



SPECTRALIX  
*Medical* | UNZ

**WINNING THE BATTLE  
AGAINST SEPTIC SHOCK**

May 2024

TSX: EDT  
[spectraldx.com](https://spectraldx.com)

# Forward Looking Statements

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# About Spectral Medical

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COMMITTED TO DECREASING THE UNACCEPTABLY HIGH MORTALITY RATES CAUSED BY SEPTIC SHOCK

Spectral's vision is to provide a personalized approach that will enable vastly improved outcomes for patients with septic shock by combining a targeted diagnostic test and therapy



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Spectral is a phase 3 company seeking U.S. FDA approval for its unique product for the treatment of septic shock, Toraymyxin™ (“PMX”)

- PMX is a therapeutic hemoperfusion device that removes endotoxin from the bloodstream and is guided by the Company's Endotoxin Activity Assay (EAA™)- the only FDA cleared diagnostic for the risk of developing sepsis
- Endotoxin causes an inflammatory reaction leading to endotoxic septic shock (ESS)... the most malignant form of septic shock

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Spectral is listed on the Toronto Stock Exchange under the symbol EDT



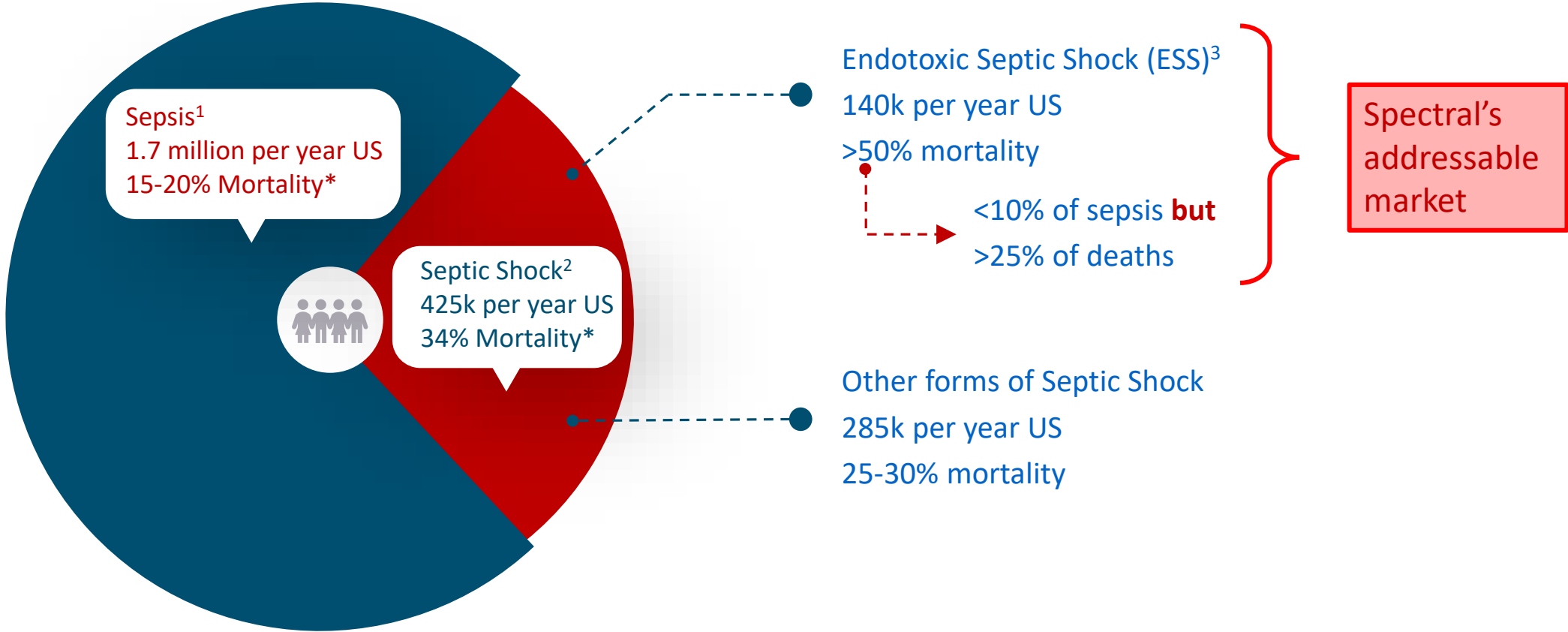
# Investment Highlights

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- Spectral addresses Endotoxic Septic Shock... the most malignant form of septic shock
  - approx. 140,000 patients each year with a mortality rate > 50%
- U.S. \$2 Billion+ annual TAM and No Competition - no FDA approved sepsis solutions in the market
- De-risked Phase 3 confirmatory trial- Tigris Trial
  - Building on knowledge gained from the earlier EUPHRATES trial, which evaluated the use of PMX in a randomized controlled trial of adults treated for endotoxemia and septic shock
  - Inclusion of 179 patients subset from Euphrates to be combined with 150 Tigris trial patients as part of FDA regulatory submission
- De-risked commercialization- Exclusive Distribution Agreement with Baxter (Feb 2020)
  - Recently amended initial term to 10 years post-FDA approval of PMX
  - Distribution agreement to transfer to Baxter's 'Vantive' spin-off (est. end 2024)... PMX partnership considered a strategic priority for 'Vantive'
- 90 Patient Milestone Achieved (Feb/24) - Baxter paid Spectral non-dilutive milestone payment to retain exclusive distribution rights... next Baxter milestone payment at FDA approval
- U.S. FDA granted Breakthrough Device Designation for PMX in July 2022
- Company has strong track record of clinical and regulatory excellence (FDA, Health Canada, CE, etc.)

# Treatment for Septic Shock... Unmet Clinical Need

Septic shock is a severe and highly fatal form of sepsis... a life-threatening condition resulting in low blood pressure, cell death and severe organ dysfunction... and is a leading cause of death in the ICU



Spectral's addressable market

\* Mortality attributed to sepsis. Usually measured within 30 to 60 days.

<sup>1</sup> Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Healthcare Quality Promotion (DHQP) August 9, 2022

<sup>2</sup> Critical Care Medicine 46(12):p 1889-1897, December 2018

<sup>3</sup> Spectral Management estimates, based on Euphrates trial data

# Commercialization Strategy

## Commercial Partner → **Baxter**

- Entered into an exclusive distribution agreement with Baxter in 2020
  - Baxter to spin-off its Renal Care and Acute Therapies businesses, into an independent, publicly traded entity (“Vantive”) anticipated ~end 2024
  - EAA + PMX products featured prominently in Baxter’s Vantive spin-off: [Renal Investor Presentation \(q4cdn.com\)](https://www.baxter.com/~/media/Investor-Relations/2023/09/23/2023-09-23-Renal-Investor-Presentation-q4cdn.com)
- Exclusive distributor of PMX in US and Canada and non-exclusive rights to distribute EAA™ globally
- Responsible to commercialize PMX entirely on its own behalf and its own expense
- Provides Spectral access to Baxter’s market capabilities thereby accelerating commercialization efforts
  - Baxter installed critical care devices in U.S. ICUs estimated @ ~50% market share
- Milestone payments to Spectral:
  - Contract signing
  - Interim 90-patient enrollment
  - FDA approval of PMX
- Robust distribution economics, with minimum pricing and minimum quantities
- Term: 10-year initial term post-FDA approval

Baxter relationship continues to be strong with collaboration on post-approval marketing plans for PMX commercialization, including: product branding, pricing and roll-out plans

# U.S. Market Opportunity: ~\$2 Billion+ Annual TAM

## Addressable Market

- U.S. Addressable Market = ~\$2 Billion<sup>1</sup> p.a.
- Baxter market share of U.S. ICU CRRT devices = ~50%
- Current healthcare spend to manage sepsis in the U.S. = ~\$20 Billion p.a.
- Eli Lilly's sepsis drug Xigris Year 1 market penetration estimated at ~9.5k patients (sales = US\$89 million)<sup>2</sup>

## Illustrative Potential US Net Economics to Spectral – PMX + EAA (per annum)

### Assumptions:

- PMX premium priced (gross margins anticipated at >70%):
  - current European pricing ~USD\$6,000 per PMX column; LASER consultant report indicated US market pricing of ~USD\$7,500 per PMX column (2016)
- Typical medical device distribution economics range from 40%-60% revenue sharing

### Illustrative US Market Penetration of EDT Addressable Market (%)

	7.5%	15.0%	30.0%	40.0%	50.0%
No. Patients	10,500	21,000	42,000	56,000	70,000
No. PMX Columns	21,000	42,000	84,000	112,000	140,000
<b>Spectral PMX EBITDA Potential</b>	<b>\$44 M</b>	<b>\$88 M</b>	<b>\$176 M</b>	<b>\$235 M</b>	<b>\$294 M</b>
No. EAA kits	52,500	105,000	210,000	280,000	350,000
<b>Spectral EAA EBITDA Potential</b>	<b>\$2 M</b>	<b>\$4 M</b>	<b>\$9 M</b>	<b>\$12 M</b>	<b>\$15 M</b>
<b>Total Spectral EAA / PMX EBITDA Potential</b>	<b>\$46 M</b>	<b>\$93 M</b>	<b>\$185 M</b>	<b>\$247 M</b>	<b>\$309 M</b>

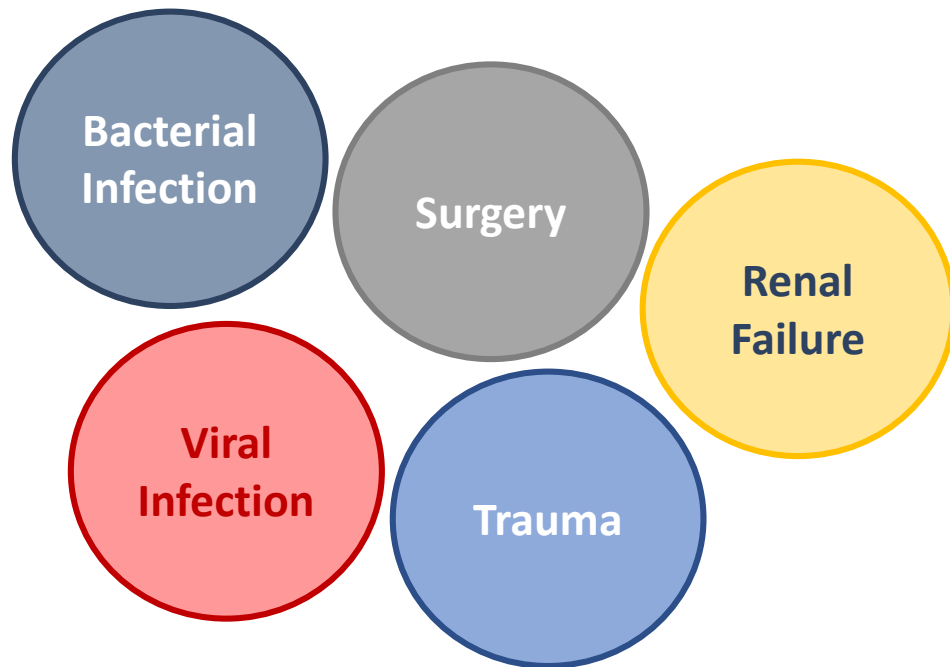
<sup>1</sup> Based on 140,000 patients x 2 PMX columns per treatment x \$6,750 price per PMX column

<sup>2</sup> Eli Lilly's Xigris was an FDA approved sepsis drug launched in 2001; the product was pulled from the market by Eli Lilly in 2011 after clinical trials showed it provided no benefit for patients in septic shock

# Endotoxin Inflammatory Response

- Endotoxins are very potent and widely spread inflammation-inducing substances; and in the course of local infections induce acute non-specific inflammation
- Triggered by the body's overactive response... this uncontrolled host response releases a potentially lethal array of pro-inflammatory molecules throughout the whole body

## Endotoxin Key Drivers



## Inflammatory Reaction

- Endotoxin shed from local bacterial infection
- Endotoxin translocation from GI tract
  - every human has 25-30 grams of endotoxin in their GI tract
  - <0.001 grams of endotoxin is enough to kill a person

## Organ Failure... or Death

- Heart
- Liver
- Kidneys
- Lungs

Toxicity to various tissues (heart, liver, kidneys, lungs) can lead to organ damage... and ultimately death



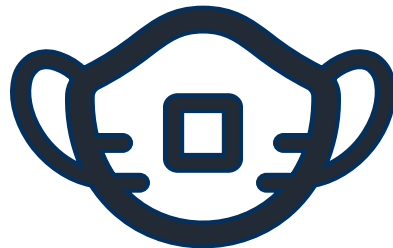
# Current Standard of Care... Limited Efficacy

- Standard of care therapies aimed at resuscitating the patient to ensure adequate blood pressure and pulmonary function.
- The battery of therapies to address **endotoxic septic shock** remain limited:

Antibiotics / Drugs



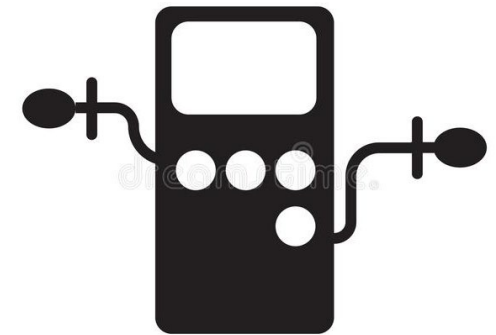
Ventilator



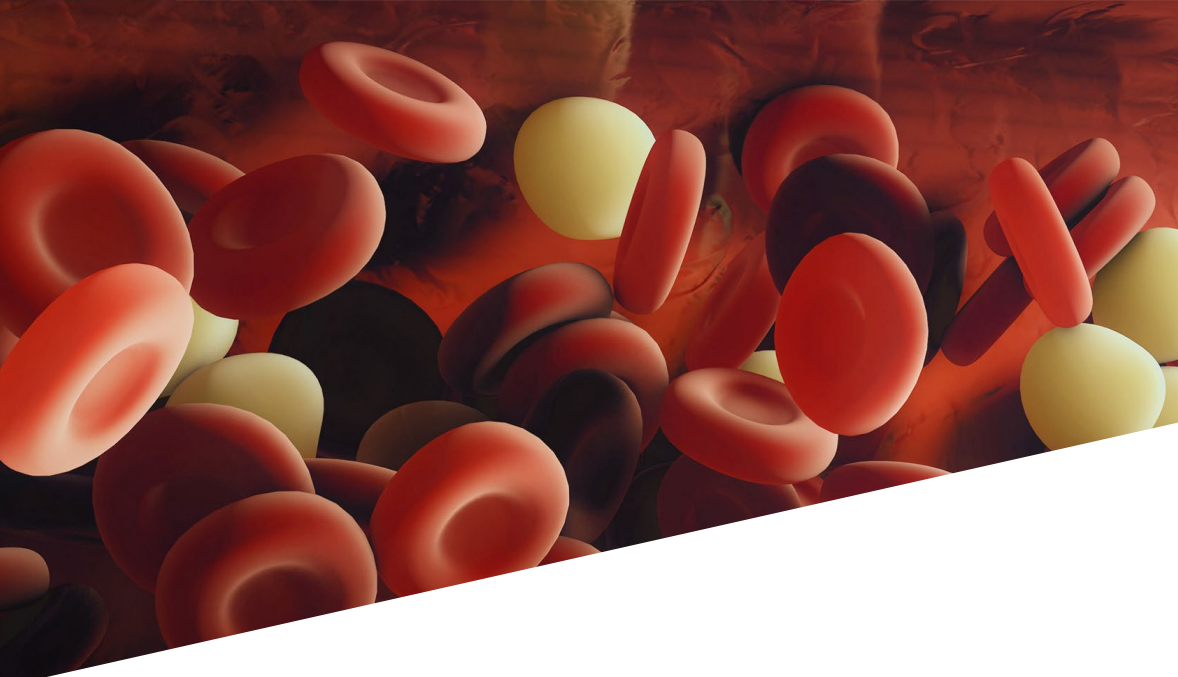
Vasopressors / IV Fluids



Dialysis



None of the standard of care therapies address the acute inflammatory agent – Endotoxin (i.e. the root cause)



# Spectral's Personalized Solution

Combining a diagnostic- EAA™ with a therapeutic device- PMX = Identification and Driver Removal

## PMX –Remove Endotoxin from the Blood

### EAA™ - Measure Endotoxin Activity

- Rapid diagnostic for endotoxin activity in human whole blood
- Predictor of ICU mortality in septic patients
- Quick results (30 mins)
- Sold globally
- Evidence of utility in thousands of patients
- FDA-approved diagnostic



- Removal of endotoxin leads to a decrease in inflammatory mediator levels, as well as improvement in vascular function and hemodynamics
- Proven efficacy to remove endotoxin – bench test results: each cartridge can remove up to 20 µg of endotoxin
- Being evaluated in a phase 3 confirmatory trial

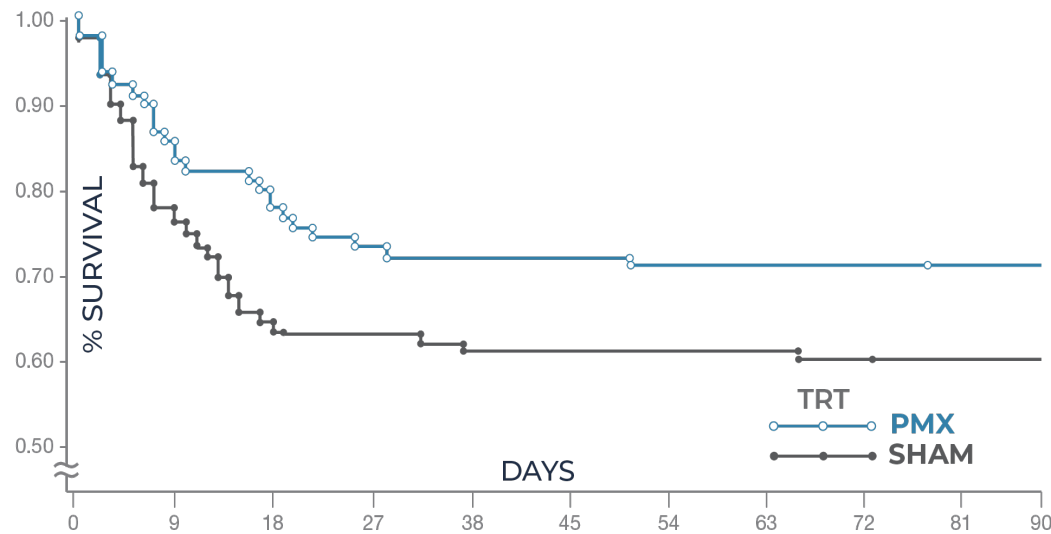
**Identify the Type of Septic Shock to Guide Therapeutic Options**

**Removal of Endotoxin the Driver of Shock and Organ Damage**

# Clinical Benefits - The EUPHRATES Trial

The EUPHRATES Trial – a double blinded, randomized trial of PMX-demonstrated that PMX cartridge therapy **decreased mortality, increased both ventilator free and renal replacement therapy free days**

194 patients with baseline EAA™ results of  $\geq 0.60$  and  $< 0.90$ , and MODS  $> 9$



- A group of patients with baseline EAA™ results between  $\geq 0.60$  and  $< 0.90$  at randomization, treated with PMX, had a 28-day mortality of 26% as compared to 37% in patients who did not receive PMX ( $p < 0.05$ ,  $n = 194$ ).
- In the same population, patients who received PMX had a 90-day mortality of 30% as compared to 41% in patients who did not receive PMX ( $p < 0.04$ ,  $n = 194$ ).

PMX Observed Data – Euphrates Trial Subset	
28-Day Absolute Mortality Reduction (“ARR”)	10%
28-Day Relative Mortality Reduction (“RRR”)	29%
Ventilator-free days**	14
Renal Replacement Therapy-free days**	9
Mean Arterial Pressure (“MAP”)*	5.0 mmHg
Vasopressor Index change*	0.8 units

\*Mean difference from Day 0 to Day 3 in patients treated with PMX as compared to patients who received SHAM

\*\*Median difference over 28 days in patients treated with PMX as compared to patients who received SHAM

# Tigris Confirmatory Trial

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The Tigris trial is a prospective, multicenter, randomized, open-label clinical trial that uses the PMX cartridge versus standard of care for patients with septic shock and endotoxemia (measured as EAA level of  $\geq 0.60$  to  $0.90$ )

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✓ Trial design agreed upon with the FDA:

- US sites only- up to 25 sites
- 150 total target patients
- Randomized 2:1
- Open label trial
- Target Endpoint: minimum 10% difference in mortality in a 28-day period vs standard of care (ARR of 10%)
- Bayesian statistical analysis

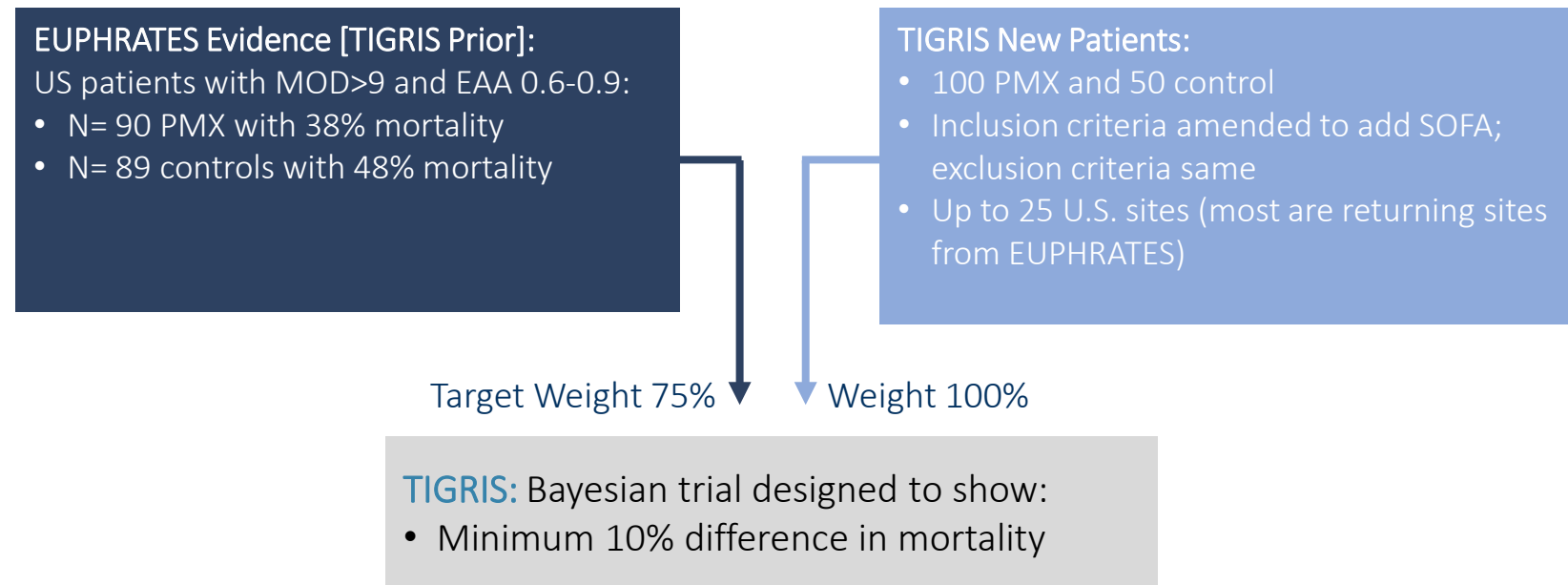
✓ Current status:

- 106 patients randomized to-date out of the 150 total target
  - Observed accelerated enrollment continued into 2024... Jan, Feb & April 2024 record enrollment months to-date
- 22 Tigris sites onboarded
  - 2 sites in late-stage onboarding process

# FDA Regulatory Pathway... De-Risked

The FDA has agreed to a Bayesian analysis approach for the regulatory submission of PMX- this allows the inclusion of a subset of 179 patients from EUPHRATES to be combined with the 150 Tigris trial patients

- Prior population consists of 179 patients from US sites in EUPHRATES (target weight\* 75%)
- 150 new patients to be added from the TIGRIS trial (106 patients have been randomized to-date)





# Bayesian Analysis: Tigris Methods Paper

Tigris trial methods paper published in Critical Care, which discusses use of Bayesian methods in clinical trial design

- **Methods:** Simulation study incorporating historical data from EUPHRATES
  - Historical data from a 179-patient subgroup of the previous trial of adult critically ill patients with septic shock, multiple organ failure and an EAA between 0.60 to 0.89
  - Trial intervention consisted of two PMX treatments (2 hours each) completed within 24 hours of enrollment
  - Simulations were run 2,000 times per scenario

## Observed hypothetical results:

- Using our planned 75% weight on the prior, an observed ARR of 7% (37%vs 44%) is approximately the boundary for reaching the 95% probability threshold for declaring PMX effective

Tomlinson et al. *Critical Care* (2023) 27:432  
<https://doi.org/10.1186/s13054-023-04717-x>

Critical Care

RESEARCH

Open Access

## Bayesian methods: a potential path forward for sepsis trials

George Tomlinson<sup>1</sup>, Ali Al-Khafaji<sup>2</sup>, Steven A. Conrad<sup>3</sup>, Faith N. F. Factora<sup>4</sup>, Debra M. Foster<sup>5</sup>, Claude Galphin<sup>6</sup>, Kyle J. Gunnerson<sup>7</sup>, Sobla Khan<sup>8</sup>, Roopa Kohli-Seth<sup>9</sup>, Paul McCarthy<sup>10</sup>, Nikhil K. Meena<sup>11</sup>, Ronald G. Pearl<sup>12</sup>, Jean-Sebastien Rachoin<sup>13</sup>, Ronald Rains<sup>14</sup>, Michael Seneff<sup>15</sup>, Mark Tidswell<sup>16</sup>, Paul M. Walker<sup>9</sup> and John A. Kellum<sup>2,27</sup>✉

### Abstract

**Background** Given the success of recent platform trials for COVID-19, Bayesian statistical methods have become an option for complex, heterogeneous syndromes like sepsis. However, study design will require careful consideration of how statistical power varies using Bayesian methods across different choices for how historical data are incorporated through a prior distribution and how the analysis is ultimately conducted. Our objective with the current analysis is to assess how different uses of historical data through a prior distribution, and type of analysis influence results of a proposed trial that will be analyzed using Bayesian statistical methods.

**Methods** We conducted a simulation study incorporating historical data from a published multicenter, randomized clinical trial in the US and Canada of polymyxin B hemadsorption for treatment of endotoxemic septic shock. Historical data come from a 179-patient subgroup of the previous trial of adult critically ill patients with septic shock, multiple organ failure and an endotoxin activity of 0.60–0.89. The trial intervention consisted of two polymyxin B hemoadsorption treatments (2 h each) completed within 24 h of enrollment.

**Results** In our simulations for a new trial of 150 patients, a range of hypothetical results were observed. Across a range of baseline risks and treatment effects and four ways of including historical data, we demonstrate an increase in power with the use of clinically defensible incorporation of historical data. In one possible trial result, for example, with an observed reduction in risk of mortality from 44 to 37%, the probability of benefit is 96% with a fixed weight of 75% on prior data and 90% with a commensurate (adaptive-weighting) prior; the same data give an 80% probability of benefit if historical data are ignored.

**Conclusions** Using Bayesian methods and a biologically justifiable use of historical data in a prior distribution yields a study design with higher power than a conventional design that ignores relevant historical data. Bayesian methods may be a viable option for trials in critical care medicine where beneficial treatments have been elusive.

**Keywords** Septic shock, Endotoxemia, Endotoxin septic shock, Statistical methods, Polymyxin-B, Hemadsorption, Trial simulation

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# Enrollment Timeline - Projections

- Uninterrupted enrollment since April 2022 (where COVID was not a factor since Tigris started) has allowed us to re-base our enrollment rate assumptions

Actual LTM Enrollment

Additional Tigris Sites

Potential Improvement in Enrollment Rate

- Actual enrollment since April 2023:
  - 0.25 patients/site/month enrollment rate**
  - As a reference, uptick from April 6<sup>th</sup> 2023 LTM enrollment rate of 0.18; and EUPHRATES enrollment rate average 0.136 patients/site/month<sup>2</sup>
- Currently 22 sites
  - 2 sites in final onboarding stage
- Potential to improve enrollment rate to 0.22 or even 0.25 per month, projected enrollment numbers for 2024-25 are as follows:

Enrol rate <sup>1</sup>	Projected Enrollment				
	Sept 2023	Jun 2024	Sept 2024	Dec 2024	Feb 2025
0.19	72	112	131	144	150
0.22	73	120	139	150	
0.25	76	129	150		

<sup>1</sup> Enrollment rate equals number of patients per site per month

<sup>2</sup> Dellinger JAMA. 2018;320(14):1455-1463)

# Market Landscape – No Direct Competitors

- Spectral has the only viable solution in Phase 3 clinical trials

	<b>SPECTRAL PMX</b>	<b>Cytosorb</b>	<b>Oxiris</b>	<b>Aethlon</b>	<b>Boa Garnet</b>	<b>Exthera</b>
Target	Endotoxin	Small molecules <70kd	Small molecules <70kd	Viruses, Viral RNA/DNA	Live organisms and PAMPs	Live organisms
Technology	Sorbent: Polymyxin bound fiber	Sorbent: Porous polymer beads	Dialyzer: modified surface	Coupled Plasma filter/ Sorbent: Lectin	Dialyzer: mannose-binding lectin (fragment)	Sorbent: beads coated with heparin
Specificity	High	Very Low	Very Low	Low	Low	Low
Removes Endotoxin	++++	+	++	-	++	-
Removes Bacteria	+/-	-	-	-	+++	+++
Patient selection	FDA approved diagnostic (EAA 30min turnaround)	Clinical criteria	Clinical criteria	Viral assays (e.g. PCR)	Proprietary pathogen detection system—not FDA cleared	Blood cultures (up to 3 days for culture report)
Outcome	Reduction in 28-day mortality	Reduction in cytokines	Reduction in small solutes	Reduction in viral load in blood	Reduction in pathogen burden in blood	Reduction in pathogen burden in blood
Addressable population US /year	Based on EAA and organ dysfunction 150,000	Unknown	Based on sepsis with renal failure requiring dialysis: 100,000	Unknown (in theory all patients with viremia)	Primary blood stream infections with resistant organisms 5-10,000	Primary blood stream infections with resistant organisms 5-10,000
World-wide use	Clinically available outside the US	Clinically available outside the US	Clinically available outside the US	Experimental	Experimental (EUA: COVID-19)	Experimental (EUA: COVID-19)
USA regulatory pathway and status	Phase-3 confirmation trial underway	No trial in sepsis underway	No trial in sepsis underway	No trial in sepsis underway	No trial in sepsis underway	No trial in sepsis underway

## Catalyst

- Achieved Tigris interim 90 patient enrollment - Baxter paid milestone payment #2 (**~Feb/24**)
- Baxter's 'Vantive' spin-off... EDT's distribution agreement to transfer to 'Vantive' spin-off
- Tigris last patient enrollment ("LPE") - 150 patients (**~Q4/24**)
- Tigris topline results (**LPE + 60 days**)
- PMX FDA submission (**~Q2/25**)
- PMX FDA approval / Baxter milestone payment #3 (**H2/25**)
- Commence PMX commercialization (**late 2025/early 2026**)

# Upcoming Catalysts

# Management Team

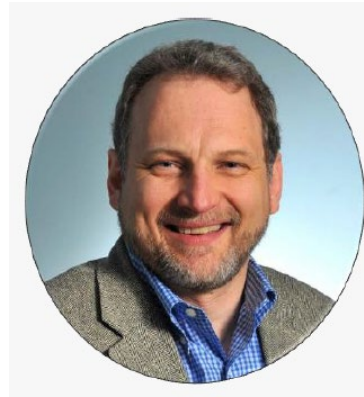
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Chris Seto

*CEO & Interim CFO*

- Over 30 years of capital market and management experience
- Former CFO of MJardin Group Inc.
- Former senior investment banking roles at Paradigm Capital, UBS Securities and CIBC World Markets
- Former Strategy & Finance senior executive at Warren Shepell Consultants (EAP)
- Received B.Comm from McMaster University; MBA from Richard Ivey School of Business
- CMA designation



John A. Kellum, MD, MCCM

*Chief Medical Officer*

- World expert in sepsis, acute kidney injury and blood purification
- Authored over 400 publications and is one of the most highly-cited investigators in the world
- Professor of Critical Care Medicine, Medicine, Bioengineering, and Clinical and Translational Science at the University of Pittsburgh
- Received his medical degree from the Medical College of Ohio; completed his residency and fellowship training at the Universities of Rochester and Pittsburgh



Esha Kamaluddin

*VP Clinical Development*

- 15+ years of clinical research and regulatory governance
- Experience ranging from CRO to industry, pharmaceuticals & medical devices, small to large scale multi-national trials in various phases of research development (Phases I-III and Bio-Equivalent clinical trials)
- Experienced in regulatory submissions to Health Canada & US FDA
- Honors Bachelor of Science from University of Toronto



# Capitalization

Ticker Symbol: EDT		
As at March 31, 2024	No. Outstanding	
Common Shares <sup>1</sup>	279,394,428	
Options <sup>2</sup>	12,069,994	
RSUs	4,123,734	
Warrants <sup>3</sup>	17,964,014	
DSUs <sup>4</sup>	3,028,090	
<b>Fully Diluted Shares Outstanding</b>	<b>316,580,260</b>	
	As at March 31, 2024	Pro Forma May/24 Financing
Cash	2,074,000	10,574,000
Total Debt <sup>5</sup>	12,972,000	21,472,000

- 1 ~31.2% of outstanding common shares held by: Toray Industries (45,630,105 shares); Birch Hill Management (36,210,017 shares); and Management & Board (5,044,011 shares)
- 2 Options weighted average exercise price = \$0.39
- 3 Warrants weighted average exercise price = \$0.49
- 4 DSUs held by Board members
- 5 Total CAD \$21.5 million comprised of convertible notes ("CN"):
  - (i) November 7, 2022 - CAD \$6.9 million (USD \$5.0 million) CN, 4 year term (Nov 2026), 7% coupon (semi-annual), \$0.48 conversion price, held by Baxter and Pinnacle Island LP;
  - (ii) September 7, 2023 - CAD \$6.2 million (USD \$4.5 million) CN: maturity (Nov 2026), 9% coupon (semi-annual), \$0.40 conversion price, held by Baxter, Pinnacle Island LP and Rosalind Capital Partners;
  - (iii) May 23, 2024 – CAD \$8.5 million CN, 4 year term (May 2028), 9% coupon (semi-annual), \$0.52 conversion price.



# SPECTRALIS

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