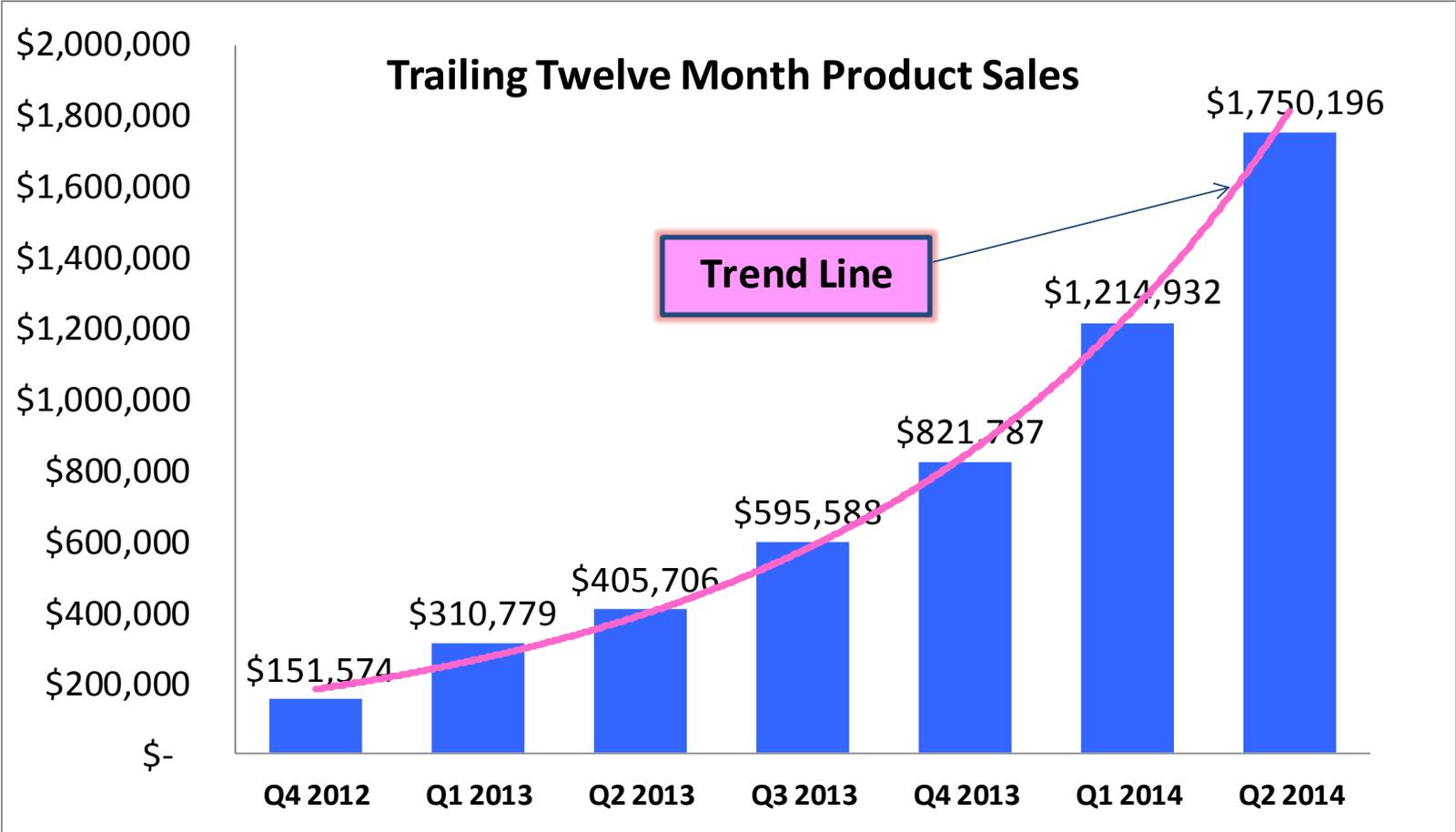
|                        | Three Months<br>Ended June 30,<br>2014 | Three Months<br>Ended June 30,<br>2013 | % Incr. |
|------------------------|--|--|---------|
| Product revenue        | \$ 663,233                             | \$ 127,969                             | 418%    |
| Grant and other income | 361,422                                | 163,514                                | 121%    |
| Total revenue          | \$ 1,024,655                           | \$ 291,483                             | 252%    |

- Second quarter 2014 total revenue of approximately \$1.0M, an increase of 252% compared to total revenues of approximately \$291K for the second quarter of 2013.
- Product sales for the second quarter of 2014 product sales were approximately \$663K, an increase of 418%, as compared to product sales for the second quarter of 2013 of \$128K
- Q2 2014 Product sales for the second quarter of 2014 were our highest ever quarterly product sales.
- Gross margin on product sales in Q2 2014 was approximately 65%.

# Continuing Strong Product Growth



# Product Sales (TTM)



# The Path to Up-listing

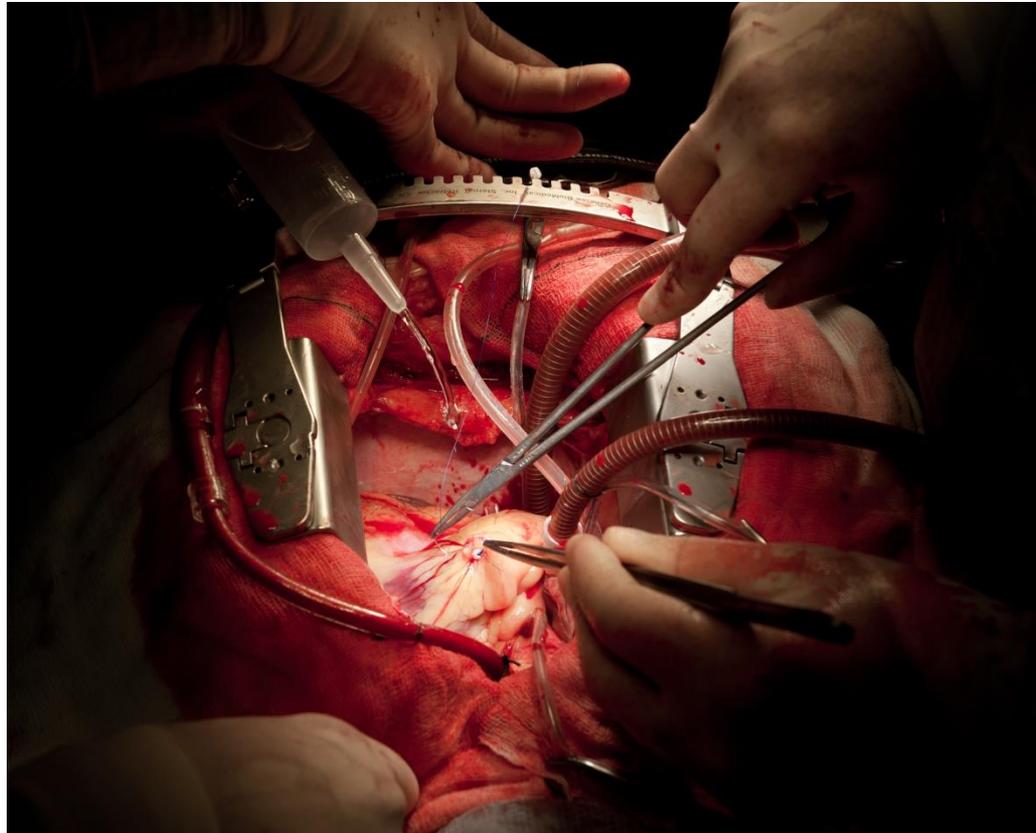
## Completed:

- ✓ Met with NYSE and NASDAQ
- ✓ Evaluation of listing requirements
- ✓ Transitioned to a new SEC counsel to provide guidance during up-listing process
  - ✓ Adopted Code of Business Conduct and Ethics
  - ✓ Updating our Insider Trading Policy
- ✓ Improvements to our system of internal control

## In Process:

- Fully Independent Audit Committee
- Selecting third party providers to assist with documentation and testing of our system of internal controls
- Increasing exposure to institutional investors
- Simplify capital structure
- Simultaneous reverse stock split with up-listing

# U.S. Cardiac Surgery Pivotal Trial



# Cardiac Surgery Stats

Approximately 1MM Cardiopulmonary Bypass Surgeries in US and EU annually

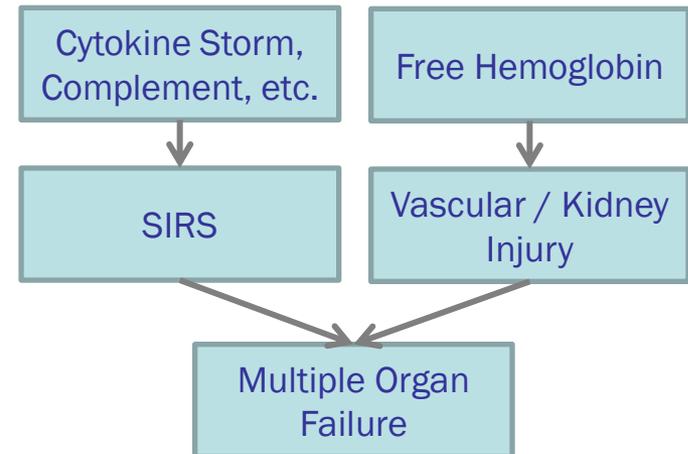
- Coronary artery bypass graft surgery
- Open valve repair, cardiac defect repair
- Heart or lung transplantation
- LVAD implantation

Patients often develop inflammation due to cytokine storm, complement activation, and free hemoglobin release during the surgery

Organ dysfunction and failure, particularly lung and kidney failure, frequently result

No technology has been able to easily and directly reduce cytokine storm, complement factors, and free hemoglobin except direct washing of blood

Leukoreduction filters are used today to remove cytokine producing white cells, but do not work and cannot directly remove cytokines



# Intra-operative versus Post-Operative

Intraoperative



Post-Operative



# U.S. Cardiac Surgery Pivotal Trial

Three potential paths to U.S. regulatory approval for CytoSorb in cardiac surgery, pending discussions with FDA. Expect to submit IDE application in Q4 2014

## 1) Inflammatory Biomarker Reduction

- Randomized controlled multi-center trial <150 patients
- Enrich for cardiac surgery patients at high risk for inflammation and hemolysis and treat DURING surgery with CytoSorb in a bypass circuit
- Primary endpoint: Reduction of inflammatory biomarkers
- Regulatory path: De novo 510(k)

## 2) Intra-Operative Usage of CytoSorb to Prevent Post-operative Complications

- Randomized controlled multi-center trial
- Enrich for cardiac surgery patients at high risk for inflammation and hemolysis and treat DURING surgery with CytoSorb in a bypass circuit
- Primary endpoint: Reduction in incidence of organ dysfunction
- Regulatory path: PMA

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## 3) Post-Operative Usage of CytoSorb to Treat Post-operative SIRS

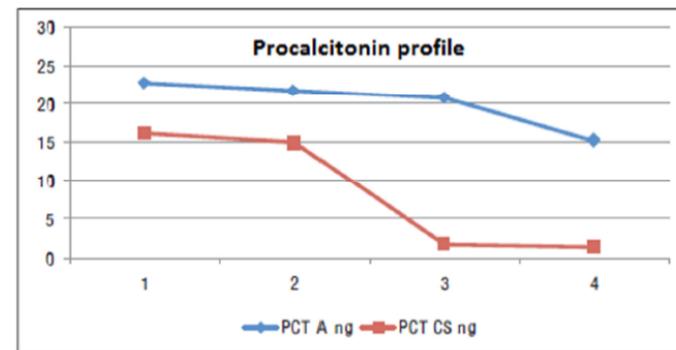
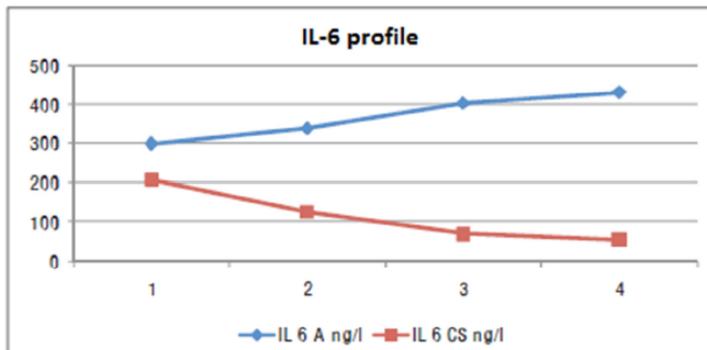
- Multi-center randomized controlled trial, PMA path
- CytoSorb is used AFTER surgery to treat patients who develop SIRS
- Primary endpoint: Relative reduction in incidence of organ dysfunction
- Regulatory path: PMA

# KardioTechnik 2014

## Retrospective 40 patient cardiac surgery study

- 20 patient (with CytoSorb) vs 20 patient (without CytoSorb) used intra-operatively with heart-lung machine
- Patients underwent high risk surgery with hypothermic cardiac arrest and antegrade cerebral perfusion
- Treatment was associated with statistically significant reduction of IL-6 and PCT in the 3 day post-operative period
- Gives visibility on U.S. pivotal trial in cardiac surgery

| CS group vs. A group | post-OP (1)    | 1 <sup>st</sup> day (2) | 2 <sup>nd</sup> day (3) | 3 <sup>rd</sup> day (4) |
|----------------------|----------------|-------------------------|-------------------------|-------------------------|
| IL-6                 | s. p = 0,033   | s. p = 0,031            | h.s. p = 0,004          | h.s. p = 0,005          |
| Fib                  | n.s. p = 0,657 | n.s. p = 0,550          | n.s. p = 0,151          | s. p = 0,019            |
| Leu                  | n.s. p = 0,788 | n.s. p = 0,652          | n.s. p = 0,536          | n.s. p = 0,234          |
| CRP                  | s. p = 0,028   | n.s. p = 0,079          | n.s. p = 0,747          | n.s. p = 0,516          |
| PCT                  | h.s. p = 0,008 | h.s. p < 0,002          | h.s. p < 0,001          | h.s. p < 0,001          |



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(Direktor: Prof. Dr. med. Christian Blatz)

## Systemic Inflammatory Response Syndrome in Heart Surgery: New possibilities for treatment through the use of a cytokine adsorber during ECC?

### ABSTRACT

The ECC is still the key technology in the performance of cardiac surgery. Currently used conventional extracorporeal circulation (CECC) systems need to be further optimized [14]. At LMU Munich positive experiences with minimized perfusion were consistently implemented. Minimized/optimized perfusion can reduce the inflammation by advanced perfusion technology [15, 16, 17, 18], but in complex interventions such as re-operations, hypothermic arrest or multiple interventions you reach the limits. Despite the use of modern perfusion technology, it is possible that a post-perfusion syndrome (PPS) can develop during long operations leading to SIRS in 2-10% of all cases. The newly introduced CytoSorb technology is a promising treatment option in patients with SIRS due to cardiopulmonary bypass surgery and increased cytokine values. Procedures involving the aortic arch, selective antegrade cerebral perfusion and hypothermic arrest require extra-long perfusion and ischemic time. It is postulated that the preventative use of a cytokine adsorber during open heart surgery with heart-lung machine has a positive impact on significant

clinical and inflammatory parameters. In a retrospective study two patient groups (n=20) were evaluated. The aim of this retrospective observational study is thus to analyze the effect of CytoSorb on the inflammatory response evolving. The IL-6 differs significantly in control and investigatory group during the postoperative course; fibrinogen reacts with significantly lower activation. The leucocyte shows a positive trend in the CytoSorb group. The CRP in the CS group showed a lower rise and a faster normalization. The procalcitonin increased with high significance in the control group.

**KEY WORDS**  
Inflammation, CECC, MAPS, Cytokines

**INTRODUCTION**  
Cardiac surgical interventions are associated with post-OP SIRS

The occurrence of the systemic inflammatory response syndrome (SIRS) is one of the most significant complications after operations in which the heart-lung machine (HLM) is employed. Clinically, the spectrum ranges from short-term limitations of organ function to multiple organ failure and death.

### Triggers and mechanisms

The triggers for this complex syndrome are multifactorial (Fig. 1). In addition to the surgical and anesthesiological operative trauma, per se, it is primarily the pathophysiological conditions of extracorporeal circulation (ECC), such as hemodilution, mechanical damage to cellular blood components, and contact of the blood with air and with artificial surfaces, that leads to the activation of the non-specific immune response and associated systemic inflammatory cascade.

Ischemia reperfusion injury and the ischemia-related release of endotoxin from the intestinal tract also represent potential triggers [1]. The systemic activation of the complement system and the formation of complement factors C3a, C5a and C5b-C9 can similarly occur within minutes [2]. C5a brings about cellular reactions in mastocytes, granulocytes and monocytes, and ultimately leads to the systemic activation of the endothelium. The activation of neutrophil granulocytes triggers the release of lytic enzymes (e.g. elastase) and oxygen radicals, thus leading to endothelial lesions, as well as to organ damage [3].

Born et al.: SIRS in heart surgery: New possibilities for treatment through the use of a cytokine adsorber during ECC?

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KARDIOTECHNIK 2/2014



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KLINIKUM DER UNIVERSITÄT MÜNCHEN®

Herzchirurgische Klinik an der LMU  
Herzklinik am Augustinum

# Ebola Virus

- Ebola is one of the most deadly viruses known with a very high mortality rate of 50-90% depending upon the strain, and very contagious (bodily fluids)
- Following an incubation phase of 2-21 days, has an abrupt onset of symptoms including high fever, chills, weakness and body pain, followed by more severe symptoms including diarrhea, cough, headache, and bleeding with vomiting of blood or blood in stool
- Patients typically die with time to death (from onset of symptoms) of 6-16 days. Culminates in a cytokine release syndrome
- Key to why Ebola is so deadly is its ability to evade the immune response, resulting in advanced infection that culminates in cytokine storm, deadly inflammation, and multiple organ failure
  - Initial suppression of the anti-viral cytokine immune response allows rampant viral replication
  - Release of soluble viral glycoproteins (sGP) that interfere with white blood cell activation and act as a decoy so that antibodies cannot neutralize the virus
- CytoSorb may have benefit by reducing cytokine storm and sGP, buying time for the immune system to kill the virus



# Could **CytoSorb**<sup>®</sup> Help?

The 2014 Ebola epidemic in West Africa, called an “international emergency” by the WHO, continues to grow and has already infected nearly 1,900 people, and claimed more than 1,000 lives. Epidemic is expected to continue throughout the year.

## Our Strategy for outreach:

- WHO
- FDA
- CDC
- Government agencies such as USAMRIID (US Army Medical Research Institute of Infectious Diseases)
- Non-profit organizations
- Hospitals treating Ebola patients inside/outside of West Africa
  - Europe
  - U.S.

# Our Bead Technology Enables a Diverse and Valuable Pipeline

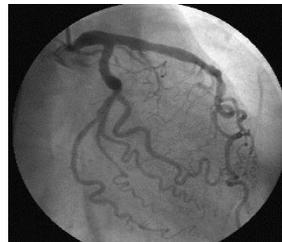


Critical Care, High Risk Surgery



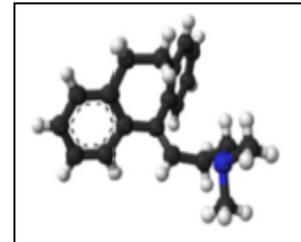
Blood Collection & Transfusion

**ContrastSorb**



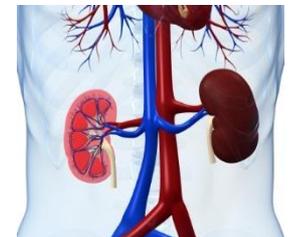
CT Imaging, Interventional Radiology

**DrugSorb**



Drug Overdose, Chemo Removal

**BetaSorb**



Improving Dialysis

CE Mark Approved

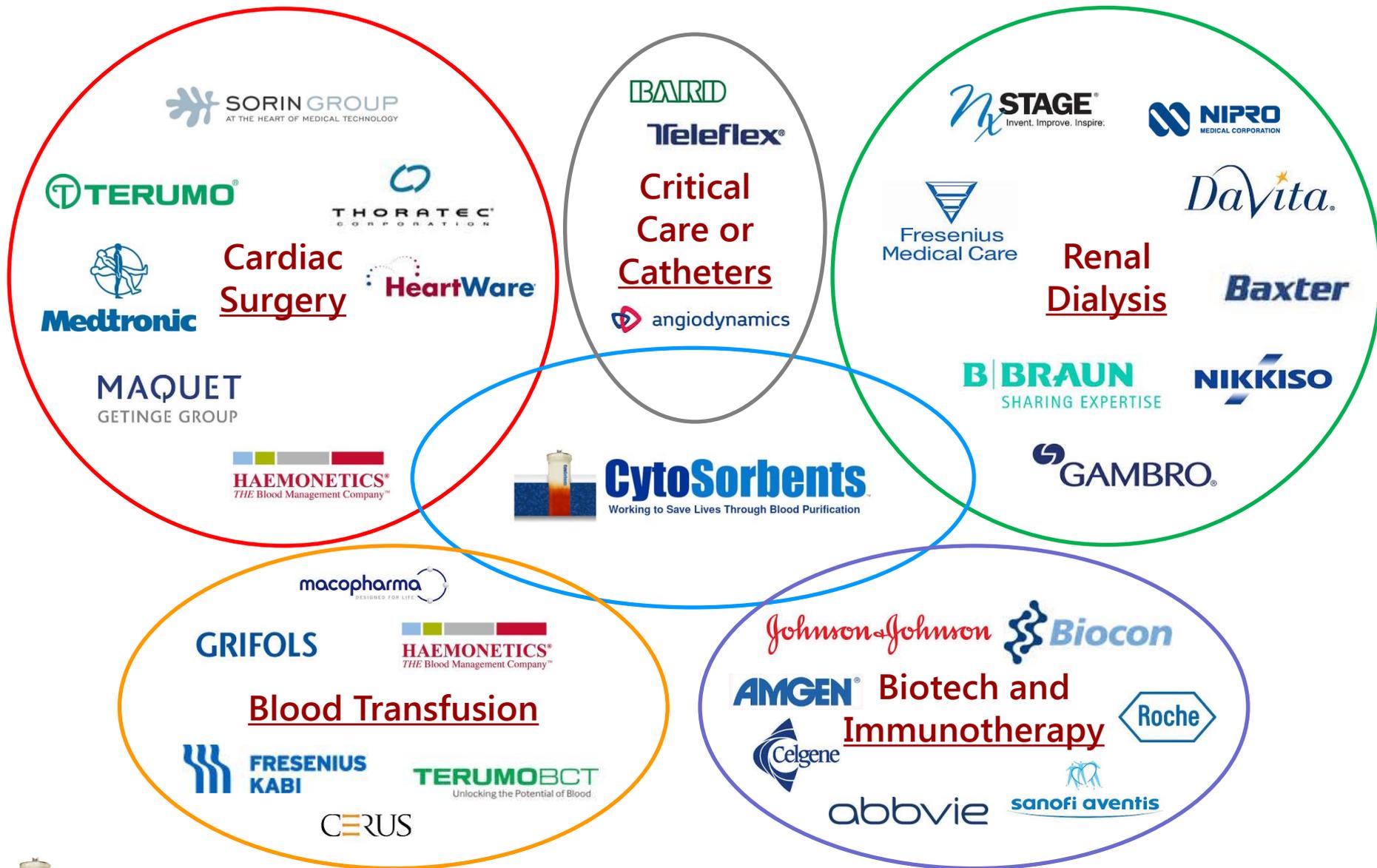
Under Development



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# Potential for Strategic Partnerships\*



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



# Acute Graft Dysfunction Case Report

Acute graft dysfunction after liver transplantation is a life-threatening event and requires emergency re-transplantation. The inflammatory response is responsible for most of the systemic complications and increased mortality

- 46 year old man with a history of liver cirrhosis underwent an initial liver transplant that failed
- Patient underwent a second emergency liver transplant, but ABO blood type incompatible
- CytoSorb was used during the re-transplantation surgery to stabilize the patient hemodynamically with weaning off of vasopressor support
- Key cytokines such as IL-6, IL-8, MCP-1, TNF and IL-10 decreased significantly
- Liver function returned to normal 5 days after surgery and left the post-anesthesia care unit after 7 days
- At 4 month outpatient follow-up, patient was doing well with normal liver function

|             | GM-CSF | IFN $\gamma$ | IL-1 $\beta$ | IL-2  | IL-4  | IL-5  | IL-6  | IL-7   | IL-8  | IL-10  | IL-12p70 | IL-13 | MCP-1  | TNF $\alpha$ |       |
|-------------|--------|--------------|--------------|-------|-------|-------|-------|--------|-------|--------|----------|-------|--------|--------------|-------|
| CytoSorb #1 | T1     | 7,55         | 0,50         | 8,73  | 30,53 | 14,37 | <2,00 | 223,18 | 51,31 | 210,69 | 188,95   | 14,43 | 19,22  | 1963,67      | 45,49 |
|             | T2     | 7,55         | <2,49        | 8,96  | 37,81 | 12,66 | <2,00 | 89,99  | 52,20 | 297,74 | 113,74   | 12,95 | 19,22  | 2369,63      | 49,70 |
|             | T3     | 7,20         | <2,49        | 6,62  | 40,35 | 13,23 | <2,00 | 75,65  | 51,31 | 53,22  | 17,54    | 14,18 | 18,84  | 257,07       | 35,13 |
| CytoSorb #2 | T4     | 5,22         | <2,49        | 2,39  | 22,27 | 14,37 | <2,00 | 56,95  | 51,31 | 119,90 | 61,34    | 12,95 | 18,45  | 509,99       | 62,71 |
|             | T5     | 6,19         | 6,80         | 7,79  | 22,43 | 21,25 | 12,94 | 31,81  | 51,31 | 299,89 | 48,65    | 13,68 | 18,84  | 399,14       | 64,65 |
| Mean M      | 5,38   | 0,50         | 2,62         | 21,81 | 13,92 | 12,94 | 7,25  | 26,54  | 20,20 | 14,23  | 12,79    | 18,07 | 281,61 | 16,09        |       |

T1: Start of surgery  
 T2: After graft reperfusion  
 T3: End of surgery  
 T4: Before 2<sup>nd</sup> CytoSorb  
 T5: After 2<sup>nd</sup> CytoSorb



# Toxic Shock Syndrome Case Report

\*

- 17 year old man suffered an injury to his ankle and unexpectedly began to develop fever
- He rapidly deteriorated and was hospitalized the next day at a major hospital in Rotterdam, Netherlands where antibiotics were started immediately. He continued to decline and was admitted to the ICU where he went into shock.
- Patient became globally red and swollen, and was suspected to have toxic shock syndrome.
- Surgical exploration of the injured ankle revealed a Staphylococcal infection, confirming the diagnosis
- Patient was still in shock and developed respiratory failure requiring intubation
- Patient was started on CytoSorb and within 5 minutes his blood pressure increased
- After three hours of treatment, the patient's swelling and redness had resolved
- Total CytoSorb® treatment was only 14 hours. Patient went on to fully recover



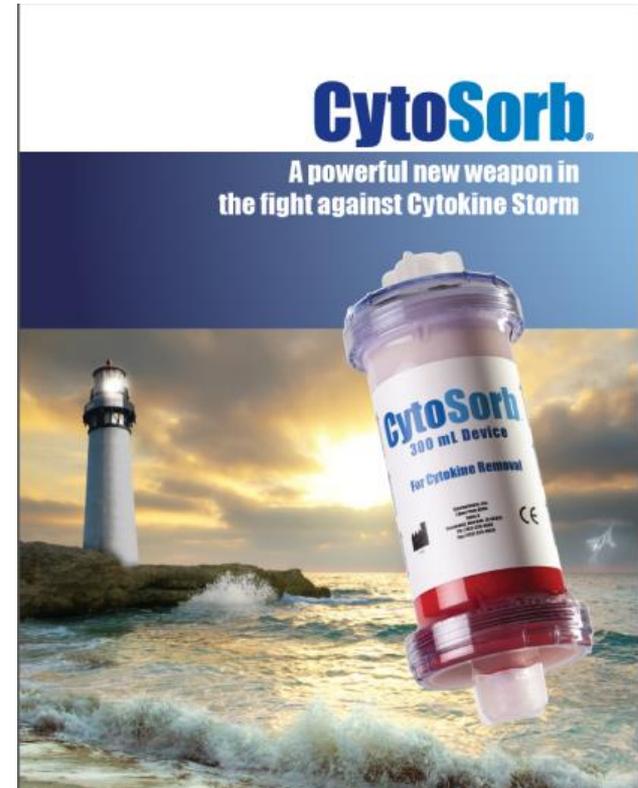
\* These pictures are not of the actual patient, but just examples of the scalded skin syndrome seen in patients with toxic shock syndrome and Staphylococcal infection

# Q&A Session

## CytoSorbents Corporation

OTCBB: CTSO

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## The Rise of An Emerging Critical Care Immunotherapy Company



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