



# **CytoSorbents Corporation** (NASDAQ: CTSO)

**A Leader in Critical Care Immunotherapy**

Q1 2016 Earnings Conference Call

May 9, 2016

# 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; 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 9, 2016 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** is A Leader in Critical Care Immunotherapy

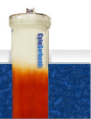


Leading the Prevention or Treatment of  
**Life-Threatening Inflammation**  
in the ICU and Cardiac Surgery using  
CytoSorb® Blood Purification



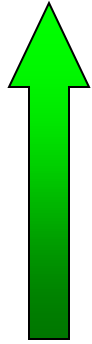
# CytoSorb® Removes the Fuel to the Fire

- CytoSorb® targets the \$20+ billion opportunity in critical care and cardiac surgery
- Approved in the European Union as the only specifically approved extracorporeal cytokine filter
- Clinically proven to remove key cytokines in the blood of critically-ill patients
- Approved for use in any situation where cytokines are elevated
- Works with standard dialysis and heart-lung machines
- Removes many other inflammatory mediators such as free hemoglobin, bacterial toxins, and complement
- Safe and well-tolerated: In ~12,000 human treatments

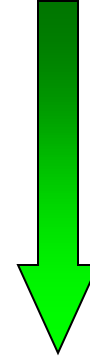




# Goal: To Prevent or Treat Organ Failure

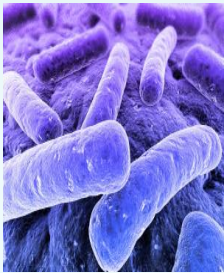


Improve  
Patient  
Outcome  
and  
Survival

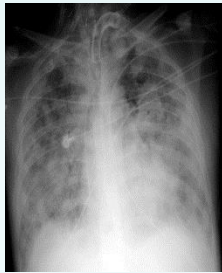


Decrease  
Costs Of  
ICU and  
Patient  
Care

Sepsis



ARDS



Burn Injury



Trauma



Pancreatitis



Influenza



Surgical



The Potential to Revolutionize Critical Care Medicine



# Operating and Financial Highlights



**CytoSorbents**

Working to Save Lives Through Blood Purification

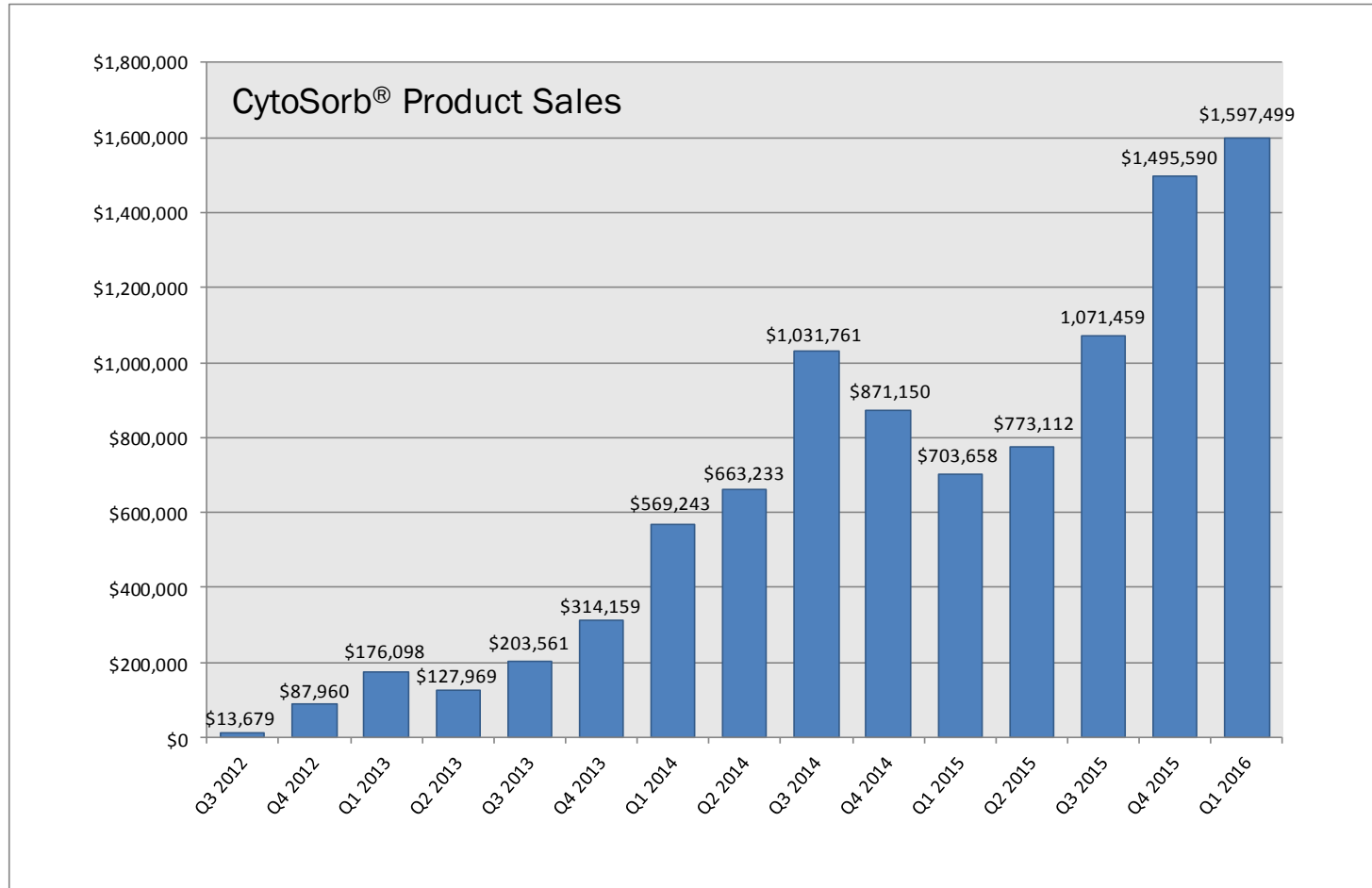
# Q1 2016 Comparative Revenue Results

	3 Months Ended March 31, 2016		3 Months Ended March 31, 2015		% Incr.
Product revenue	\$ 1,597,449		\$ 703,658		127%
Grant and other income	212,733		19,416		996%
Total revenue	\$ 1,810,182		\$ 723,074		150%

- CytoSorb® product sales were \$1.6M for the quarter ended March 31, 2016, a 127% increase over product sales of \$704K for the quarter ended March 31, 2015
- Q1 2016 annualized product sales run rate is approximately \$6.4M, as compared to Q1 2015 product run rate of approximately \$2.8M
- Total revenue for the quarter ended March 31, 2016, which includes both product sales and grant revenue, was \$1.8M as compared to \$723K for the quarter ended March 31, 2015, an increase of 150%
- Q1 2016 gross margin rose to approximately \$1.0M, an increase of \$572K as compared to gross margin of \$419K for the first quarter of 2015
- Gross profit margins on product sales were approximately 62% for the quarter ended March 31, 2016.

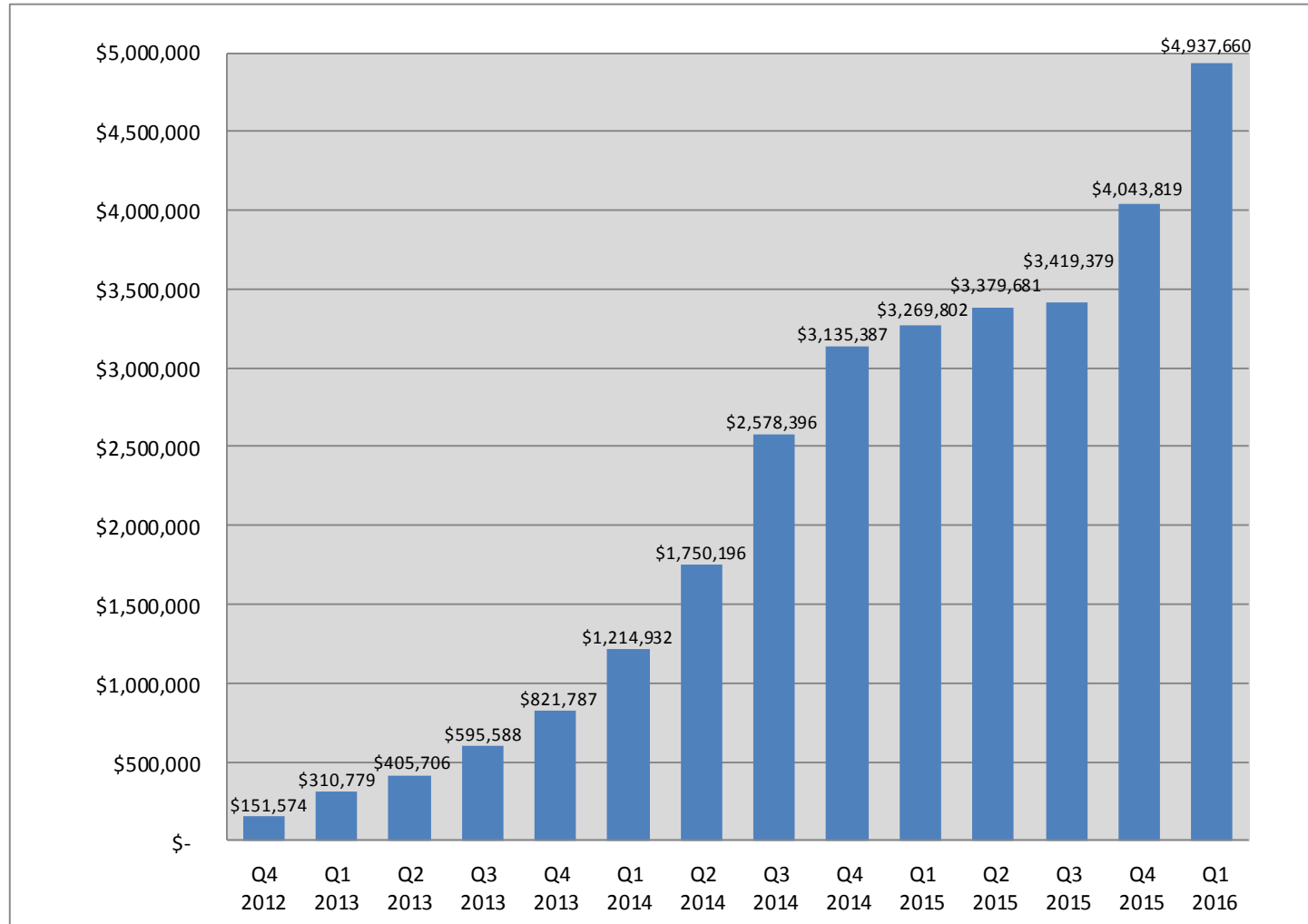
# Quarterly Product Sales

Fourth Consecutive quarter of product sales growth  
Third consecutive quarter of record sales





# Trailing Twelve Months Product Sales

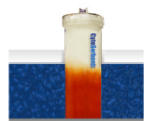


# Working Capital and Cap Table

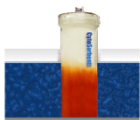
Working Capital as of					
	3/31/16	12/31/15	12/31/14	12/31/13	12/31/12
Current Assets:					
Cash and short-term investments	\$ 6,027	\$ 7,509	\$ 5,550	\$ 2,183	\$ 1,729
Grants and accounts receivable, net	760	649	819	453	51
Inventories	1,060	1,191	538	245	682
Prepaid expenses and other current assets	194	512	700	605	476
Total current assets	8,041	9,861	7,607	3,486	2,938
Current Liabilities(1):					
Accounts payable	861	685	698	787	801
Accrued expenses and other current liabilities	770	723	825	362	350
Deferred revenue	-	-	1	272	-
Total current liabilities	1,631	1,408	1,524	1,421	1,151
Net Working Capital	\$ 6,410	\$ 8,453	\$ 6,083	\$ 2,065	\$ 1,787
(1) Excludes warrant liability, a current liability that does not have cash implications.					

## Cap Table 3/31/2016

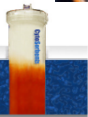
(unaudited)	Fully Diluted Common Shares
Common Stock	26,406,056
Options	2,485,448
Warrants	1,100,166
	28,991,670



# Operating Highlights



# 3<sup>rd</sup> International CytoSorb Users Meeting





# ISICEM 2016

**ISICEM News**  
The official daily newsletter of the 36th ISICEM Tuesday 15 March 2016 Day 1

**Welcome to Brussels...**

because of the interplay between industry and the clinic, and we want to continue that bond. We begin today, as we always do, with a rich and informative opening session that will be a particular highlight of the program, filled with key lectures, as well as the eagerly-anticipated Report of the Round Table Conference on Recovery after Critical Illness. Held in the expansive yet intimate Henry Le Raulx Auditorium, it is perhaps the only chance during the four days that we can all sit together to share in several vital topics, so I do look forward to seeing you there. But there is also much more to come, and depending on your specialty, interests or treatment goals, I'm sure there will be plenty of options to stimulate your interest. Finally, I must thank you all for your understanding with regards to the elevated security this year. We do hope it did not cause any inconvenience for you. I wish you a very enjoyable and enlightening meeting, and invite you to join us this evening for the opening cocktail welcome in the scientific exhibition area.

**Jean-Louis Vincent**  
ISICEM Chairman  
Professor of intensive care medicine  
Dept of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles  
President of the World Federation of Societies of Intensive and Critical Care Medicine

At the 2016 edition of the International Symposium on Intensive Care and Emergency Medicine (ISICEM), it is with great pleasure that I welcome you to the Square for a comprehensive program packed with the latest and greatest topics in the field. Over the next four days, physicians, nurses, and allied healthcare providers from all over the world will join together for a fascinating program of lectures, tutorials, workshops, debates, and more, with hundreds of individuals taking to the stage to share their expertise. As always, discussions will center on a multitude of front-line issues, facilitating an open forum in which we can all share the most clinically relevant advances, research developments, therapeutic nuances, and management techniques. Of course, we thank our sponsors for helping make this possible – and we encourage you to spend some time in the scientific exhibition to see the latest medical and scientific equipment, pharmaceutical products, books, and services related to intensive care and emergency medicine led by technology and techniques. Finally, I wish you a very enjoyable and enlightening meeting, and invite you to join us this evening for the opening cocktail welcome in the scientific exhibition area.

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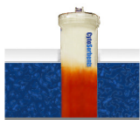
**CytoSorbents**  
**NEW CLINICAL DATA**

**Satellite Symposium**  
**REGAIN CONTROL in SIRS and Sepsis: New insights into the CytoSorb® Therapy**  
Thursday, March 17th 2016  
12:30pm – 01:30pm, Copper Hall

CytoSorbents  
www.cytosorbents.com



# CytoSorbents ISICEM Research Symposium



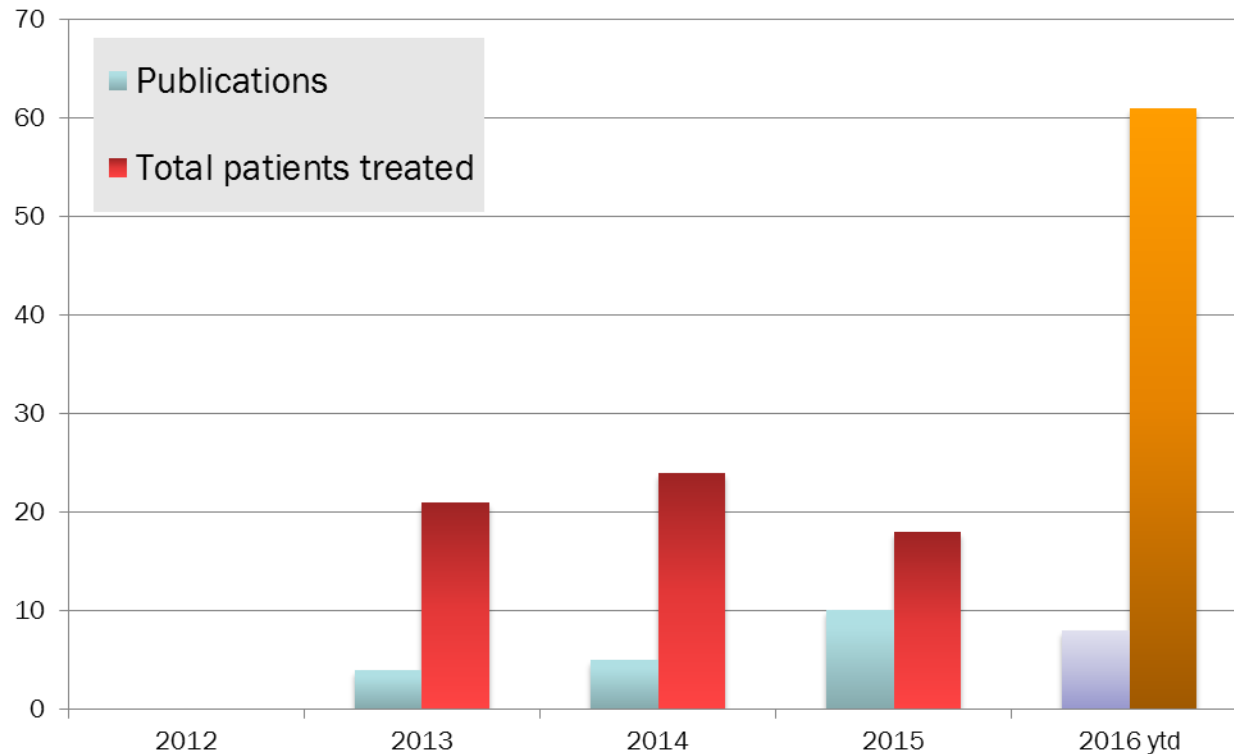


# Fresenius Medical Care

- Fresenius initiated the marketing push behind CytoSorb® at the International Symposium on Intensive Care and Emergency Medicine (ISICEM) Conference in Brussels in March
  - CytoSorb® was featured in the Fresenius exhibition booth on the multiFiltrate Acute Therapy System
- They also sent approximately 18 people to our 3<sup>rd</sup> International CytoSorb Users Meeting
- Fresenius has been marketing CytoSorb® in country specific conferences such as the one in Poland last month
- Fresenius has confirmed that it plans to beginning selling in France, Poland, Denmark, Finland, Norway and Sweden later this month



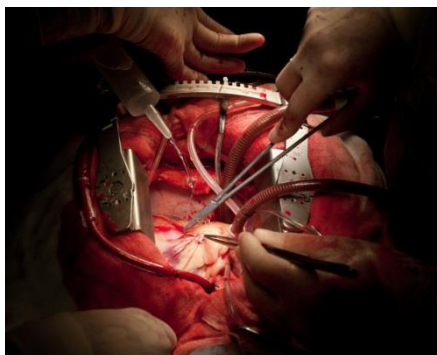
# Published Clinical Data Continues to Grow



# REFRESH I Trial Update

## REduction in FREe Hemoglobin

- 40-patient, eight-center study evaluating the safety and efficacy of intra-operative use of CytoSorb® in a heart-lung machine during complex cardiac surgery in elective, non-emergent cardiac surgery > 3 hours
  - Aortic reconstruction, CABG redos, multiple valve replacements, etc
- Goal: Safe reduction of plasma-free hemoglobin and other inflammatory mediators that can cause post-operative complications



# REFRESH I Trial Update

## REduction in FREe Hemoglobin Trial



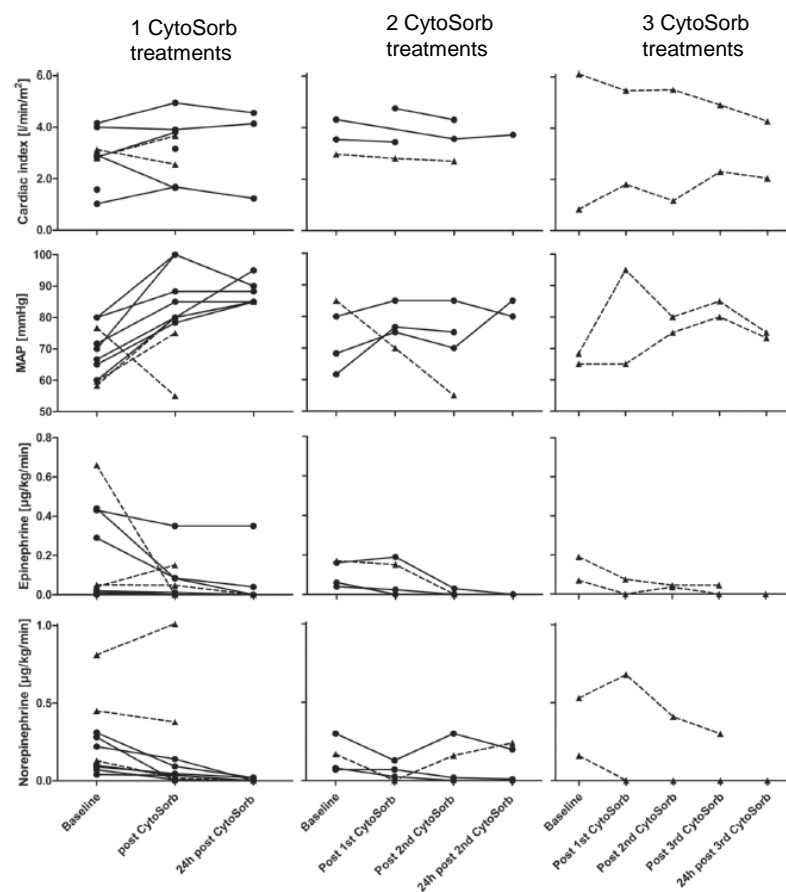
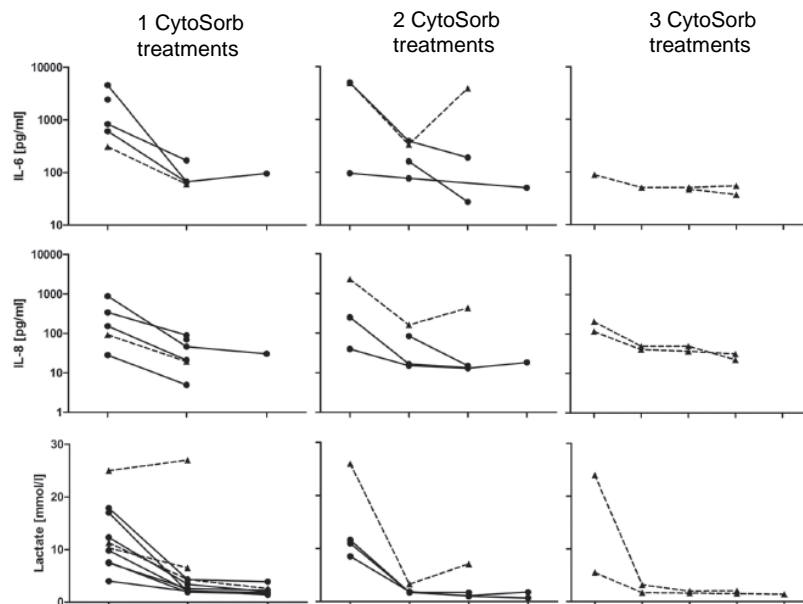
- Working with major cardiac surgery centers
  - Baylor College of Medicine and Texas Heart Institute
  - Baystate Medical Center
  - Columbia University
  - Cooper University Hospital
  - University of Kentucky
  - University of Maryland
  - University of Pennsylvania
  - University of Pittsburgh Medical Center
- All sites currently active in the trial
- Trial is nearly two-thirds enrolled at 63%
- Expected to complete enrollment by mid-2016, with database lock and top-line results available in Q3 2016

# New Clinical Data in Cardiac Surgery

- Interim analysis of 165 patients enrolled into a 3-arm randomized controlled study at University of Cologne, Germany evaluating the intra-operative use of CytoSorb during open heart surgery, reported a statistically significant reduction in sternal wound infections, a major and expensive complication following cardiac surgery
- A 10 patient cardiac surgery evaluation study led by Prof. Christophe Baufreton, MD, PhD, cardiothoracic surgeon and Vice Dean of Research from C.H.U - Angers, France, in a complex cardiac surgery patient population similar to those in the REFRESH I study
  - Improved hemodynamic stability especially with 2 patients undergoing valve surgery due to endocarditis
  - Reduction in the need for vasopressors and expensive extracorporeal life support
- Medical University of Vienna recently published data from a 37-patient randomized controlled study using CytoSorb intra-operatively during low-to-medium risk cardiac surgery and demonstrated safety and technical feasibility. Inflammation in general was not a problem for any of these low-to-medium risk patients

# Post-op SIRS (Cardiac Surgery) Case Series

A retrospective case series was recently published on 16 consecutive cardiac surgery patients who developed post-operative SIRS following prolonged cardiopulmonary bypass, with shock requiring vasopressors and acute kidney injury requiring hemofiltration



## Key Findings:

- Therapy was well-tolerated and safe
- Marked decrease in IL-6 and IL-8 during the course of CytoSorb treatment
- Hemodynamic stabilization and reduction in vasopressors and lactate

\* Traeger, K, et. al., "Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series", Int J Artif Organs, April 2016; e-published before print



# Removal of Bilirubin

- The liver is a major detoxification organ
- Patients with either chronic liver failure due to alcoholic cirrhosis, NASH, or viral hepatitis, as well as acute liver failure, due to infection, liver cancer, alcohol, poisoning, shock, and other causes will have high levels of unconjugated bilirubin which can be neurotoxic
- This manifests clinically as jaundice
- CytoSorb is very effective in reducing bilirubin, cytokines, and other potential toxins that a compromised liver cannot, and is being considered as an adjunct therapy or standalone therapy in liver failure
- Liver failure is estimated to be the 12<sup>th</sup> leading cause of death in the U.S., and the 4<sup>th</sup> leading cause of death in China



## Removal of bilirubin with a new adsorbent system: in vitro kinetics

S Faenza<sup>1</sup>; E Mancini<sup>2</sup>; D Ricci<sup>2</sup>; C Gemelli<sup>3</sup>; A Cuoghi<sup>3</sup>; S Magnani<sup>4</sup>; M Atti<sup>4</sup>

<sup>1</sup>Teaching Hospital Policlinico S.Orsola-Malpighi, Department of Surgery, Intensive Care and Transplantation, Bologna, Italy,

<sup>2</sup>Department of Nephrology, Dialysis, Hypertension, Bologna, Italy,

<sup>3</sup>Science and Technology Park for Medicine, Mirandola, Italy

<sup>4</sup>Aferetica, Bologna, Italy

### INTRODUCTION

A new sorbent (CytoSorb, CytoSorbents USA), based on blood-compatible porous polymer-beads and able to adsorb hydrophobic molecules, could be a valid artificial support in many conditions of organ failure through the reduction of cytokines and other toxic molecules directly from blood. Today, extracorporeal systems for this purpose are based on plasma-adsorption.

We performed an in vitro study on bilirubin kinetics from plasma to verify the system's adsorption capacity and the ability to remove protein-bound solutes.

### METHODS

We performed 3 in vitro tests. Experiments 1 & 2 were conducted with equimolar solution of Albumin-Bilirubin, containing only unconjugated Bilirubin, strongly Albumin-bound [1], in order to verify the removal of protein-bound solutes.

In test 3, 24h long, we tried to reproduce clinical conditions, with higher concentration of Bilirubin and lower of Albumin to study kinetics and mass balance.

Solutions were recirculated in a hemoperfusion circuit (Fig. 1) including a peristaltic pump and CytoSorb at a flow rate of 100 ml/min. Samples were collected pre and post cartridge at different times: 0, 15, 30 min and then every hour until the end.

### RESULTS

All of the experiments showed the adsorption capacity of the system concerning Bilirubin (Table 1) and the removal kinetics is shown below (Fig.2).

Experiments 1 & 2 demonstrated the capacity of the system to adsorb protein-bound solutes. In this condition, the removal of Bilirubin is possible only breaking the strong Albumin-Bilirubin complex.

Test 3, similar to a real clinical condition, showed a Bilirubin adsorption of 2.499 mg, equivalent to the total removal of blood Bilirubin in a 70 kg patient with an initial concentration of 49.98 mg/dl. The major reduction of Bilirubin was in the first 8h but the cartridge maintained an adsorption capacity until the end of the experiment, whereas there was a minimal loss of Albumin (1.5%). Moreover, we could not demonstrate any release of the adsorbed Bilirubin in 24h.

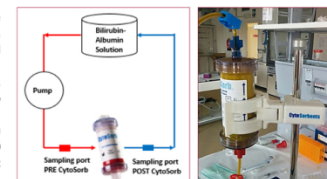


Fig.1: In vitro hemoperfusion circuit and CytoSorb

	1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>
Bilirubin, mmol/l	0,4	0,8	0,8
Albumin, mmol/l	0,4	0,8	0,4
Flow Rate, ml/min	100		
Volume of Solution, lt	6		
Duration, h	8	8	24
Bilirubin Mass Balance, mg	944	1.020	2.499

Table 1: Data and Bilirubin Mass Balance of the experiments

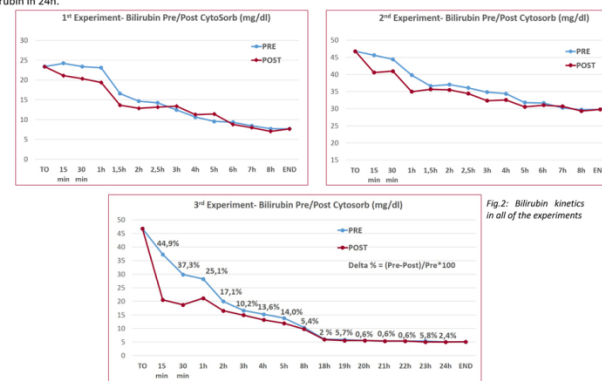


Fig.2: Bilirubin kinetics in all of the experiments

### CONCLUSIONS

This in vitro study shows the effectiveness in removing Bilirubin without any substantial Albumin loss, the resin ability to break the Albumin-Bilirubin complex and to adsorb irreversibly Bilirubin. CytoSorb might represent a valid and simple aid in supporting also liver dysfunction, with no need of plasma separation. In vivo studies are ongoing to confirm these in vitro results.

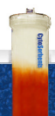
### REFERENCES

[1]Weber et al. Biomacromolecules 2008, 9 1322-1328.



ALMA MATER STUDIORUM  
UNIVERSITÀ DI BOLOGNA

36th International Symposium on Intensive Care and Emergency Medicine  
Brussels, 15-18 March 2016, P192



**CytoSorbents**  
Working to Save Lives Through Blood Purification

# Septic Shock Series

- 8 patient case series: 2 severe sepsis, 6 septic shock
- CytoSorb® used with continuous renal replacement therapy (CRRT) for 24 hours at a time, with a median treatment time of 2 days
- Those that benefited showed an improvement in hemodynamics, with a rapid reduction of vasopressors, a reduction in procalcitonin (a sepsis biomarker) and an improvement in renal function
- Mortality was 25%. The two patients that died showed no positive response to the therapy
- Authors suggest a “timely use” of CytoSorb and additional studies to confirm their findings



## Case series of patients with severe sepsis and septic shock treated with a new extracorporeal sorbent

T Laddomada ; A Doronzio ; B Balicco

San Marco Hospital, Anesthesia and Intensive Care Service, Zingonia, Italy

### Introduction

In-Vitro and In-Vivo studies have shown that the reduction of toxic levels of cytokines directly from blood with the use of a new extracorporeal sorbent, CytoSorb (CytoSorbents Corp), could be useful to regain control during a complicated inflammatory condition in patients with severe sepsis and septic shock [1,2].

In this case series, we evaluated patients admitted to our ICU from January to November 2015 treated with CytoSorb. The aim was to analyze the system's influence in clinical outcomes, as mean arterial pressure (MAP), vasopressors need and inflammatory markers, like procalcitonin (PCT).

### Methods

We included 8 patients (4 female, 4 male): 2 severe sepsis and 6 septic shock. Patients' data are reported in Table 1 as median values (lower and upper quartiles). All patients were non-responding to the Standard of Care for the treatment of severe sepsis/septic shock.

Therefore, CytoSorb was used as adjunctive therapy in combination with continuous renal replacement therapy (CRRT), in order to control the cytokines storm and improve hemodynamic stability and MAP, often associated with a marked reduction in vasopressor requirements.

It was installed in series connection after the dialyzer in the CRRT circuit for 24h (median duration of the treatment: 48h). Clinical parameters were collected before and after every treatment with CytoSorb.

Age, years	65,5 (52,25-67,25)
Type of patient	6 Surgical /2 Medical
ICU stay, days	17 (9,5- 27,5)
Vasopressors need, days	5 (3,25-10,5)

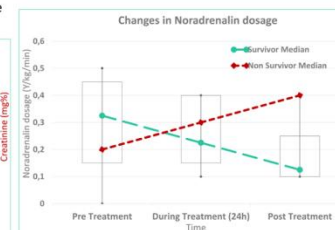
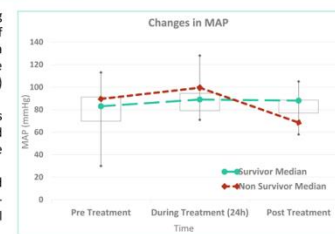
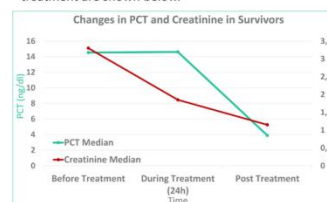


### Results

6 treated patients with CytoSorb survived and during the treatment there was an overall improvement of MAP from 83 (73,5-89) to 88 (82-89,5) mmHg, with a rapid reduction in vasopressors dosages: noradrenaline decreased from 0,33 (0,15-0,46) to 0,13 (0,10-0,18) while dopamine from 7,5 (6-8) to 3 (1,5-5) V/kg/min. Moreover, there was a marked decrease of PCT levels from 14,53 (7,64-67,5) to 3,90 (1,62-23,05) ng/dl and an improvement in renal function, thanks to the combination of CytoSorb with CRRT.

In non-survivors, MAP was hard to stabilize and decreased from 89,5 (77,75-101,25) to 68,5 (63,25-73,75) mmHg and there was an aggravation in overall patients' conditions.

Changes of the main clinical parameters during the treatment are shown below.



### Conclusions

To our experience, a timely use of CytoSorb in combination with the standard therapy could have benefits in improving patients hemodynamic and helping a more rapid stabilization of the patient. However, more in vivo studies are needed to confirm these results.

### References

- [1] Kellum et al. Crit Care Med 2004 32(3):801-5
- [2] Schadler et al. Critical Care 2013 17 (Suppl 2):P62

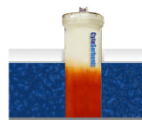
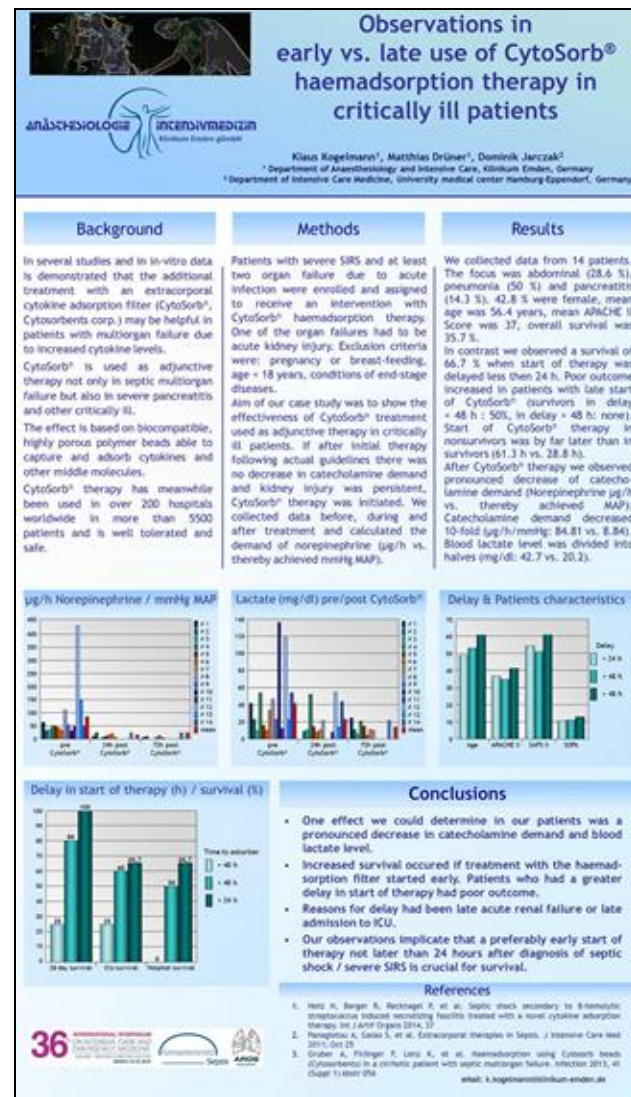
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# Septic Shock and SIRS Case Series

- 14 patient case series: Abdominal sepsis (29%), pneumonia (50%), pancreatitis (14%), other (7%)
- Patients were critically-ill, with a mean APACHE II score of 37, predicting a mortality of > 85% in sepsis
- Observed a pronounced 10-fold decrease in vasopressor requirement and a reduction in blood lactate levels by 50%
- Overall survival was 36%, but when therapy was started within 24 hours of, survival was 67%
- The investigators recommend early usage (<24 hours after admission), similar to how CytoSorb is being used today



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# Visit CytoSorb.com for Case of the Week



[The Therapy](#) [The Studies](#) [The Adsorber](#) [Support](#)

## Case of the week 17/2016

CytoSorb in pneumogenic septic shock after ethyltoxic bone marrow depression and increased comorbidity (alcohol abuse, 3-fold ACVB)

Dr. Matthias Lutze, Head of Department for Anaesthesiology and Intensive Care Medicine, Hospital Teterow, Germany

This case study reports on a 53-year-old male patient (medical history of 3-fold ACVB and pacemaker implantation) who presented at the hospital with ethyltoxic pancytopenia, acute alcohol withdrawal delirium and hypostatic bilateral pneumonia.

### Case presentation

- Immediate transfer to intensive care unit – at this point of time the patient was awake, responsive, tachycardic and hallucinating
- Instant initiation of anti-delirious therapy (gamma hydroxybutyrate, Haloperidol) as well as administration of ampicillin/sulbactam

## Archive

16/2016

### **CytoSorb in postoperative septic shock after pylorus-preserving pancreaticoduodenectomy**

Dipl. med. Hermann Begau, Head of surgical Intensive Care Medicine, Agaplesion Diakonie Clinics Kassel, Germany

[... more](#)



- We have had excellent feedback from both physicians and investors on the many exciting case reports presented in the CytoSorb “Case of the Week” on the [www.cytosorb.com](http://www.cytosorb.com) website
- These cases highlight the ongoing successes that clinicians continue to have as they treat earlier or more aggressively
- Our goal, using these reports, our Proceedings of the International CytoSorb Users meeting publication, and our Case Study Summary booklet is to broadly teach our users how and when the therapy is being used most effectively



# CytoSorb®

## SIRS and Sepsis: Regain Control!



**CytoSorbents**

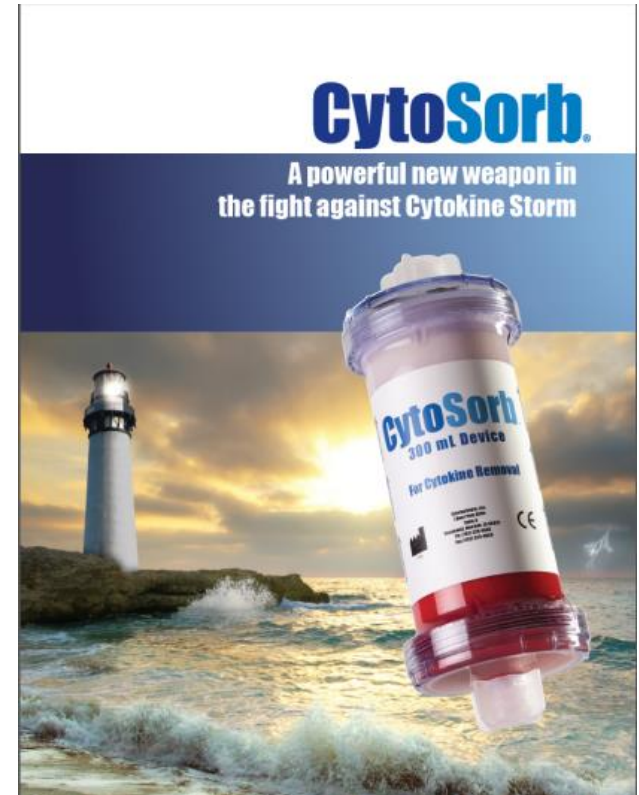
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# Q&A Session

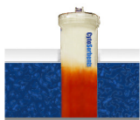
**CytoSorbents Corporation**

**NASDAQ: CTSO**

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**A Leader in Critical Care Immunotherapy Company**



**CytoSorbents**  
Working to Save Lives Through Blood Purification