## **CytoSorbents Corporation**

NASDAQ: CTSO

Working to Save Lives
Through Blood Purification
Investor Presentation
September 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.



## **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

- NASDAQ-traded (CTSO): Market cap of ~\$160M
- International footprint across two wholly-owned operating subsidiaries
  - CytoSorbents Medical, Inc Monmouth Junction, NJ
    - Headquarters, ISO 13485 manufacturing, QA/QC, R&D
  - CytoSorbents Europe GmbH: International sales office Berlin, Germany
    - CytoSorbents Switzerland GmbH
- Flagship product, CytoSorb®, is E.U. approved, distributed in 38 countries
- Strategic Partnerships with Fresenius Medical Care, Biocon Ltd, and Terumo
- Strong government support with \$18M+ in grants and contracts
- ~70 employees and consultants worldwide
- Pursuing U.S. approval of CytoSorb® in cardiac surgery via REFRESH I & II
- ~\$9M in cash at the end of Q2 2016
- Expecting acceleration of international growth this year with record trailing 12-month sales of \$6.0M vs \$3.3M a year ago, and gross margins of 68%



#### Leadership Background



#### Phillip Chan, MD, PhD - Chief Executive Officer and President

Former Partner at the \$80M NJTC Venture Fund, leading life science investments for 5 years. Co-founder of Andrew Technologies, commercializing its HydraSolve™ lipoplasty device in the U.S. MD/PhD from Yale School of Medicine, internal medical residency at the Beth Israel Deaconess Medical Center at Harvard.



#### Vincent Capponi, MS - Chief Operating Officer

20+ years experience in the medical device, pharmaceutical and imaging fields. Led the first regulatory approval for the heparin flush syringe, used worldwide in hospitals, and managed manufacturing of > 1 million units/week



#### Kathleen Bloch, MBA, CPA - Chief Financial Officer

20+ years as CFO of private and public companies. Former Laureate Biopharma CFO, a contract biopharmaceutical manufacturer, and CFO of Silverline Windows, a \$750M revenue window manufacturing company with 9 manufacturing plants nationally



#### Robert Bartlett, MD - Chief Medical Officer

World-renowned pioneer of extracorporeal membrane oxygenation therapy (ECMO) – used worldwide in ICUs in refractory lung failure. Former Director of the Surgical Intensive Care Unit at University of Michigan, with extensive experience in cardiothoracic surgery and critical care medicine including the treatment of sepsis



#### Christian Steiner, MD - Vice President of Sales and Marketing

15+ years experience in sales and marketing of extracorporeal therapy and critical care sales at Teraklin for MARS, the first liver failure dialysis technology, and at Pulsion Medical (hemodynamic monitoring)



#### Christopher Cramer, MS, MBA – Vice President of Business Development

15+ years experience in business development and commercial experience. Former Senior Director of New Venture Development at Johnson & Johnson, and previously at PwC Consulting



#### **Board of Directors**



#### Al Kraus - Chairman (Audit, Governance, Compensation Committees)\*

25+ years leadership experience in the dialysis and medical device industries. Former CEO and Board director of CytoSorbents, NOvoVascular, Althin Medical, and former COO and U.S. manager of Gambro, Inc., one of the leading dialysis companies in the world, taking them public through an IPO in the U.S. in the 1980's and growing sales 4x.



#### Michael Bator, MBA (Compensation Committees)\*

Chief Financial Officer of Trek Therapeutics, a private pharmaceutical company. 15 year Wall Street veteran, most recently as Managing Director - Healthcare Research at Jennison Associates, a US mutual and pension fund management company, with \$109 billion in equities and \$66 billion in fixed income assets. Formerly a management consultant at several agencies, including the Boston Consulting Group.



#### Phillip Chan, MD, PhD - Chief Executive Officer and President

Former Partner at the \$80M NJTC Venture Fund, leading life science investments for 5 years. Co-founder of Andrew Technologies, commercializing its HydraSolve™ lipoplasty device in the U.S. Internal medicine physician with MD/PhD from Yale School of Medicine, internal medical residency at the Beth Israel Deaconess Medical Center at Harvard.



#### Edward Jones, MD, MBA (Audit, Governance Committees)\*

Clinical Professor of Medicine at Temple University Hospital and attending nephrologist at the Albert Einstein Medical Center and Chestnut Hill Hospital. Past Board member of the National Kidney Foundation of the Delaware Valley, Past President of the Renal Physicians Association, and Chairman of Kidney Care Partners



#### Alan Sobel, MS, CPA (Audit Committee Chair, Governance Committee)\*

Audit Committee Chair. Managing Member of Sobel & Co., LLC, a full-service accounting, audit, tax, and business consulting firm serving individuals, small and mid-sized businesses, and SEC-registered companies. Former Chairman of the Audit Committee of the New Jersey Society of Certified Public Accountants

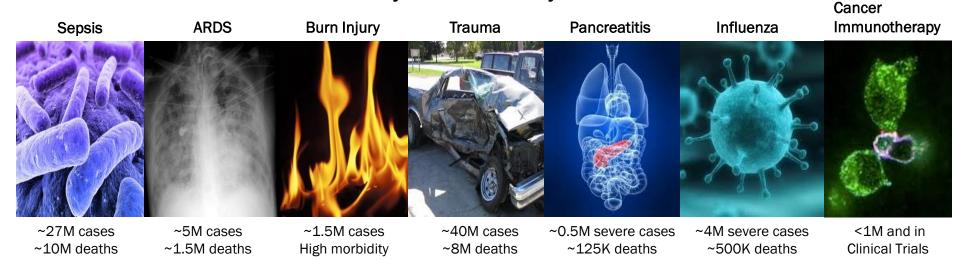


# Controlling Deadly Systemic Inflammation



## Severe Inflammation: Deadly in the ICU

Millions worldwide admitted to the intensive care unit annually with deadly inflammatory conditions



- Massive inflammation causes cell death and organ failure. Patients are kept alive with "life support" – machines like mechanical ventilation, dialysis, and vasopressors, that do not help them get better, but keep them alive until hopefully the body starts to heal itself
- Because of the lack of effective therapies, approximately 1 in every 3 patients dies
- Staggering costs: Lack of "active" therapies lead to patients lingering days to weeks in the ICU at \$4,300 per day in the U.S.<sup>1</sup>

Critical care (U.S.): \$108B per year <sup>1</sup> Sepsis: \$20.3B <sup>2</sup> Lung failure: \$8.8 billion <sup>2</sup> Kidney failure: \$4.7 billion <sup>2</sup>



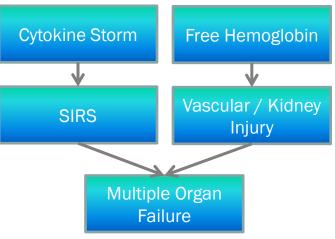
<sup>&</sup>lt;sup>1</sup> Halpern, NA, et al., Crit Care Med 2016, 44(8):1490-99.

<sup>&</sup>lt;sup>2</sup> Torio, CM and Andrews, RM. "National Inpatient Hospital Costs: The Most Expensive Conditions" (2013) Healthcare Cost and Utilization Project (HCUP) and Agency for Healthcare Research and Quality.

#### Cardiac Surgery Drives Dangerous Inflammation

- ~1.5M Open Heart Surgeries performed globally
  - 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, resulting in:
  - Hemolysis and free hemoglobin
  - find the second second
  - Levels of nitric oxide, causing decreased blood flow to vital organs
- Severe inflammation and reduced blood flow can lead to kidney, lung, and/or heart failure in many patients following surgery







## Cytokines Fuel the Fire of Inflammation

- Cytokines are small proteins that normally help stimulate and regulate the immune system and control inflammation
- Cytokines are a dual edged sword
  - They are required for proper immune system function
  - However, in mild to moderate excess, cytokines can cause or exacerbate disease (e.g. autoimmune diseases)



 But cytokines in vast excess, called "cytokine storm" can lead to a massive uncontrolled systemic inflammatory response syndrome (SIRS).



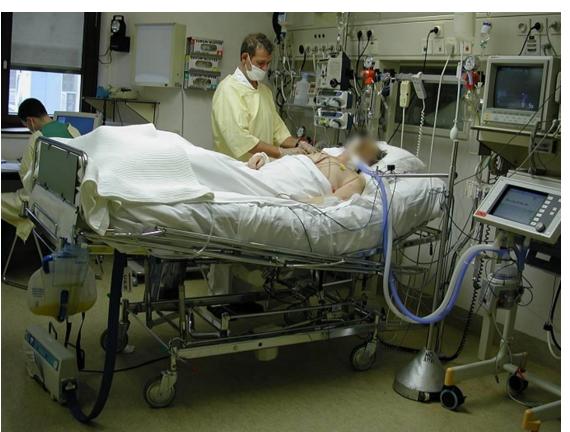
#### Massive Inflammation Causes Organ Failure

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 it today



#### CytoSorb® Removes the Fuel to the Fire

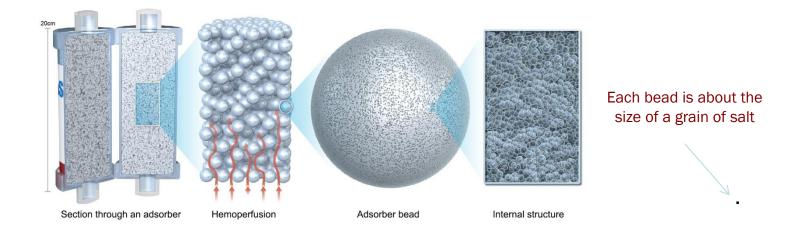
- Targets \$20+ billion opportunity in critical care and cardiac surgery
- European Union approved as the only specific cytokine filter for elevated cytokines
- Clinically proven to remove key cytokines in blood of critically-ill patients
- Removes many other inflammatory mediators such as free hemoglobin, bacterial toxins, and bilirubin
- Safe and well-tolerated: In 14,000+ human treatments, most in critically-ill patients and more than 2,500 treatments during open heart surgery





#### Powerful 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

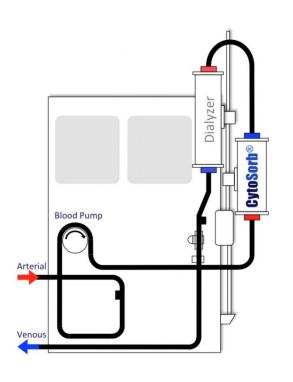


- Protected by 32 issued US patents and multiple applications pending
- Manufactured at our ISO 13485 certified facility in New Jersey
- One of the highest grade medical sorbents on medical market today



## **CytoSorb**® is Plug and Play with Existing Machines

#### **Easy to Use, No Special Equipment or Training Required**



- Place a temporary dialysis catheter in a major vein
- Connect the device to a standard dialysis machines 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 hr treatment
- Each treatment uses a new cartridge

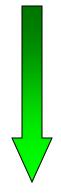


## Goal: To Prevent or Treat Organ Failure

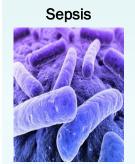


Improve
Patient
Outcome
and
Survival





Decrease Costs Of ICU and Patient Care













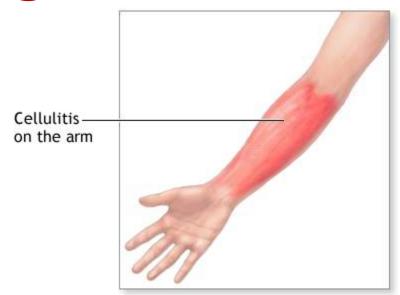


The Potential to Revolutionize Critical Care Medicine



#### Case Report: Necrotizing Fasciitis

- A 19-year old man developed a painful infection on his right hand and was rushed to a hospital with high fever and malaise
- Started on broad spectrum antibiotics for a suspected deep infection in the carpal tunnel
- Rapid onset of multi-organ failure with shock, kidney dysfunction and respiratory failure with infection quickly spreading up his arm
- Extensive surgical debridement confirmed betahemolytic Streptococcal infection, but conditioned worsened requiring increasing vasopressors and CRRT for kidney failure
- Failing therapy, CytoSorb was started. After first treatment, blood pressure significantly improved and after two treatments, vasopressors were reduced by 90% and IL-6 declined from 2,300 pg/mL to 36 pg/mL



- Renal function returned after the second CytoSorb treatment and mechanical ventilation was weaned 4 days later
- Patient recovered and amputation of his arm was avoided



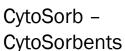
#### **Blood Purification Competition**

Sorbents

**HMCO Filters** 

Coupled Plasma
Filtration Adsorption



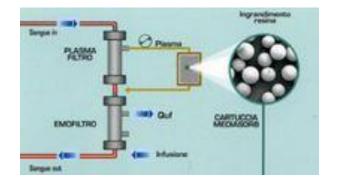




EMiC2 - Fresenius



SepteX - Gambro



CPFA - Bellco I.M.P.A.C.T - Hemolife

CytoSorb is the leader in cytokine and mid-molecular weight toxin removal. It has significant advantages of hemocompatibility, high blood flow/low resistance, massive surface area, ease of use, and compatibility with most extracorporeal blood pumps (e.g. dialysis, CRRT, and heart-lung machines)



#### \$18 Million in U.S. Government Support

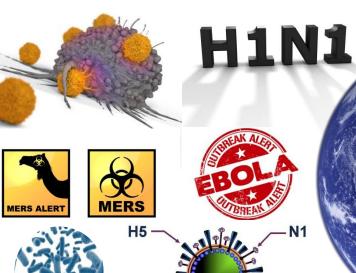
- DARPA awarded \$3.8M five year (2012-present) contract as part of "Dialysis-Like Therapeutics" program to treat sepsis by removing cytokines and pathogen-derived toxins
- U.S. Army awarded ~\$1.7M SBIR contracts for trauma and burn injury research and hyperkalemia (2011-present)
- U.S. Air Force funding a 30-patient human pilot study (~\$3M) in trauma (2013-present); FDA approved trial



- 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 \$1.7M Phase I & II SBIR contracts to advance HemoDefend purification technology with the goal of improving the quality and safety of blood transfusions (2013- present)
- JPEO-CBD awarded \$150K Phase I SBIR contract for fungal mycotoxin removal
- Defense Health Agency awarded a \$150K Phase I SBIR contract to treat hyperkalemia

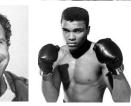


The World Needs CytoSorb®































## Key Catalyst #1:

## Drive CytoSorb Revenues



## CytoSorb® An Excellent Business Model

- Huge market
   Sold to hospitals & critical care doctors. Targets "need to have" life-or-death issues
- Little to no competition
- Critical care physicians understand the problem
- Plug and play, high margin, disposable "razorblade"

  Hospital's existing hemodialysis infrastructure is the "razor", no new hardware
- Technicians already know how to use the device
- Hospitals pay for the device and then receive reimbursement
   Depending on the application and devices used, revenue potential per patient ~\$1-5K
- Affordable yet profitable with blended gross margins of 68%, target > 80%
- Highly centralized intensive care units easy for small sales force to access



#### Direct Sales: Germany, Austria, Switzerland

\$1.0-1.5 billion



Dr. Christian Steiner, MD Vice President - Sales and Marketing and General Manage



Stefan M Baudis



Dr. Joerg Scheier, MD



Dr. Volker Humbert, MD





Dominik Gutzler



Dr. Rainer Kosanke, PhD



Alexandru Bojan



Hans-Juergen Kraus



Matthias Hoeldtke

Andreas Pendleder

Regional Sales Manager Western Germany







Steffen Martens

Petra Hoffman



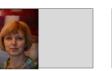
Regional Sales Manager



Oliver Lupoli



Andreas Gassmann



Anke Applehoff



CytoSorbents' direct sales force focused on most

major university and public hospitals in Germany,

Austria and Switzerland. German market alone is

**Christian Koptik** 



Harriet Adamson



Franziska Preissing





Eva Wechsler



Ilona Otto



Sales Assistant/Customer Support



## CytoSorb® Distributed in 38 Countries







































## Geographic Expansion – A Growth Engine

January 2016

Contributing to Revenue				Not Yet Contributing to Revenue			
#	Country	Population (M)		#	Country	Population (M)	
1	Germany	81		16	France	66	
2	Austria	9		17	Poland	39	
3	Switzerland	8		18	Sweden	10	
4	United Kingdom	64		19	Denmark	6	
5	Italy	60		20	Norway	5	
6	Turkey	75		21	Finland	5	
7	India	1,200		22	Russia	144	
8	Sri Lanka	21		23	UAE	9	
9	Netherlands	17		24	Qatar	2	
10	Romania	20		25	Kuwait	3	
11	Ireland	5		26	Oman	4	
12	Moldova	4		27	Bahrain	1	
13	Australia	23		28	Iraq	33	
14	New Zealand	5		29	Jordan	7	
15	Saudi Arabia	29		30	Yemen	24	
				31	Vietnam	90	
				32	Israel	8	
Total 1,621				Total	456		

September 2016

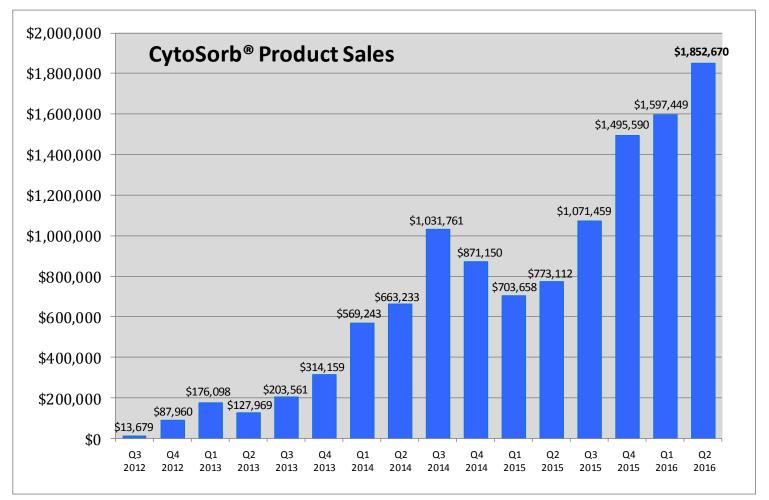
Contributing to Revenue				Not Yet Contributing to Revenue			
#	Country	Population (M)	1	#	Country	Population (M)	
1	Germany	81		29	UAE	9	
2	Austria	9		30	Qatar	2	
3	Switzerland	8		31	Kuwait	3	
4	United Kingdom	64		32	Oman	4	
5	Italy	60		33	Bahrain	1	
6	Turkey	75		34	Iraq	33	
7	India	1,200		35	Jordan	7	
8	Sri Lanka	21		36	Yemen	24	
9	Netherlands	17		37	Israel	8	
10	Romania	20		38	Iceland	0.3	
11	Ireland	5					
12	Moldova	4					
13	Australia	23					
14	New Zealand	5					
15	Saudi Arabia	29					
16	France	66					
17	Poland	39					
18	Sweden	10					
19	Denmark	6					
20	Norway	5					
21	Finland	5					
22	Russia	144					
23	Spain	46					
24	Portugal	10					
25	Vietnam	90					
26	Hungary	10					
27	Czech Republic	11					
28	Slovakia	5					
	Total	2,068			Total	91.3	

We continue to add new and existing distributors into the "contributing to revenue" category and many other countries



#### **Quarterly Product Sales**

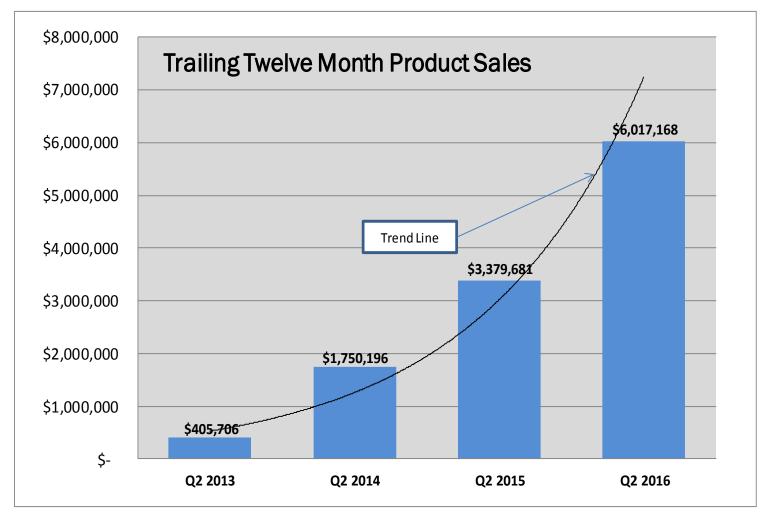
Fifth consecutive quarter of product sales growth Fourth consecutive quarter of record sales





## Trailing Twelve Months Product Sales

Over the past three years, the compound growth rate of return ("CAGR") on product sales was 145%





#### Potential for Growth Acceleration

- In Germany alone, there are ~154,000 cases of severe sepsis or septic shock each year. Here, we have:
- ✓ Established reimbursement
- Customers including majority of major university and many public hospitals
- ✓ Significant key opinion leader support
- ✓ Strong direct sales team and support infrastructure

2,100 acute care hospitals in Germany; top 400 have >400 beds 300-600 sepsis patients per hospital annually CytoSorb ASP > \$1,000 per cartridge.

\$3,000-5,000 average total CytoSorb treatment cost per patient

If adopted as standard of care, each hospital  $\approx$  \$1-3 million for sepsis alone



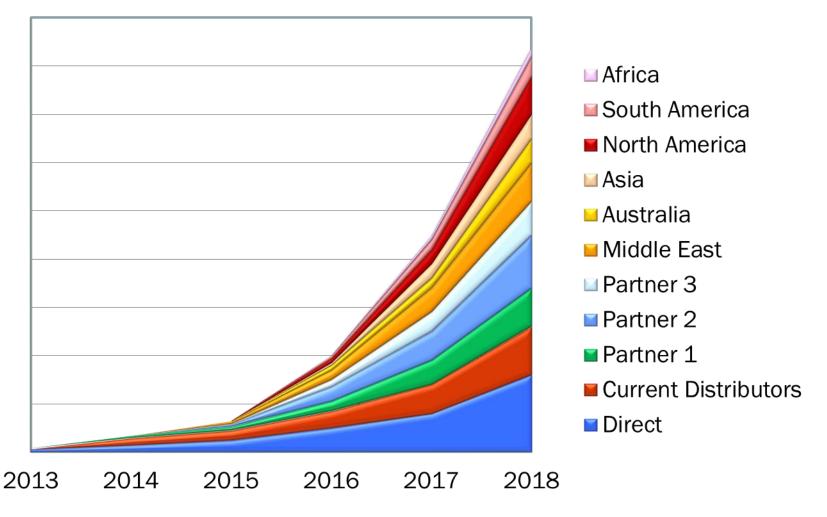
#### Strong Gross Margins to Drive Breakeven

- Because we control our own manufacturing, we expect to drive direct sale gross margins of CytoSorb® (currently > 70%) to more than 80%, with reduced costs, improved manufacturing efficiencies, and economies of scale, helping to significantly boost blended gross product margins (currently at 62%)
- Targeting operating flow cash breakeven within 2-3 years, after which CytoSorbents could become a very profitable company, where nearly 70 cents on every \$1 in sales can drop to the bottom line
- To accelerate sales growth, we plan to finance and invest in clinical studies that are intended to help CytoSorb become standard of care. These studies could be funded by us or through strategic partners



#### Growth Driven by Direct, Distributor, Partner Sales

#### Theoretical Revenue Growth Based on Layering\*





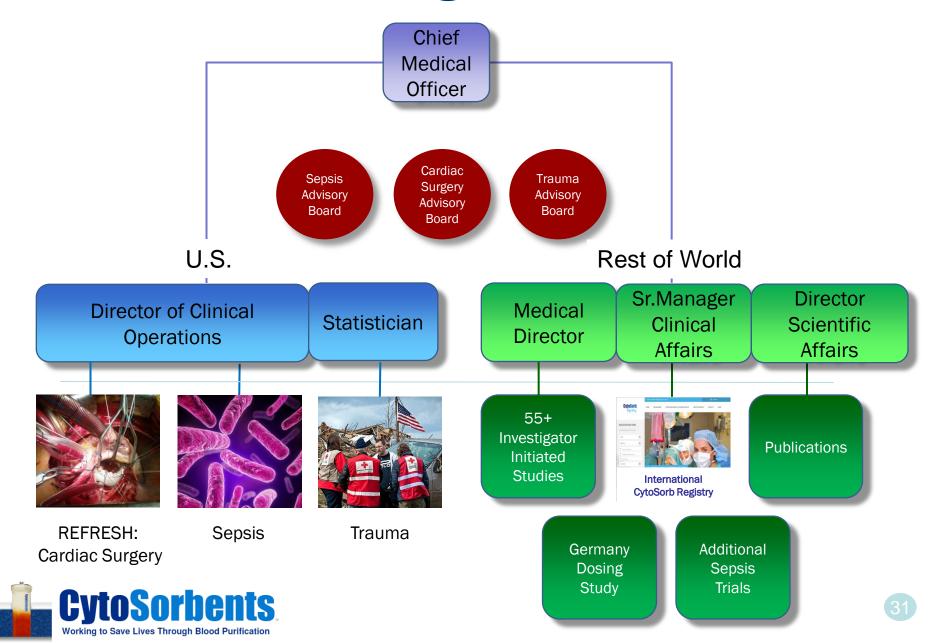
<sup>\*</sup> This graph is provided only to demonstrate the concept of revenue layering. It does NOT represent revenue forecasts or guidance

## Key Catalyst #2:

Drive Clinical Data to Support CytoSorb As Standard of Care



#### Robust Clinical Program and Team



## 3rd International CytoSorb Users Meeting







#### **ISICEM 2016**



## CytoSorbents ISICEM Research Symposium



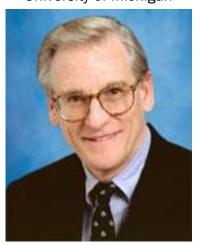


#### Leading US Advisors in Cardiac Surgery

Dr. Joe Zwischenberger, M.D.
- SAB Chair
University of Kentucky



**Dr. Robert Bartlett, M.D.**University of Michigan



Dr. Paul Checchia, M.D. Texas Children's Hospital in Houston



**Dr. Jonathan William Haft, M.D.**University of Michigan



**Dr. Nicholas Smedira, M.D.**Cleveland Clinic Foundation



**Dr. Craig Smith, M.D.**Columbia University



Dr. Peter Wearden, M.D., Ph.D. U. of Pittsburgh Medical Center



#### REFRESH I Trial Update



#### REduction in FREe Hemoglobin

- 40-patient, eight-center study evaluating the safety and efficacy of intra-operative use of CytoSorb<sup>®</sup> 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.
- Primary endpoints: Safety and reduction of plasma-free hemoglobin 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
- In May, DSMB analyzed safety data from the first 24 patients and found no safety concerns and recommended completion of the trial
- Currently, enrollment is complete with a target total of 40 patients who have completed all aspects of the trial. Expect to announce top-line data during the EACTS conference in Barcelona (Oct 1-5)
- Pending the successful completion of REFRESH I and agreement with the FDA, the REFRESH 2 trial is expected to start early next year



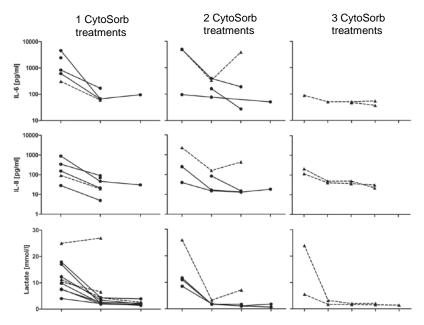
### Recent Clinical Data in Cardiac Surgery

- 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



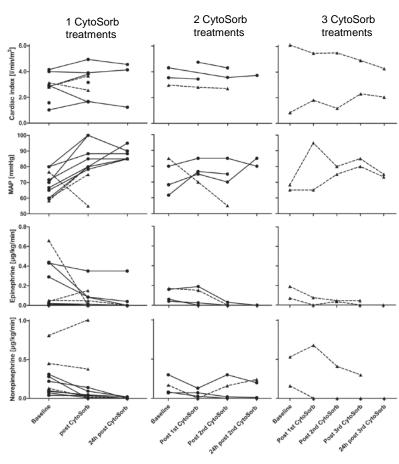
### Post-op SIRS (Cardiac Surgery) Case Series

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



### Leading Advisors in Critical Care

John Kellum, MD (Chair) University of Pittsburgh



Mitchell Cohen, MD University of San Francisco



Raul Coimbra, MD, PhD University of San Diego

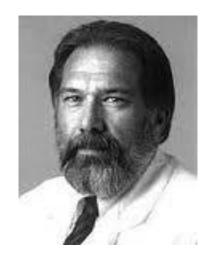


Ronald Maier, MD
University of Washington, Seattle





**Ernest Moore, MD**University of Colorado



Emil Paganini, MD
Cleveland Clinic Foundation



Joseph Parrillo, MD
Hackensack Heart and
Vascular Hospital



Claudio Ronco, MD St. Bartolo Hospital, Vicenza, Italy



### New Trials for Severe Sepsis & Septic Shock

- Sepsis, the overzealous immune response to a serious infection, is a
   Top Ten cause of death by causing organ injury, organ failure, and death
- Largest, most complex, critical care market; ~30 million people afflicted worldwide each year, estimated 10 million deaths
- Currently no approved products to treat sepsis

U.S. and European clinical trials being planned to advance CytoSorb as

standard of care for sepsis





### CytoSorb Attacks Sepsis Broadly



Inflammatory cytokines (organ failure) & other factors



Immunosuppressive cytokines & re-establish immune responsiveness



Many bacterial toxins (organ failure)



Re-establish proper leukocyte trafficking to prevent cell-mediated organ injury



Improvement in hemodynamics



Reduction in capillary leak

No other single therapy has demonstrated this broad range of activity



### Refractory Septic Shock

At the 26<sup>th</sup> Symposium for Intensive Medicine + Critical Care in Bremen, Germany, Dr. Sigrun Friesecke, Senior Intensivist in the Greifswald University Hospital MICU reported on a prospective, single arm study in 22 patients with refractory late-stage septic shock

- Patients had refractory shock despite high doses of vasopressors, respiratory failure requiring mechanical ventilation or ECMO, anuric kidney failure requiring dialysis, and lactate > 8 mmol/L
- A similar population (n=16) receiving standard of care, 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.\*
- Results from the CytoSorb Greifswald Study
  - 28-day survival was 41%, a 30-40% absolute improvement over expected (0-10%)
  - Resolution of shock in 68% of patients treated with CytoSorb
  - Reduction of IL-6 from an initial average of 87,000 pg/mL to below 10,000 pg/mL after 24 hours
    of treatment

<sup>\*</sup> 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.





### 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

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#### 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 replace 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)	

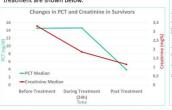


#### Results

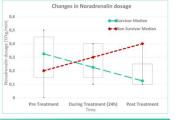
6 treated patients with CytoSorb survived and during the treatment there was an overall improvement of MAP from 83 (73,5-89) to 88 (82-89,5) mmHg, with a rapid reduction in vasopressors dosages: noradrenaline decreased from 0,33 (0,15-0,46) to 0,13 (0,10-0,18) while dopamine from 7,5 (6-8) to 3 (1,5-5) Y/kg/min. Moreover, there was a marked decrease of PCT levels from 14,53 (7,64-75) 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

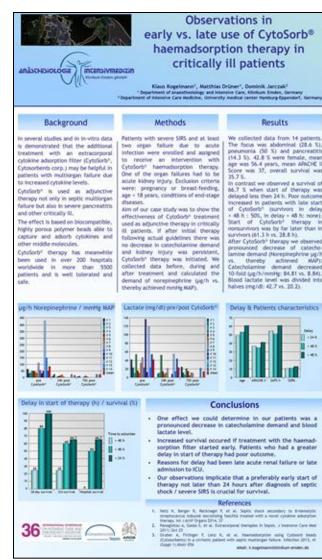
- [1] Kellum et al. Crit Care Med 2004 32(3):801-5
- [2] Schadler et al. Critical Care 2013 17 (Suppl 2):P62

36th International Symposium on Intensive Care and Emergency Medicine Brussels, 15-18 March 2016, P193



### Septic Shock and SIRS Case Series

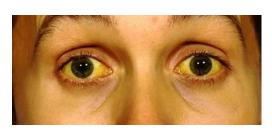
- 14 patient case series: Abdominal sepsis (29%), pneumonia (50%), pancreatitis (14%), other (7%)
- Patients were critically-ill, with a mean APACHE II score of 37, predicting a mortality of > 85% in sepsis
- Observed a pronounced 10-fold decrease in vasopressor requirement and a reduction in blood lactate 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





### 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

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- <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 hydrophobimolecules, could be a valid artificial support in many conditions of organ failure through the reduction of cytokines and other toximolecules directly from blood. Today, extracorporeal systems for this purpose are based on plasma-adsorption.

We performed an in vitro study on bilirubin kinetics removal 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 11. 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.





Fig. 1: In vitro hemonerfusion circuit and CytoSor

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

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



Table 1: Data and Bilirubin Mass Balance of the experimen







#### CONCLUSIONS

This in vitro study shows the effectiveness in removing Billrubin without any substantial Albumin loss, the resin ability to break the Albumin-Billrubin complex and to adorbit rivervishly Billrubin. 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.

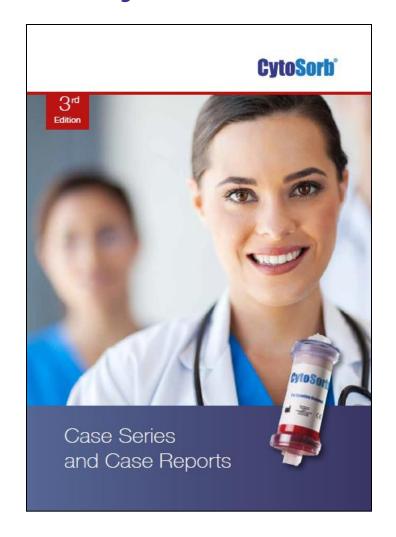
[1]Weber et al. Biomacromolecules 2008, 9 1322-1328



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### Many Published Peer-Reviewed Articles











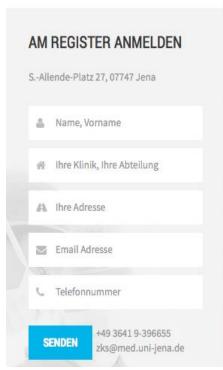
### CytoSorb Website - A Wealth of Info

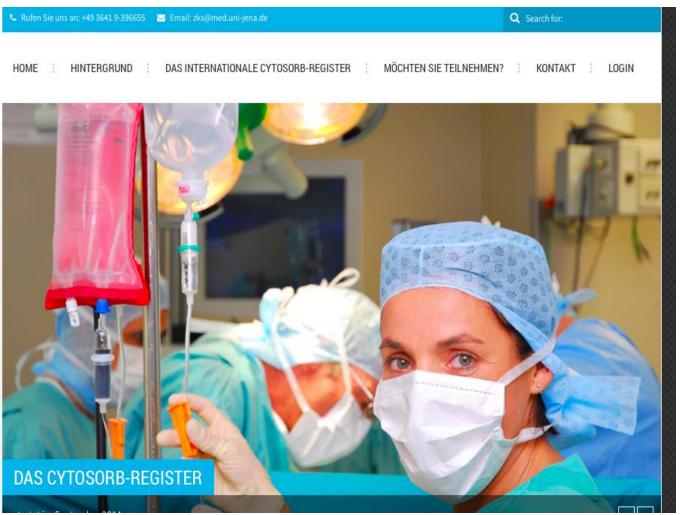




### The International CytoSorb® Registry

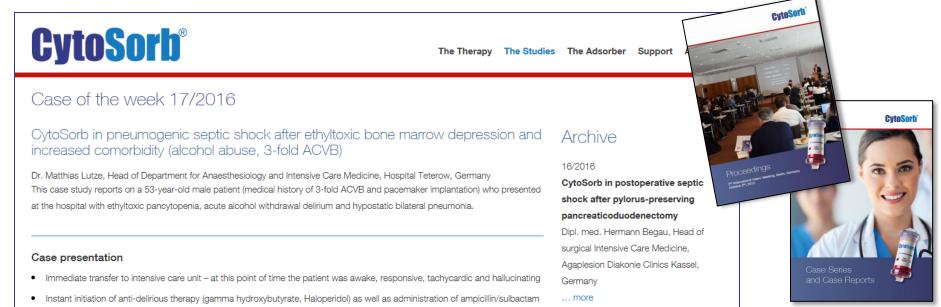








Visit CytoSorb.com for Case of the Week



- 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 <a href="https://www.cytosorb.com">www.cytosorb.com</a> 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



### Key Catalyst #3:

# Leverage Pipeline to Establish Strategic Partnerships



# Beads Enable a Broad and Valuable Pipeline



Critical Care, High Risk Surgery

#### **HemoDefend**



Blood Collection & Transfusion

#### **ContrastSorb**



CT Imaging, Interventional Radiology

#### **CytoSorb-XL**



Severe

Hyperkalemia

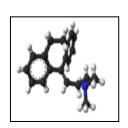
Potassium

Sorbent

K+

Sepsis, Critical Care, High Risk Surgery

**DrugSorb** 



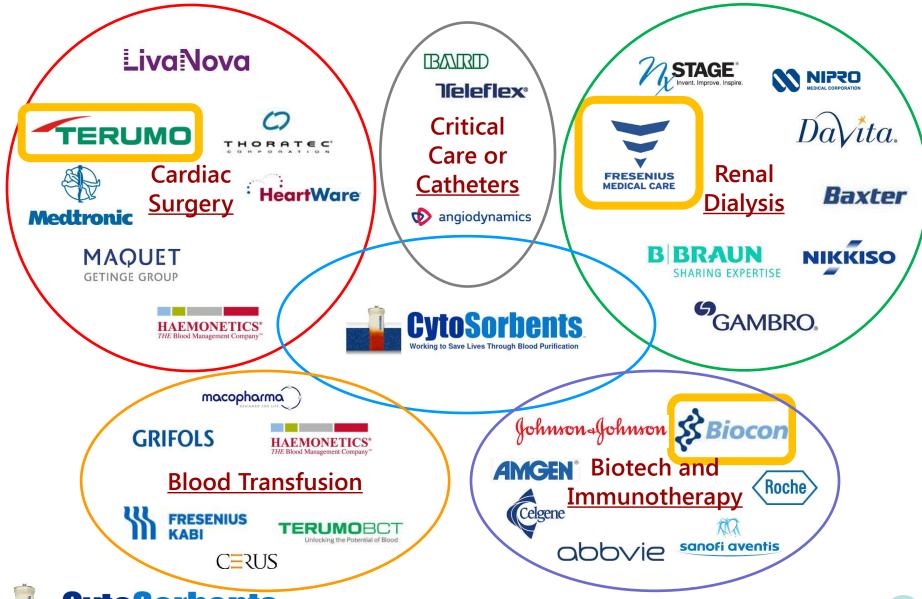
Drug Overdose, Chemo Removal

**BetaSorb** 



Improving Dialysis

### Three Major Partnerships, Potential for More





### TERUMO Partnership

 Entered into a multi-year partnership with Terumo Cardiovascular Group, a global leader in medical devices for cardiac and vascular surgery with \$5 billion in annual sales across more than 160 countries, for exclusive distribution of CytoSorb® for cardiac surgery applications in France, Denmark, Norway, Sweden, Finland, and Iceland



Arik Anderson – President of Perfusion and Surgical Devices Division at Terumo

"Our collaboration with CytoSorbents enables us to offer this innovative, easy-to-use blood purification therapy to address our customers' most challenging cardiac cases. CytoSorb integrates with the heart-lung machine platform, giving surgical teams, for the first time, the ability to safely reduce dangerous inflammatory mediators in real-time as they are being generated during cardiac surgery. We believe Terumo's extensive relationships in cardiac surgery centers, combined with the benefits and simple implementation of CytoSorb, will accelerate adoption of CytoSorb as a cost-effective, standard-of-care therapy to control severe inflammation in patients undergoing cardiac surgery."

- Terumo has committed to annual minimum purchases to maintain exclusivity
- Strong validation of our technology and opens door to potential expansion to other countries, such as Japan – the second largest medical device market in the world



### Fresenius Medical Care Partnership

- Currently in a multi-year partnership with Fresenius, the world's largest dialysis company, for exclusive distribution of CytoSorb<sup>®</sup> in critical care in France, Poland, Denmark, Norway, Sweden, and Finland
- CytoSorb® is a key part of Fresenius' growth strategy in critical care
- Fresenius has committed to annual minimum purchases to maintain exclusivity
- Leveraging Fresenius' critical care leadership and industry-leading sales force and distribution
- Potential for broader future synergy and expansion
- In May, Fresenius launched CytoSorb® with a 30-person ICU sales force that is also selling Fresenius products





## **Biocon** Partnership Update



- Biocon is the largest biopharmaceutical company in India
- Significant growth in India with expansion into Sri Lanka
- Currently funding and conducting the first investigator initiated study in India
- Established a separate sales division to focus specifically on all aspects of CytoSorb market development and sales
- Embarking on another KOL speaker series in India



### Advanced Development of CytoSorb-XL

- CytoSorb-XL is a next generation porous polymer bead technology combining lipopolysaccharide (LPS) endotoxin removal with the robust cytokine, toxin, and inflammatory mediator reduction achieved by CytoSorb®
- Endotoxin is a very potent stimulator of cytokine storm, often resulting in septic shock in serious Gram negative bacterial infections related to abdominal or urinary tract infections, pneumonia, and hospital acquired infections
- In a head-to-head comparison, CytoSorb-XL matched the level of endotoxin reduction of the leading endotoxin adsorber, Toraymyxin™ (Toray, Japan) in an in vitro plasma recirculation system
- CytoSorb-XL is expected to eliminate the need for stand-alone endotoxin specific filters by offering superior performance and removal of endotoxin and a broad range of inflammatory mediators that drive uncontrolled deadly inflammation
- CytoSorb-XL and its novel endotoxin binding chemistry are the subject of a broad composition of matter patent application, intended to protect the technology worldwide for the next two decades. CytoSorb-XL is intended to succeed CytoSorb®



### Key Catalyst #5: Increase Investor Awareness





### NASDAQ Capital Market Listed

Clean capital structure with good liquidity for investors





### Included in Russell Microcap Index

### CytoSorbents Corporation Set to Join Russell Microcap Index

6/19/15

CytoSorbents Corporation (NASDAQ: CTSO), a critical care immunotherapy leader commercializing its CytoSorb® blood purification technology to reduce deadly uncontrolled inflammation in hospitalized patients around the world, is set to join the Russell Microcap® Index at the conclusion of the Russell indexes annual reconstitution on June 26, 2015, according to a preliminary list of additions posted on June 12, 2015.

Membership in the Russell Microcap Index, which remains in place for one year, means automatic inclusion in the appropriate growth and value style indexes. FTSE Russell determines membership for its Russell indexes primarily by objective, market-capitalization rankings and style attributes.

Dr. Phillip Chan, Chief Executive Officer of CytoSorbents stated, "We are pleased to be included in the Russell Microcap Index, a significant corporate achievement that is expected to increase visibility and exposure of our company and life-saving technology to the broader investment community. This complements our continued institutional investor outreach, where the response has been extremely positive to date."

Russell indexes are widely used by investment managers and institutional investors for index funds and as benchmarks for active investment strategies. Approximately \$5.7 trillion in assets are benchmarked to the Russell's U.S. indexes. Russell Indexes are part of FTSE Russell, a leading global index provider.

For more information on the Russell 1000 and the Russell indexes reconstitution, go to "Recon Central"





### Increasing Institutional Ownership

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

Owner Name	Date	Shared Held	Change (Shares)	Change (%)	Value (in 1,000s)
VANGUARD GROUP INC	06/30/2016	537,707	5,446	1.02	2,828
RAYMOND JAMES & ASSOCIATES	06/30/2016	324,603	247,052	318.57	1,707
ADVISOR GROUP, INC.	06/30/2016	301,845	301,845	New	1,588
GEODE CAPITAL MANAGEMENT, LLC	06/30/2016	125,772	0	0.00	662
DOUGLASS WINTHROP ADVISORS, LLC	06/30/2016	70,540	70,540	New	371
BLACKROCK FUND ADVISORS	06/30/2016	53,915	15,203	39.27	284
SKYLANDS CAPITAL, LLC	06/30/2016	48,350	(4,150)	(7.91)	254
CALIFORNIA PUBLIC EMPLOYEES RETIREMENT SYSTEM	06/30/2016	46,100	0	0.00	242
BANK OF NEW YORK MELLON CORP	06/30/2016	29,469	(477)	(1.59)	155
BLACKROCK INSTITUTIONAL TRUST COMPANY, N.A.	06/30/2016	26,460	0	0.00	139
LADENBURG THALMANN FINANCIAL SERVICES INC	06/30/2016	24,069	469	1.99	127
NORTHERN TRUST CORP	06/30/2016	23,709	0	0.00	125

7.0%
Institutional
Ownership
(6/30/16)

42 Institutional holders

1.8M shares



Increasing Media Coverage

### **Forbes**



Jennifer Hicks Contributor

I write about science, robotics & innovative technologies in Europe.

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TECH 8/24/2016 @ 4:09PM | 2,950 views

This Blood Filtering System Could Help Lower The Risk of Death From Inflammatory Infections



A new blood filter. (Image credit: Kurt Paulus, Munich)

Trauma to the body comes in many forms – severe burns, gun shot wounds, liver failure, drug overdose, sepsis – which can be deadly. Treating these types of trauma to the body means people end up in the intensive care unit (ICU).



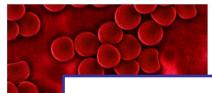
Exclusive: Cytosorbents CEO On How Its Blood Purification Technology Can Change Healthcare

The Street

Phil Chan CEO, CytoSorbents

Jayson Derrick (/users/jayson-derrick) , Benzinga Staff Writer Follow.

August 15, 2016 8:54am | Comments



USA and CANADA \*\*

CytoSorbents' blood filter is saying liv

<u>oroactiveinvestors</u>

CytoSorbents' blood filter is saving lives and money

07:14 07 Jul 2

CytoSorb is a blood filter designed to reduce the "fuel to the fire" of deadly inflammation. It is approved for use in the EU, with distribution in 34 countries worldwide.

Medtech Insight

Related CTSO (/stock/CTSO)

(http://cdn3.benzinga.com

Pharma intelligence

### CytoSorbents Expanding Marketing Reach Of CytoSorb Blood Purifier

by Reed Mi

@MedtechReed reed.miller@informa.com

#### Executive Summary

CytoSorbents is sponsoring the REFRESH I trial of its CytoSorb extracorporeal cytokine adsorber in the US, which the company hopes will support approval of a pivotal trial of the device for reducing reduce plasma free hemoglobin and cytokines in patients undergoing complex cardiac surgery.





# Increasing Analyst Coverage



\$3.11-\$8.19

#### **EQUITY RESEARCH** INITIATION Cytosorbents Corporation

	C	ytosorbents Corporation
Eiotechnology CTSO - NYSE Closing Price 05/23/2016 Rating: 12.Month Target Price: 52.Week Range: Market Cap (M): Shares O(S (M): Float: Avg. Daily Volume (000): Dividend: Dividend: Risk Profile: Fiscal Year End:	May 23, 2016	New Paradigm in Sep-  nith a Buy Rating and a \$8.00 Price Target.  VyfoSorbents is now commercializing its CE-approved product CyfoSorbents is now commercializing its CE-approved product CyfoSorbents in the EU (direct in Germany, Austria and Switzerland) and in a tool 22 countries worldwide (ex.US) for complications related to life-threated to the EU (direct in Germany, Eustria man, burn injury, liver failure, inflammatory diseases such as sepsis, trauma, burn injury, liver failure, inflammatory diseases such as sepsis, trauma, burn injury, liver failure, inflammatory diseases and care for complication of care for septimental complex complex products of care for the standard of care for the complex products of the standard of care for the care for the standard of care for the care for the standard of care for the care for the standard of the care for
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CytoSorbents is now commercializing its CE-approved product CytoSorb Cytosoruents is now commercializing its UE-approved product. Cytosoru in the EU (direct in Germany, Austria and Switzerland) and in a total of in the EU (direct in Germany, Austria and Gwitzerians) and in a total of 32 countries worldwide (ex.US) for complications related to life-threatening. ar countries worrowne (er.co) for compresents teased to interactioned inflammatory diseases such as sepsis, trauma, burn injury, liver failure, and CytoSorb has the potential to become part of the standard of care for sepsis, Cytosoro nas the potential to Decome part of the standard of care for sepsis, a top-10 cause of death worldwide. It is an extracorporeal blood purifier (a a top-10 cause of death workwide, it is an extracorporeal tilloop purner; a filter) that targets the immunological "cytokine storm" that accelerates organ and tailure and uttimately death. By extending the treatment of the purpose organization and nature and unimitately usage, by extending the treatment window for these patients, the product could be the difference between life

2017E 2016E ,810A

CytoSorb has yet to build sales traction. Revenues last year from both direct various has yet to build sales traction. Revenues last year from both direct sales and distributorship amounted to a total of only \$4M. Introducing a new sales and distributorship amounted to a total of only \$4M.





May 10, 2016

Swayampakula Ramakanth, Ph.D. 212-356-0544 sramakanth@hcwresearch.com

Earnings Update Medical Device

CytoSorbents Corp (CTSO)

212-356-0521 slee@hcwresearch.com

Fresenius to Rollout in May; REFRESH to Report in 3Q16; Reiterate Buy

05/09/2016 Stock Data NASDAQ

Financial update and changes to our model. CytoSorbents reported 1Q16 financial results and held a conference call on May 9. The company reported revenues of \$1.8M, higher than our estimate of



### WBB Securities, LLC

Stephen G. Brozak • sbrozak@wbbsec.com • (908) 518-7610

INITIATING COVERAGE - FEBRUARY 25, 2015

CytoSorbents Corporation (NasdaqCM: CTSO)

Initiating Coverage with a Speculative Buy Rating and One-Year Price Target of \$13.00



d and	One-Teal Target Price	\$13.00
9	12 Month Target	\$4.40-\$12.87
11.00	12 Month Trading Range	2007.87
10.50	Market Capitalization (Mil)	\$207.01
10.00	Market Capitalis	

### Zacks Small-Cap Research

Brian Marckx, CFA bmarckx@zacks.com Ph (312) 265-9474

June 2, 2016

10 S. Riverside Plaza, Chicago, IL 60606

CytoSorbents Corporation (CTSO-NASDAQ)

CTSO: Fresenius Commences Sales, DSMB Recommends Continuation of REFRESH I

Based on our 10-year DCF model, which uses a 13% discount rate to account for certain risks and uncertainties that CytoSorbents faces, and a 2% terminal growth rate, the shares are valued at approximately \$12.50.

Current Price (06/01/16) Valuation

#### OUTLOOK

\$4.48 \$12.50

We view 2015 as somewhat of a re-grouping year on the income statement authough regrouping should be put into context, that product sales grew 29%—and which would have been almost a few first and which would have been almost sales grew 29%—and which would have been almost great grea that product sales grew 25% – and which would have been almost 50% growth if not for an Fx headwind. And if not for the sales force ours grown it not for an Ex neadwind. And it not for the sales force disruption earlier in the year, product sales growth would likely have been even significantly stronger.

We expect to see accelerating product sales growth as well as more We expect to see accelerating product sales grown as wen as miles strides on the operational front in 2016. In addition to Fresenius coming online, expansion into other geographic territories (in coming online, expansion into other geographic territories (iii addition to those detailed by Fresenius), an expected continued accepting to those peralled by Fresemus), an expected continued regular flow of clinical data (including that from the patient registry as regular now or clinical oasta (including that from the patients regular) a well as REFRESH I), potential additional production gains from the direct sales force, sales through Biocon could also accelerate direct sales torce, sales through blocon could also accelerate further. And the cardiac-surgery channel also holds significantly nuturer. And the cardisc-surgery chariner also horize significantly potential. Consummation of a partnering agreement could further this opportunity.



52-Week Range:

Cash (M):

### Working to Save Lives Through Blood Purification

### **CytoSorbents** Has Tremendous Potential

CytoSorbents is a hybrid: Combines the greater visibility and lower risk of a medical device company with product sales with the upside potential of biotech

- Massive untapped \$20 billion unmet, medical need in critical care
- Generating significant international CytoSorb® sales growth with 68% gross margins
- Fueling growth through more usage, clinical data, and continued geographic expansion
- Pursuing CytoSorb® FDA approval through our REFRESH I and II cardiac surgery trials
- Fresenius, Terumo, and Biocon partnerships validate tech and open future possibilities
- Greater market awareness and financing for success

CytoSorb is helping to save lives throughout the world



