

OTCQB: "SIGY"



*Jim Joyce  
CEO, Inventor*

*Emerging Growth Conference  
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A close-up photograph of a medical device, likely a dialyzer or filter, with various colored tubes (red, white, blue, yellow) connected to it. The device has a cylindrical body with a textured surface. The background is blurred, showing more of the medical equipment.

***Medical Devices to Treat  
Life-Threatening Conditions***

A blurred background image of a medical device, possibly a dialyzer or filter, with various colored tubes (red, white, blue) and connectors (blue, yellow).

## ***Two Classes of Product Candidates***

- 1. Devices to treat pathogen-associated disorders beyond the reach of drugs*
- 2. Devices to improve patient responses to cancer therapies*

The background of the slide features a blurred image of medical equipment, including a red tube with a blue connector and a yellow connector, and a clear plastic container with a red lid. The text is overlaid on this background.

## ***Pathogen-associated disorders beyond the reach of drugs***

- *Preparing to initiate first-in-human studies of **Sigyn Therapy™***
- *Dual clearance of inflammatory mediators & pathogen sources of life-threatening Inflammation*
- *Candidate treatment indications include #1 cause of hospital deaths in the United States*

## *To improve patient responses to cancer therapies*

- ***ImmunePrep™*** – platform to enhance delivery of immunotherapeutic antibodies to treat cancer

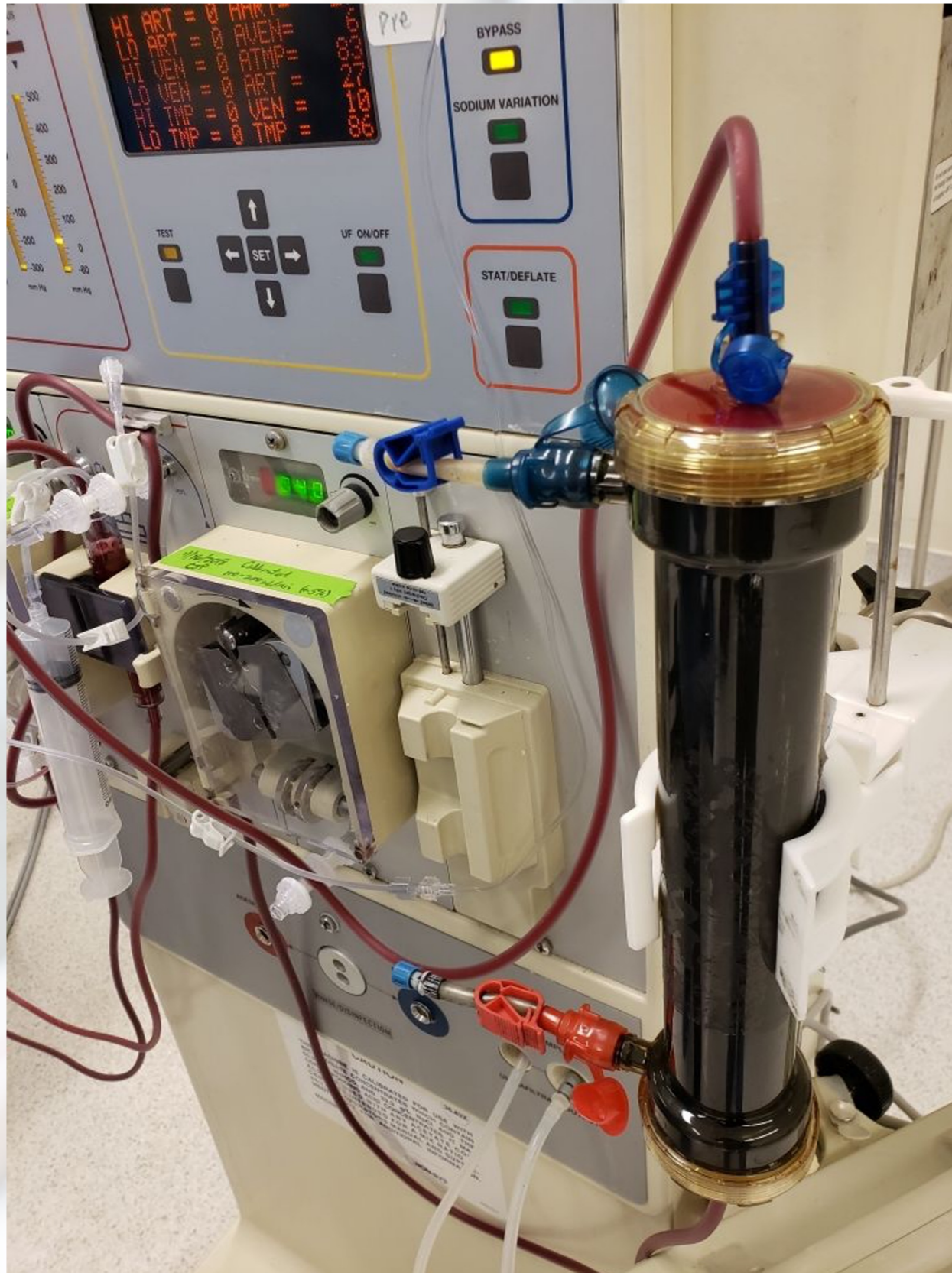
*(Top selling cancer drugs)*

- ***ChemoPrep™*** designed to enhance delivery of chemotherapeutic agents

*(Most commonly administered cancer drug)*

- ***ChemoPure™*** to reduce chemotherapy toxicity

***Sigyn Therapy™***



*University of Michigan Animal Studies*

## **Sigyn Therapy™ in Action**





A patient is lying in a hospital bed, connected to a dialysis machine. The machine is white and has several red and white tubes connected to it. The patient's arm is visible, and they are wearing a white wristband. The background is a bright, clinical setting.

***“Simultaneous Clearance of Inflammatory Mediators & Pathogen Sources of Life-Threatening Inflammation”***

## *In Vitro* Human Blood Plasma Validations

*Viral Pathogens*

*Bacterial Toxins*

*Hepatic Toxins*

*Inflammatory Mediators*

*CytoVesicles*

Leading Cause of Hospital Deaths

**Sepsis**

Emerging Global Health Threat

**Drug-Resistant Bacteria**

Common Cause of Sepsis

**Endotoxemia**

**Therapeutic Opportunities**

Increasing Incidence

**Drug-Resistant Viruses**

## Next Step: First-In-Human Studies

*Investigational Device Exemption (IDE) drafted for FDA submission (modular feasibility study)*

*Enrollment of 12-15 dialysis-dependent end-stage renal disease (ESRD) subjects with endotoxemia and concurrent inflammation*

*Three site locations identified: Hartford, CT – San Antonio, TX – Las Vegas, NV*

## ESRD – Things To Know!

*> 50% of ESRD patients suffer from endotoxemia and/or chronic inflammation (currently untreatable)*

*>550,000 ESRD patients receive ~85 million dialysis treatments in the U.S. each year*

## ESRD – Things To Know!

*~30% of ESRD patients die within a year of dialysis initiation*

*Cardiovascular disease (CVD), followed by sepsis are leading causes of ESRD deaths*

*Endotoxemia and concurrent inflammation are hallmark causes of these conditions*

## North American Dialysis Market Dominated By Two Organizations



“FMS” Market Cap: ~\$11 Billion



“DVA” Market Cap: ~\$11 Billion

## Potential Value to the Dialysis Industry

*Sigyn Therapy™ offers potential new revenue channel*

*Provides pathway into non-dialysis markets*

*Reduced ESRD patient hospitalizations = Recouped Revenues*

*Revenues gains from extended life of ESRD patients*



# Value for Each Month of Extended Life - DaVita

**\$11.6 Billion**  
2022 Revenues  
North America

**199.4K ESRD Patients**

**30 Million Dialysis  
Treatments**

**\$58.2K Per Patient  
Revenue**

**+ \$960 Million**  
per month of extended life

# Value for Each Month of Extended Life - Fresenius

\$14.5 Billion  
2022 Revenues  
North America

208.3K ESRD Patients

US

31.8 Million Dialysis  
Treatments

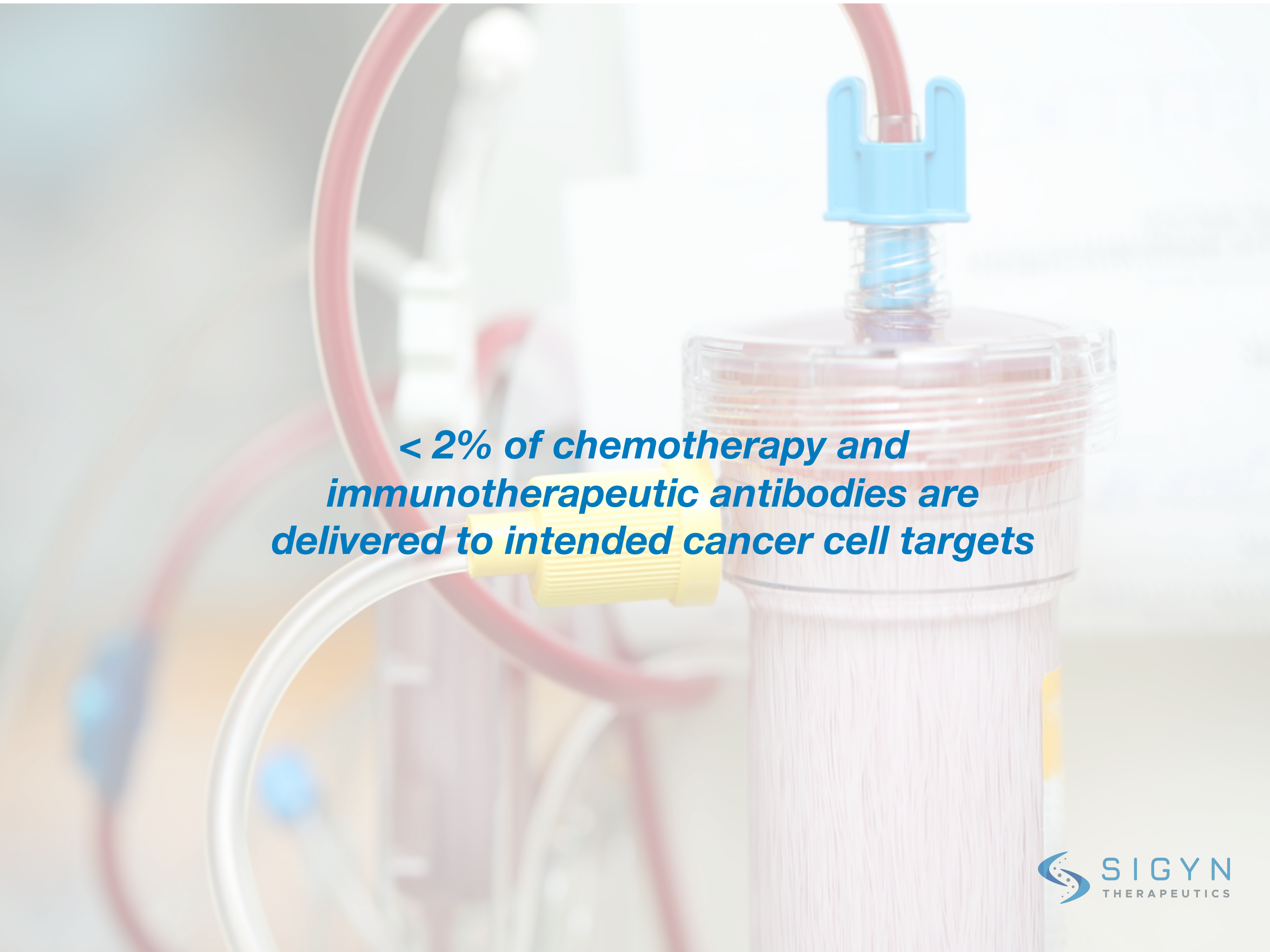
\$69.6K Per Patient  
Revenue

**+ \$1.2 Billion**  
per month of extended life

A close-up photograph of a medical device, likely a dialyzer or filter, featuring a clear plastic cylindrical reservoir. A red tube is connected to the top of the reservoir via a blue plastic fitting with a spring mechanism. A white tube is connected to the side of the reservoir via a yellow plastic fitting. The background is blurred, showing other parts of the medical equipment.

***Devices to improve patient responses to cancer therapies***

***Something you need to know!***

A close-up photograph of a medical infusion set. The central focus is a clear plastic chamber with a blue spring-loaded cap at the top. A red tube is inserted into the cap. A yellow connector is attached to the side of the chamber, leading to a white tube. The background is blurred, showing more of the medical equipment.

***< 2% of chemotherapy and immunotherapeutic antibodies are delivered to intended cancer cell targets***

## Enhancing Performance of Cancer Drugs

*We designed devices to optimize delivery of chemotherapy and therapeutic antibodies*

*We extract circulating decoys that sequester drugs from reaching intended cancer targets*

*Clinical objective: improve drug delivery, reduce toxicity, and extend life*

## Chemotherapy – Things to Know

*Most common class of drug administered to cancer patients*

*Patient benefit limited by toxicity and poor tumor-site delivery*

*Tumor-derived exosomes obstruct delivery*

# Rationale to Deplete Cancer-Released Exosomes

- **They Block & Sequester Chemotherapy Delivery**
- **Export Chemotherapy from Tumor Cells**
- **Prime Contributor to Treatment Resistance**



# Cancer-Released Exosomes



**JCI** The Journal of Clinical Investigation  
Published by The American Society for Clinical Investigation | Founded 1908

[J Clin Invest.](#) 2016 Apr 1; 126(4): 1208–1215.  
Published online 2016 Apr 1. doi: [10.1172/JCI81135](https://doi.org/10.1172/JCI81135)

PMCID: PMC4811149  
PMID: [27035812](https://pubmed.ncbi.nlm.nih.gov/27035812/)

**The biology and function of exosomes in cancer**

[Raghu Kalluri](#)

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Department of Cancer Biology, Metastasis Research Center, University of Texas MD Anderson Cancer Center, Houston, Texas, USA.

*"the blood of cancer patients is estimated to contain about 4,000 trillion exosomes"*

➤ **Miles of Chemotherapy Interference**

\* Based on average size of 100 nanometers



**OUR SOLUTION**

***ChemoPrep™ & ChemoPure™***

***“SYSTEMS AND METHODS TO  
ENHANCE CHEMOTHERAPY DELIVERY  
AND REDUCE TOXICITY”***

*Patent Filed: October 2022*

# OUR SOLUTION

## ChemoPrep™

*Administered prior to chemotherapy infusion*

*Pre-treatment sweep of tumor-derived exosomes from the bloodstream*

*A Treatment Goal: Improve chemo delivery w/ ½ dose = 50% reduction in toxicity*

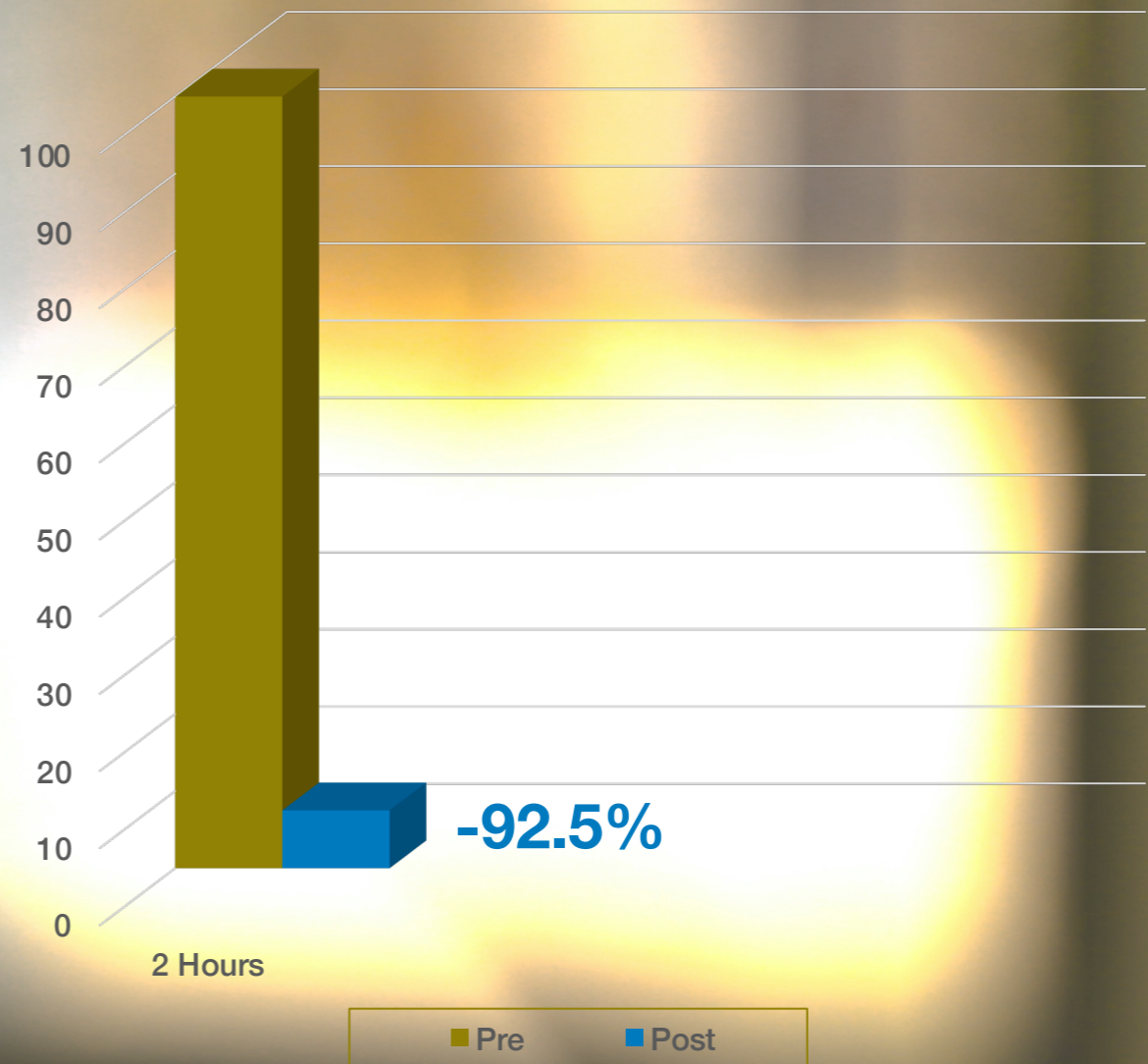
# OUR SOLUTION

**ChemoPure™**

*Post-treatment sweep of off-target chemotherapy to further reduce toxicity*

# OUR SOLUTION

## SIGYN LIPOSOME REMOVAL *Pre-Clinical Data*



*\* Note: Liposomes also serve as a model for exosome depletion*

## Therapeutic Antibodies – Things to Know

*Represent 9 of 15 top selling cancer drugs and most valued M&A assets of 2023*

*Inclusive of monoclonal antibodies , checkpoint inhibitors & antibody drug conjugates*

*Over 1,000 antibodies being evaluated in human studies*

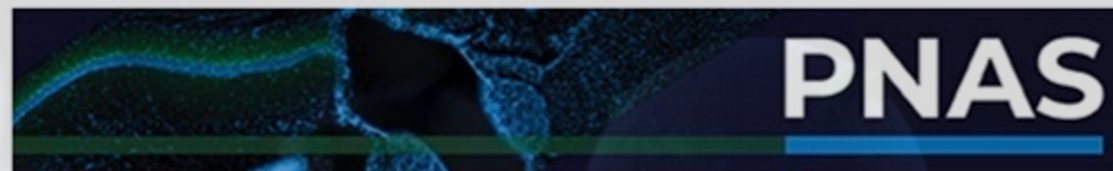
## Therapeutic Antibodies – Things to Know

*Less than 2% of doses are reported to be delivered to target binding site*

**Circulating factors that express the antigen binding site of the antibody decoy delivery**

*Decoys include anti-drug antibodies, soluble proteins, and exosomes*

# CANCER-RELEASED EXOSOMES



[Proc Natl Acad Sci U S A](#). 2011 Sep 13; 108(37): 15336–15341.

Published online 2011 Aug 25. doi: [10.1073/pnas.1102855108](https://doi.org/10.1073/pnas.1102855108)

PMCID: PMC3174603

PMID: [21873242](https://pubmed.ncbi.nlm.nih.gov/21873242/)

Exosomal evasion of humoral immunotherapy in aggressive B-cell lymphoma modulated by ATP-binding cassette transporter A3

[Thiha Aung](#),<sup>a,1</sup> [Bjoern Chapuy](#),<sup>a,b,1</sup> [Daniel Vogel](#),<sup>a</sup> [Dirk Wenzel](#),<sup>c</sup> [Martin Oppermann](#),<sup>d</sup> [Marlen Lahmann](#),<sup>a</sup> [Toni Weinhage](#),<sup>a</sup> [Kerstin Menck](#),<sup>a</sup> [Timo Hupfeld](#),<sup>a</sup> [Raphael Koch](#),<sup>a</sup> [Lorenz Trümper](#),<sup>a</sup> and [Gerald G. Wulf](#)<sup>a,2</sup>

***"Approximately half of all of the plasma rituximab was found to be fixed to exosomes 3 hours after the end of the rituximab infusion"***



# OUR SOLUTION

***ImmunePrep™***

***“DEVICES FOR ENHANCING THE  
ACTIVITY OF THERAPEUTIC  
ANTIBODIES”***

***Patent Filed: May 2023***

# OUR SOLUTION

## ImmunePrep™

*Administered prior to antibody infusion*

*Incorporates market-cleared antibody to sweep drug decoys out of the bloodstream*

*Reverse decoy mechanism increases availability of infused antibody to bind targets*

***Conclusion***

A close-up photograph of a medical device, likely a dialyzer or filter, with various colored tubes (red, white, blue, yellow) connected to it. The device is made of clear plastic and has a textured surface. The background is blurred, showing more of the medical equipment.

***Medical Devices to Treat  
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## ***Two Classes of Product Candidates***

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## ***Pathogen-associated disorders beyond the reach of drugs***

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## *Improving patient responses to cancer therapies*

- ***ImmunePrep™*** – platform to enhance delivery immunotherapeutic antibodies to treat cancer  
(#1 source of cancer drug revenues)
- ***ChemoPrep™*** designed to enhance delivery of chemotherapeutic agents  
(Most commonly administered cancer drug)
- ***ChemoPure™*** to reduce chemotherapy toxicity

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