



SERES
THERAPEUTICS

Seres Therapeutics Investor Presentation
January 2025



Disclaimers

Forward Looking Statements

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Transforming patient outcomes using proprietary consortia of live biotherapeutics

Strong Foundation

- Validated platform highlighted by VOWST® FDA approval as first ever oral microbiome therapy with outstanding clinical results
- VOWST asset sale strengthened balance sheet and streamlined organization
- Cash into Q1 2026

Positive SER-155 Phase 1b Data in Allo-HSCT

- 77% relative risk reduction for bloodstream infections
- Well tolerated safety profile; no treatment-related SAEs and engraftment
- Biomarker data supports impact on epithelial barrier integrity
- FDA Breakthrough Designation

Blockbuster SER-155 Opportunity

- Accelerate SER-155 development in allo-HSCT
- Potential to initiate multiple clinical trials in next 12-18 months for additional indications
- SER-155 represents multi-billion net sales opportunity across indications (e.g., autologous-HSCT, blood cancers, CAR-T recipients)

Expansive Platform Potential

- Systemic inflammation and immune homeostasis biomarker data support the potential in inflammatory and immune diseases, such as IBD (e.g., ulcerative colitis and Crohn's disease)
- SER-147 designed to prevent infections in chronic liver disease

Pursuing SER-155 strategic partnership to accelerate next study in allo-HSCT and expand to multiple target populations

Validated therapeutic modality and platform: Seres pioneered the development and FDA approval of VOWST as the first-ever oral live microbiome therapeutic



VOWST™
(fecal microbiota spores, live-brpk)

FDA approved (April 2023)
to prevent the recurrence of
C. difficile infection in adults

DRAMATIC CLINICAL BENEFIT –
Preventing infection recurrence

Approximately
88%

sustained clinical response rate
(*C. diff.* recurrence, at up to 8 weeks)

VOWST asset sale (completed September 2024) provided capital to support pipeline advancement and resulted in a more streamlined, focused organization

VOWST asset sale completed September 30, 2024: transformational for Seres – provides resources to support SER-155 advancement



- **VOWST asset purchase agreement provided infusion of capital and supports SER-155 development**
- **Asset sale extended operational runway into Q4 '25; now into Q1 '26**
- **Retires debt and other obligations**

KEY FINANCIAL TERMS

\$100M upfront payment to Seres, less ~\$20M in net obligations due to an affiliate of SPN*

\$15M equity investment by SPN at closing

\$60M prepaid sales-based milestone at closing

\$75M in deferred payments due in 2025 (less ~\$1.5M in employment-related payments)

\$275M in potential future sales-based milestone payments (subject to reductions for interest on prepaid milestone payment)

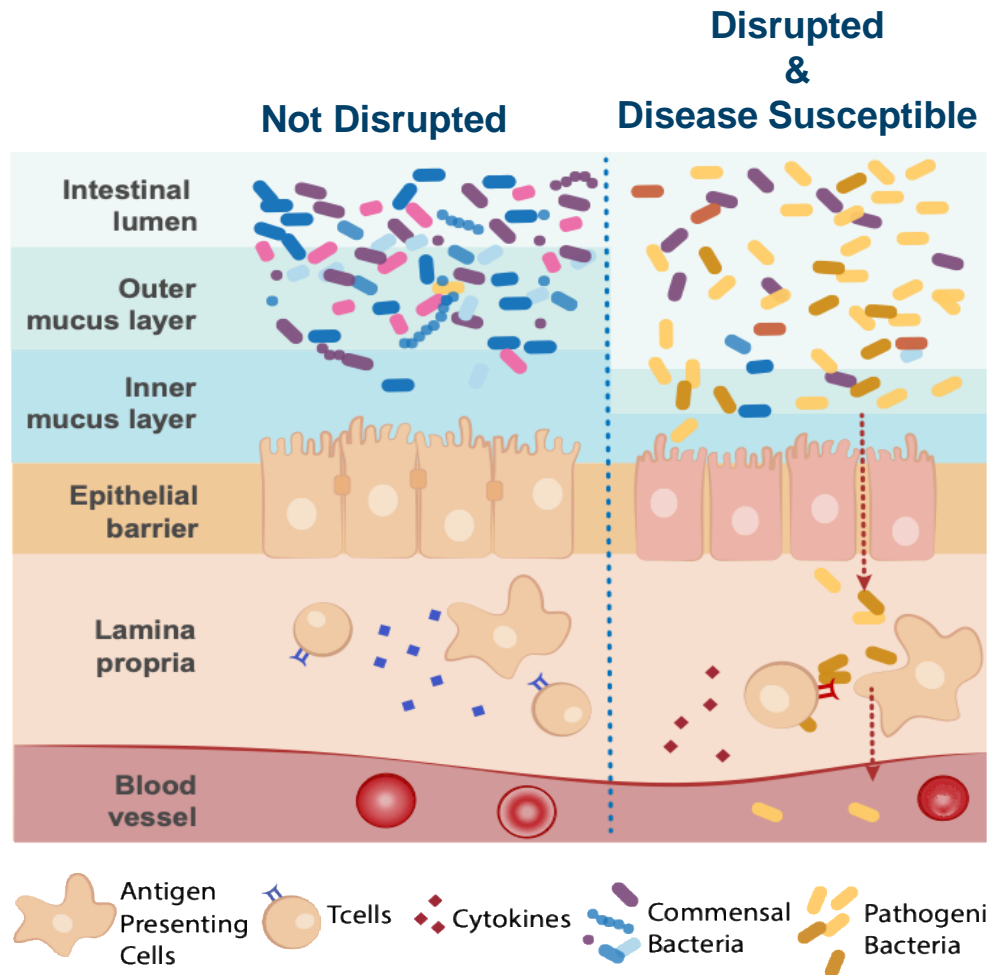
Transaction results in a more streamlined, focused Seres organization and lower cash burn rate

The gut microbiome has substantial untapped therapeutic potential to both prevent and treat diseases

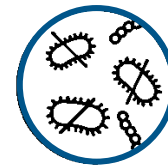


The genetic content of the **microbes** living within and on your body is at least **100-fold greater** than that contained in the human genome

Disrupted gastrointestinal microbiome is mechanistically linked to infections and disease



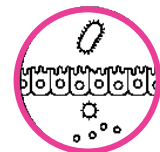
Impacted Biology & Disease Relevance



Pathogen or “undesirable”
microbe abundance



Lost epithelial barrier &
mucosal integrity

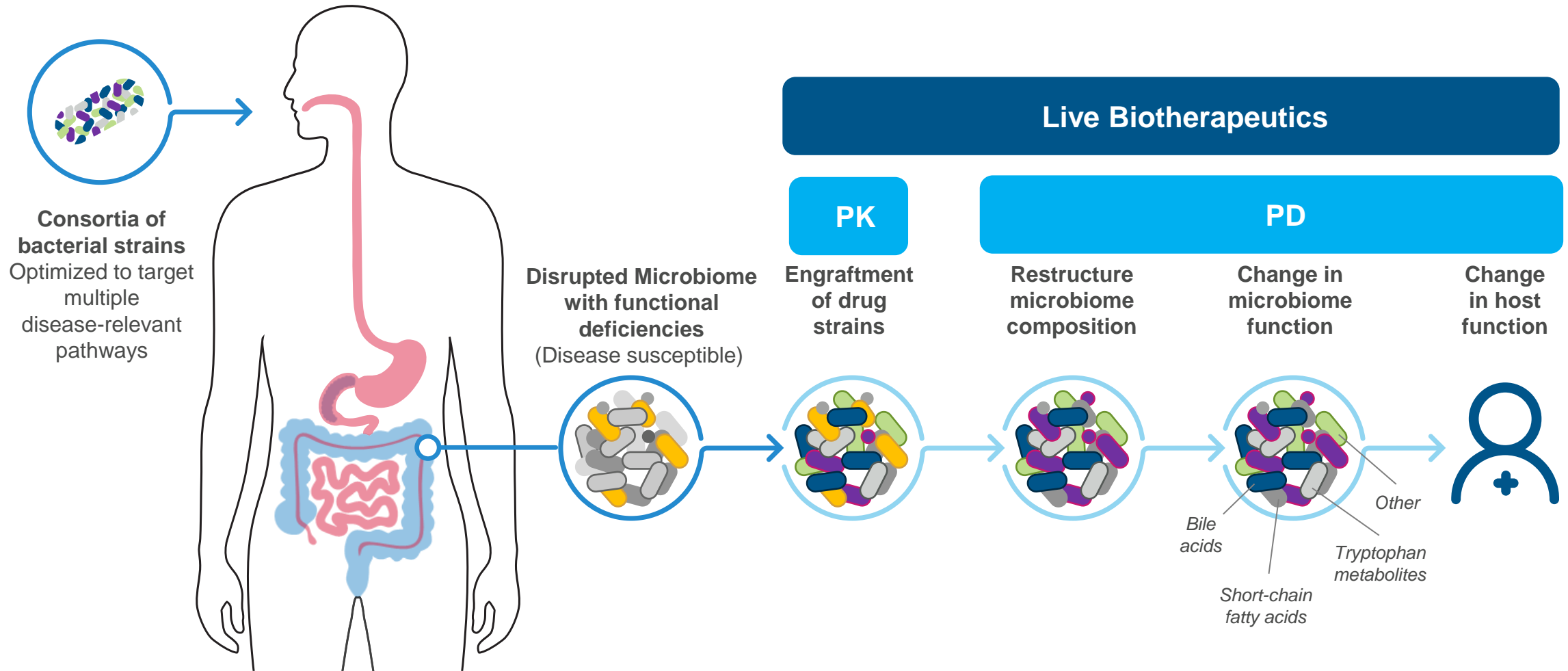


Unfavorable immune
responses

Increased **pathogen abundance**,
in combination with
impaired barrier integrity
and **decreased immune function...**

...enables bacterial and
antigen translocation leading
to infections & inflammation

Consortia of live commensal bacteria can be used as therapeutics



Seres' biotherapeutics and pipeline candidates are expected to have well tolerated safety profile, reducing development risk

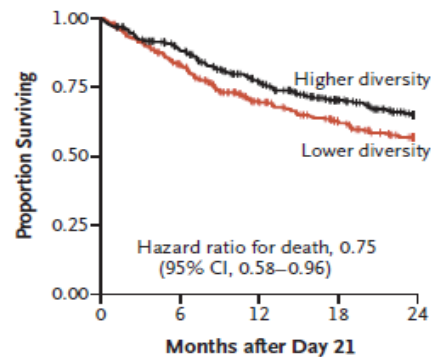
- ✓ Based on GI bacteria naturally **found in healthy humans**, and not associated with disease
- ✓ VOWST product profile includes **well tolerated safety** without drug-related serious adverse events
- ✓ **Well tolerated safety profile in multiple clinical trials** and patient populations, including medically vulnerable allo-HSCT recipients

Safety profile has potential to mitigate a primary cause of drug development failure

Seres' initial focus is preventing infections in allo-HSCT; potential is broad

Allo-HSCT

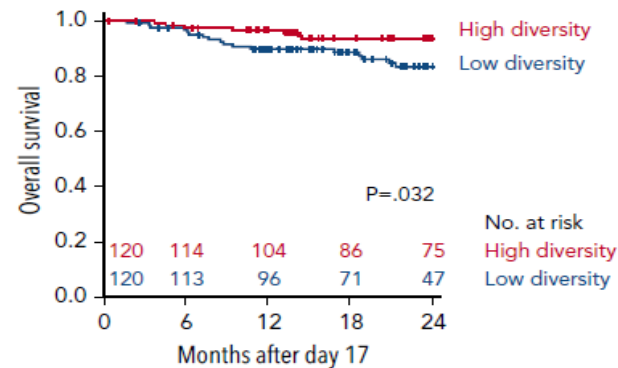
Survival by microbiome diversity



Lower microbiome diversity post allo-HSCT is associated with increased blood stream infections and decreased overall survival

Autologous HSCT

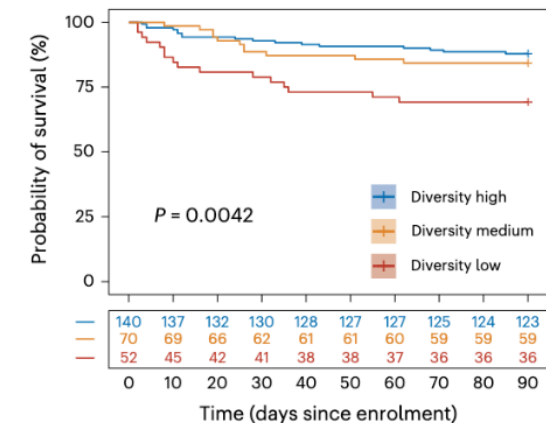
Survival by microbiome diversity



Lower microbiome diversity post auto-HSCT is associated with worse overall and progression-free survival

Chronic Liver Disease

Survival by microbiome diversity



Microbiome diversity decreases with disease severity and is associated with increased risk of infection & death

Common biology across vulnerable populations: pathogen domination in the GI microbiome, loss of epithelial barrier integrity, impacted immune function

Near-term focus on SER-155 as anchor biotherapeutic program; achieved Breakthrough and Fast Track designations



- Reduces risk of recurrent *C. diff* infections
- Well tolerated safety profile

provides clinical proof of concept

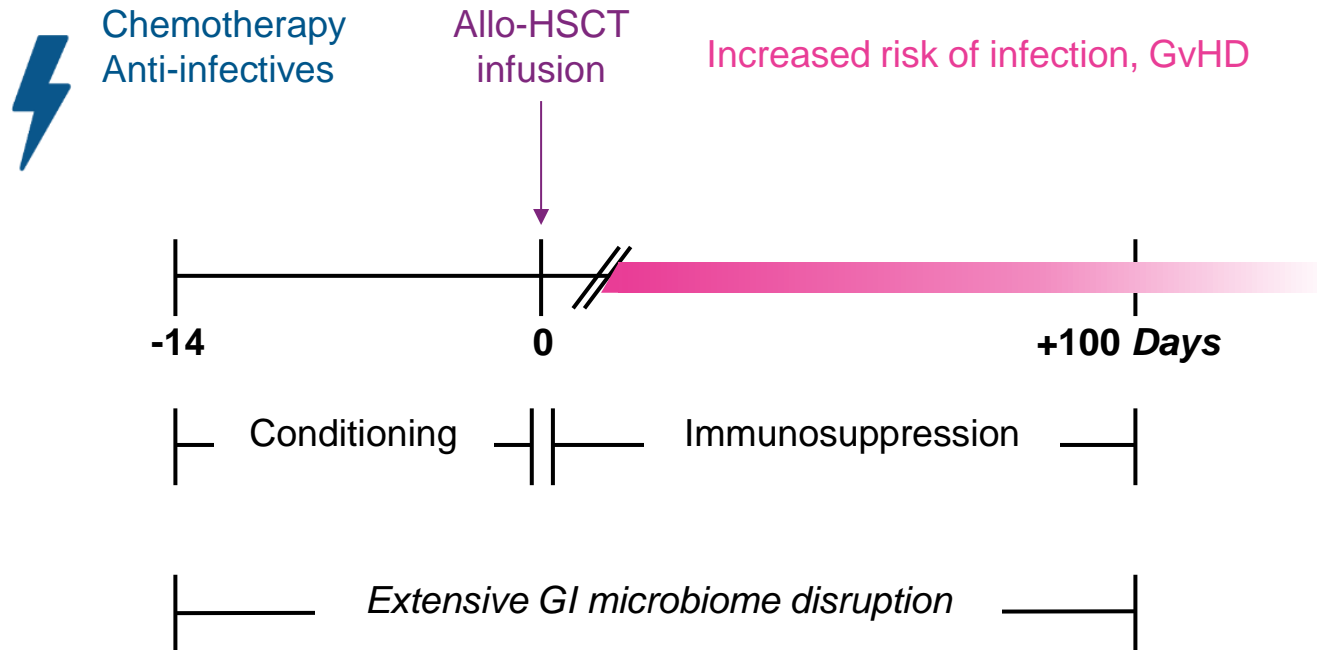


Program	Lead Indication & Development Stage	Therapeutic Objectives	Potential Additional Indications
SER-155	<u>Allogeneic HSCT:</u> Phase 1b Cohort 2 (placebo controlled) data announced Sept. '24 and exploratory biomarker data in Jan '25	Reduce incidence of serious bacterial infections (e.g., BSIs), febrile neutropenia, and GvHD	<ul style="list-style-type: none"> • Autologous HSCT • Blood cancers • CAR-T
SER-147	<u>Chronic liver disease:</u> IND-enabling activities	Reduce incidence of serious bacterial infections (e.g., SBP, BSIs) and related complications	<ul style="list-style-type: none"> • Solid organ transplant • ICU patients • Long-term care patients

Briefing Book Submitted – engaging with FDA in Q1 '25 to explore **potential for SER-155 to have single registrational study for efficacy**, following successful precedent from VOWST

Allo-HSCT regimen can result in life-threatening complications

Allo-HSCT treatment regimen



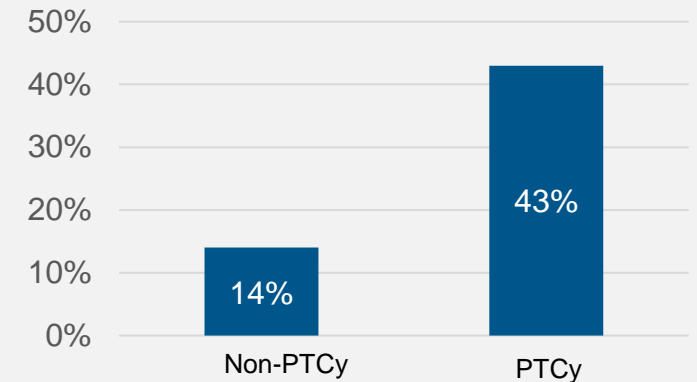
- **Only ~60% survival** 3 years post-transplant
- Significant **immune compromise**
- **~10% transplant mortality for adults** in first 100 days post-transplant
- **Infections are leading cause of death** in first 100 days post-transplant for adults
- Other leading causes of death are disease relapse and organ failure

Bloodstream infections (BSIs) are a leading cause of death post-transplant and are increasing in incidence

Incidence

- **BSI risk increasing** due to recent adoption of post-transplant cyclophosphamide (PTCy) for GvHD prophylaxis
- ~50% of infections are gut-seeded
- 50-80% febrile neutropenia incidence

Bacterial BSI in first 30 days post-HSCT



Salas et al 2024

Impact

- Infection is **leading cause of death** in first 100 days post-HSCT for adults
- **~7.5% mortality rate** from bloodstream infections
- Complications including infection associated with longer hospital stay and ICU utilization, driving **substantial cost increase**

Standards of care to prevent bloodstream infections in allo-HSCT patients are poor and decreasing in efficacy



Joint ASCO* and IDSA recommendation

- **Fluoroquinolones (FQ)** recommended for antibacterial prophylaxis
- Prophylaxis recommended during window of expected neutropenia



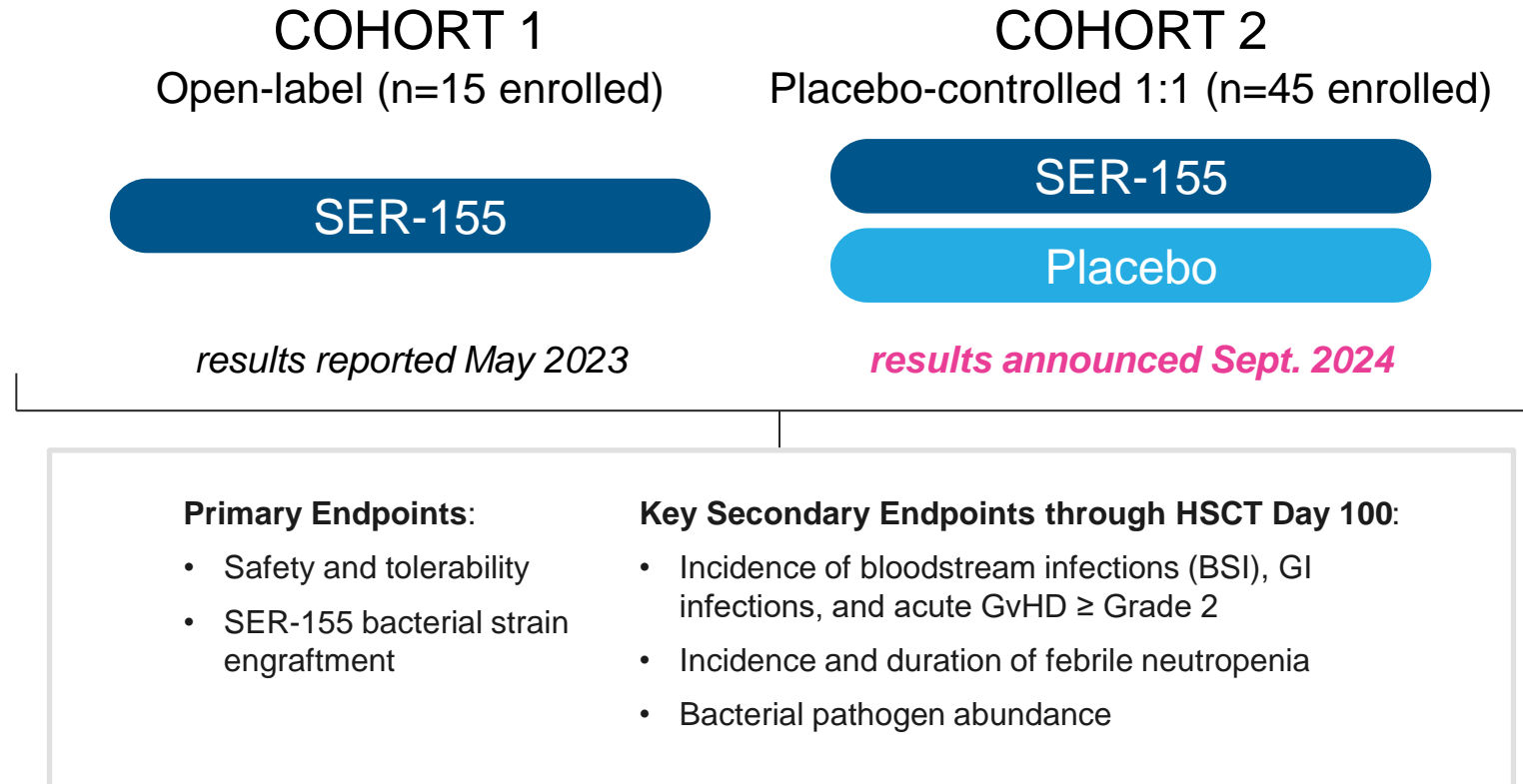
EBMT guidelines and Infectious Disease Working Party recommendations

- 2022 Workshop recommends **move to "targeted" antibacterial prophylaxis**
- Multiple analyses suggest reduced infections from antibacterial prophylaxis but no overall survival benefit

Trends

- High BSI rate happening despite broad FQ prophylaxis in the US
- Prophylaxis efficacy decreasing as bacteria become resistant to antibiotics
- PTCy adoption for GvHD prophylaxis is increasing BSI rates

SER-155 Phase 1b study evaluated safety, pharmacology, and efficacy in adult allo-HSCT recipients



SER-155 Safety: SER-155 was generally well tolerated with no treatment-related SAEs

Treatment-emergent adverse events (TEAEs)

- All but one subject in the placebo arm experienced at least 1 TEAE
- Most common for SER-155 treated subjects ($\geq 50\%$ and with $\Delta \geq 5\%$ greater than placebo): diarrhea (86% vs. 74% placebo), nausea (62% vs. 53% placebo)
- 1/40 (3%) subject experienced a TEAE leading to treatment discontinuation (active = 0; placebo = 1)
- 3/40 (8%) subjects experienced a TEAE leading to study discontinuation (active = 1; placebo = 2)

Serious adverse events (SAEs)

- 19/40 (48%) subjects experienced an SAE: 11/21 (52%) SER-155-treated subjects vs. 8/19 (42%) placebo-treated subjects; none considered related to SER-155 (no SUSARs)
 - Most common SAE SOC: infections & infestations (24% active vs. 37% placebo)
 - 3 deaths prior to Day 100 (active = 1; placebo = 2), 1 death after Day 100 (active), none considered related to SER-155

Adverse events of special interest (AESIs)

- AESIs (bloodstream infections, GI infection, invasive infection): 14/40 (35%) subjects
- Rates of AESIs were lower in SER-155 arm vs placebo arm (29% vs 42% respectively)
- No SER-155 species were identified in culture from any subject

SER-155 Efficacy: SER-155 associated with 77% relative risk reduction in bacterial BSIs and reduction in systemic antibiotic exposure

Bloodstream infections

Significant decrease in bacterial bloodstream infections in SER-155-treated subjects vs. placebo with **77% relative risk reduction**

Antibiotic exposures

Significantly lower mean cumulative exposure (days) and exposure rate to systemic antibacterials / antimycotics for SER-155-treated subjects vs. placebo

Febrile neutropenia

Numerically lower incidence rate of febrile neutropenia in SER-155-treated subjects vs. placebo

Bloodstream infections from HSCT Day 0 to Day 100: Lower incidence in SER-155 treated subjects vs. placebo

Bloodstream infections from Day 0 to Day 100 (# patients)	SER-155 n=20 n (%)	Placebo n=14 n (%)
Subjects with confirmed BSI	2 (10.0%)	6 (42.9%)
95% confidence interval	(1.2, 31.7)	(17.7, 71.1)

mITT-1 population

Odds ratio	0.15
95% confidence interval	(0.01, 1.13)
p-value	0.0423

Organisms in SER-155 patients: Finegoldia magna; E. coli/Strep mitis

Organisms in placebo patients: E.coli; Enterococcus faecium/staph haemolyticus/Candida krusei; Staph aureus; Staph haemolyticus; Pseudomonas aeruginosa; E coli

Cumulative exposure to systemic antibacterials / antimycotics through HSCT Day 100: Lower incidence in SER-155 treated subjects vs. placebo

Cumulative Antibacterial or Antimycotic Exposure (HSCT Days)	SER-155 n=20 n (SD)	Placebo n=14 n (SD)
Mean (SD)	9.2 (5.44)	21.1 (20.31)
Median	9.0	14.0
Min, Max	0, 19	0, 74

Mean Difference (95% CI)

-11.9 (-23.85, -0.04)

mITT-1 population

p-value

0.0494

- Cumulative exposure is the sum of all days a subject received systemic antibacterials and/or antimycotics between HSCT Day 0 through Day 100; counting once per day regardless of number of agents taken
- 95% confidence interval and p-value based on independent samples t-test of the difference in mean days between SER-155 and placebo

Cumulative exposure rate to systemic antibacterials / antimycotics through HSCT Day 100: Lower incidence in SER-155 treated subjects vs. placebo

Cumulative Antibacterial or Antimycotic Exposure Rate	SER-155 n=20 Rate (SD)	Placebo n=14 Rate (SD)
Mean (SD)	0.090 (0.0530)	0.305 (0.2898)
Median	0.089	0.244
Min, Max	0.00, 0.18	0.00, 0.90

Mean Difference (95% CI)

-0.2 (-0.38, -0.05)

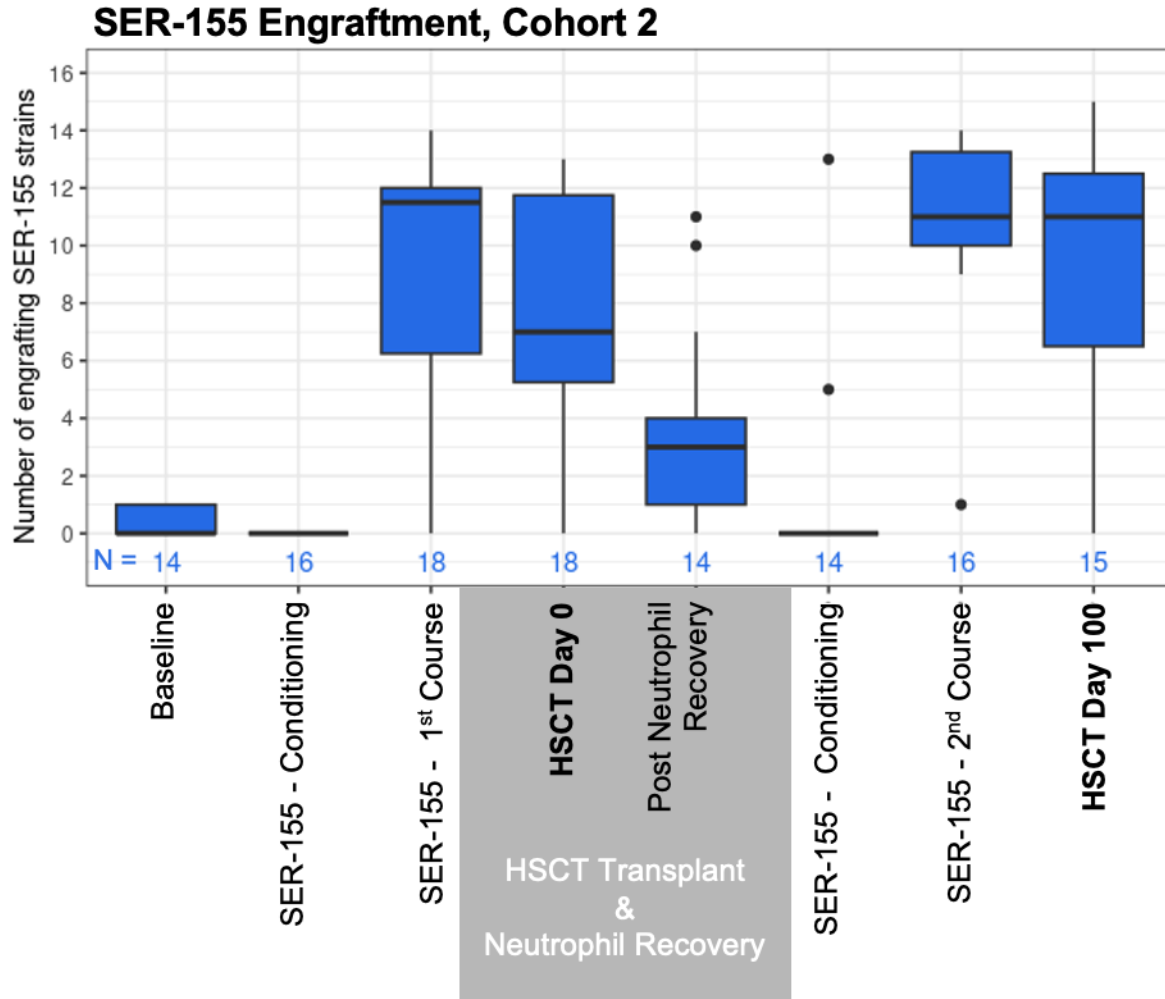
mITT-1 population

p-value

0.0163

- Cumulative exposure rate is calculated as the sum of all days a subject received systemic antibacterials and/or antimycotics on or after HSCT Day 0 (counting once per day, regardless of number of antibacterial/antimycotic medications taken in a day) through HSCT Day 100 over the total number of days a subject was on the study from HSCT Day 0 to the earliest of EOS, or HSCT Day 100
- 95% confidence interval and p-value are based on independent samples t-test of the difference in mean days or mean rate of cumulative exposure between SER-155 and Placebo

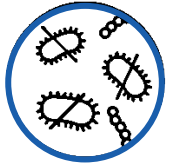
SER-155 Pharmacokinetics: Primary objective achieved - drug bacteria strain engraftment was robust and as expected



- The majority of SER-155 strains engrafted and were durable through chemotherapy exposure
- Engraftment decreased but was detectable post-neutrophil recovery, suggesting sustained engraftment through period of greatest BSI susceptibility
- The second course of SER-155 was effective at increasing strain engraftment following neutrophil recovery
- Engraftment durable out to day 100 following transplant

SER-155 Pharmacodynamics: the Ph1b study included multiple measures of drug pharmacodynamics

SER-155 Mechanism of Action Targets



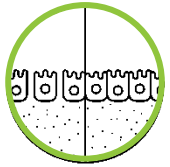
Inhibit Pathogens or “Undesirable” Microbes

Preclinical Optimization



Measurements on Ph1b clinical study

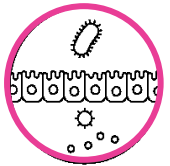
Genomic measurements of pathogen abundance in gastrointestinal tract, including domination by pathogenic bacteria



Repair & Protect Mucosal Epithelial Barrier Integrity



Concentration of fecal albumin in subject stool, reflecting barrier damage and leakage of serum albumin into the GI tract

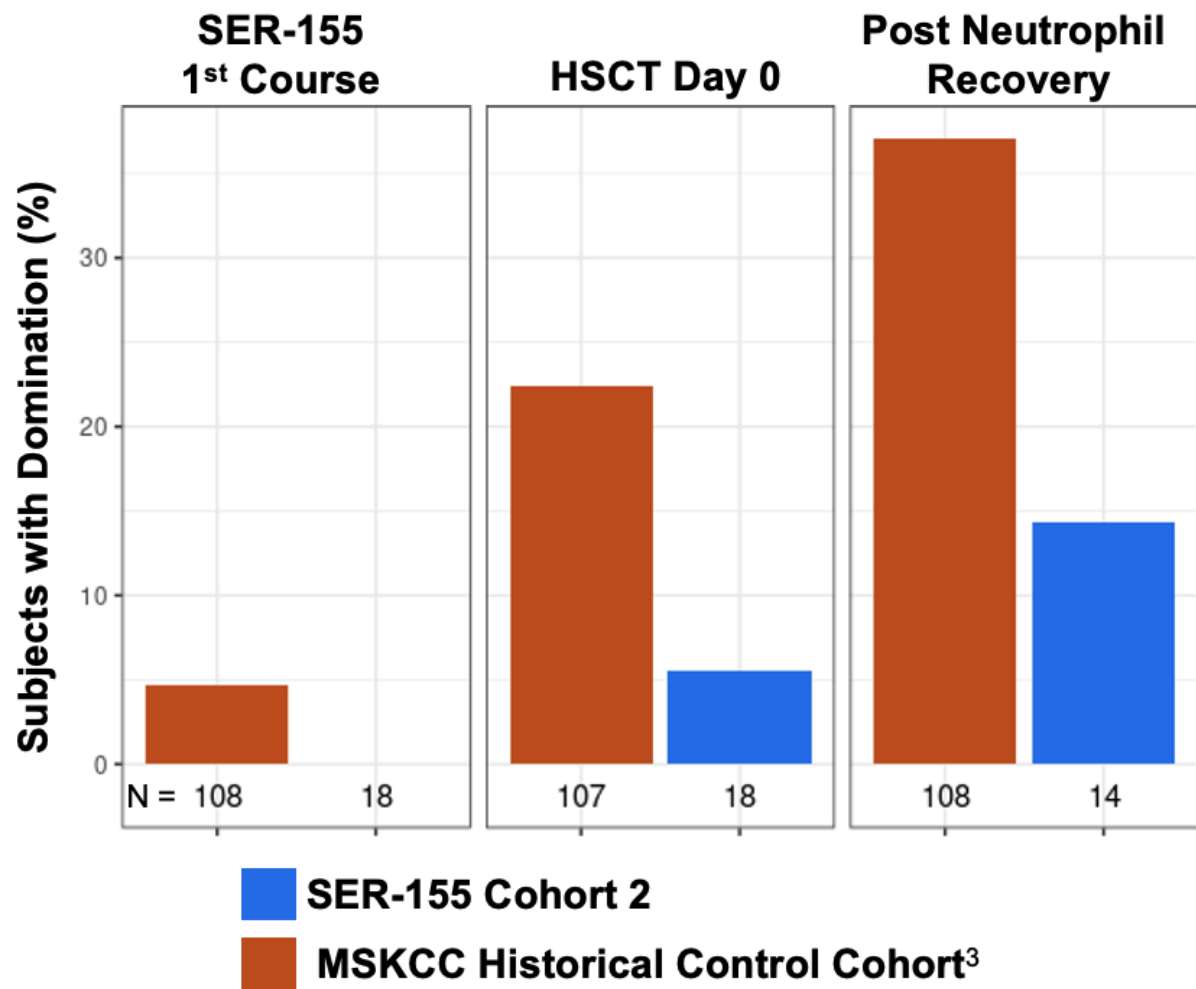


Modulate Immune function



Concentrations of plasma cytokines, chemokines and signaling molecules reflecting GI inflammation, systemic inflammation, and immune homeostasis

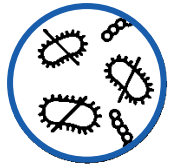
SER-155 Pharmacodynamics (pathogen domination): prevalence in SER-155 Cohort 2 was substantially lower relative to Historical Control Cohort



- Pathogen domination (i.e., relative abundance in the GI $\geq 30\%$) has been associated with risk of BSIs and other negative clinical outcomes^{1, 2}
- Observed pathogen domination events were low in both the placebo and SER-155 arms with no significant differences observed
 - *The ability to detect pathogen domination in the placebo arm was constrained due to the imbalance in the number of available stool samples between the arms.*
- Pathogen domination was substantially lower in SER-155 Cohort 2 compared to Historical Control Cohort³

SER-155 Pharmacodynamics: results from the Phase 1b study support clinical efficacy results

SER-155 Mechanism of Action Targets



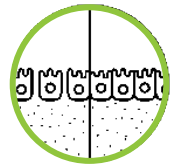
Inhibit Pathogens or “Undesirable” Microbes

Clinical Support for MoA



Key Observed Results

Domination by pathogenic bacteria was **reduced** in SER-155 subjects relative to historical comparators from MSKCC, suggesting SER-155 inhibits pathogen growth and subsequent infection

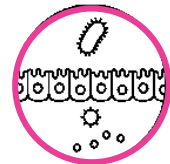


Repair & Protect Mucosal Epithelial Barrier Integrity



New Data

Fecal albumin levels were significantly **reduced** in SER-155 subjects, suggesting SER-155 repairs and protects the GI epithelial barrier from damage, preventing bacterial translocation and subsequent infection



Modulate Immune Function



New Data

Pro-inflammatory cytokines and chemokines were significantly **reduced** following SER-155 treatment*; additional effects observed in markers of immune homeostasis*. Data suggest SER-155 promotes systemic anti-inflammatory responses and immune homeostasis

US HCPs seek significant reduction of infection risk without compromising patient safety and would incorporate such a therapeutic into standard of care

Profile of SER-155

Efficacy

- **Reduce incidence of bloodstream infections:** target 20% BSI rate vs. current 40% rate
- **Reduce systemic antibiotic use** that is contributing to rising resistance
- **Reduce incidence of febrile neutropenia:** target 60% FN rate vs. current 80% rate

Safety

- **No major adverse event signals**
- Expect translation to **fewer deaths** in the active study arm

Health economics

- **Shorten hospital stay, reduce readmissions & reduce ICU utilization**

SER-155 Phase 1b data suggest potential to deliver this profile in a pivotal study

HCPs see SER-155 as a potentially transformative means to eliminate complications that get in the way of achieving transplant success

Primary Value Driver for SER-155

Reducing the risk of HSCT-related complications, thus ensuring successful engraftment and long-term health of the patient

A relative risk reduction of 50% in BSIs is seen as “transformative” and would support broad inclusion in standard protocols for allo-HSCT patients



Health Care Providers

Streamlines the transplant process so they can spend more time treating the patient’s underlying conditions and **less time dealing with potential morbidities**



Patients

One less thing to worry about for patients already dealing with a lot; additional **financial and QoL benefits** due to shortened hospital stays



Healthcare System

Reduced healthcare costs due to shorter hospital stays, fewer ICU visits, fewer antibiotic days and lower incidence of severe negative outcomes



The benefit would be massive because people die from these infections and so preventing them, the biggest benefit is mortality. The rest of the stuff with ICU admits and sepsis protocols and all...I think some of that also gets averted. That would be huge.”



*“This would probably be **standard of care**. It would be all eligible patients minus those who cannot tolerate it or are allergic.”*

US payers confirm high unmet clinical need for infection prophylaxis in allo-HSCT recipients and robust profile of SER-155

High clinical burden and unmet need

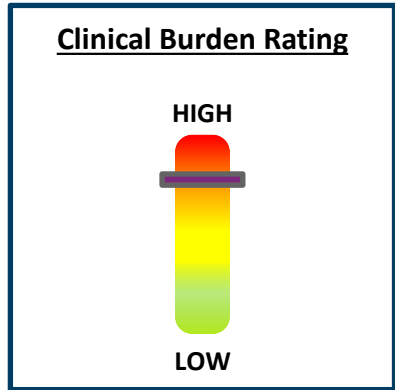
- High perceived clinical burden of BSIs within the allo-HSCT patient population is driven by high frequency of occurrences and poor associated outcomes
- Lack of an efficacious prophylactic therapy that successfully limits incidence of BSIs is considered a key unmet need and current driver of clinical burden
- Top unaided clinical concerns raised by payers include risk of febrile neutropenia, sepsis, and antibiotic-resistant infection

Profile of SER-155 positively received

- Proposed risk reduction of BSIs and related endpoints were seen as clinically meaningful and supportive of value proposition
- *“The reductions in primary and secondary endpoints are encouraging and brings hope that you are going to escape this risky scary complication of cancer therapy.”*

Site of dispensing drives reimbursement pathway

- Oral administration is viewed as convenient by payers, with most expecting coverage under outpatient pharmacy benefit given oral administration likely outside of the hospital setting



Viral prophylaxis provides precedent in medically vulnerable patients

Prevymis - increasingly used for viral infection prophylaxis (e.g., allo-HSCT and solid organ transplant populations)



**\$605M '23
WW sales**

- Reduces CMV infection in allo-HSCT recipients
- Lowers mortality rate

- Overall cost of allo-HSCT is high (~\$400K US year 1 allo-HSCT costs)
- Transplant-related complications (e.g., infections) raise cost by ~\$180K
- Infections result in longer hospital stays, readmissions, increased ICU utilization

SER-155 has blockbuster commercial potential, driven by a robust SER-155 profile and substantial unmet needs in allo-HSCT and additional groups

- ✓ **High unmet need** to prevent frequent and serious infections
- ✓ ~40K annual transplants worldwide; 3% annual growth from aging population and transplant success rates
- ✓ **Costly procedure** (~\$400K US year 1 allo-HSCT per patient cost) with **high incremental costs** of infections (incremental ~\$180K/patient)
- ✓ SER-155 has potentially "**transformational**" **profile** with robust efficacy and safety
- ✓ Highly concentrated universe of transplant centers conducting stem cell transplant procedures allows for an **efficient commercial model** with rapid education on new standard of care

Indication expansion: potential 10x addressable population

	Allo-HSCT	Autologous HSCT	Broader leukemia & lymphoma population*
WW annual diagnoses or transplants	~40,000	~60,000	~500,000
US annual diagnoses or transplants	~9,300	~13,500	~87,000 initial focus
Unmet needs addressed by SER-155	Prevent mortality and cost of post-transaction infections	Prevent mortality and costs of post-transplant infections	Reduce morbidity, mortality, and cost of infections and febrile neutropenia from chemotherapy

*Includes acute myeloid leukemia, multiple myeloma, and aggressive B cell non-Hodgkin lymphomas (diffuse large B-cell lymphoma, mantle cell, Burkitt's lymphoma)

Sources: CIBMTR, US NCI SEER, Thandra et al 2021 report of WHO data, Niederwieser et al *Haematologica* 2022; WHO Global Cancer Observatory; American Cancer Society

Accelerating SER-155 clinical development with positive Ph1b outcomes

Aim to **accelerate SER-155 development** in allo-HSCT

- Potential to follow successful precedent from VOWST development with single registrational study for efficacy

Engage with FDA on advancement of SER-155 allo-HSCT program

- **Received Breakthrough Therapy designation in December 2024**
- Applied for Orphan Drug designation

Intend to evaluate SER-155 in **additional patient populations** with high risk of serious bacterial infections

**Seeking SER-155
strategic partnership to
accelerate next study in
allo-HSCT
and expand to multiple
target populations**

Advancing SER-147 to prevent infections in chronic liver disease patients

Substantial unmet need

0.5M  2.1M 

~50% experience bacterial infections in a 6 month period

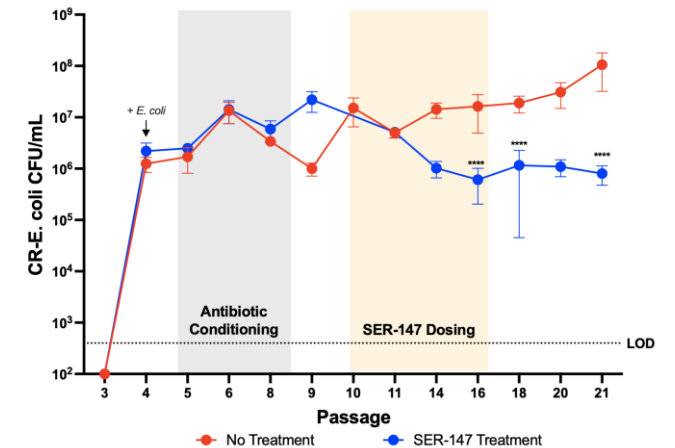
~20-25% of infections are spontaneous bacterial peritonitis (SBP) and bloodstream infections likely to be gut-seeded

Promising preclinical data

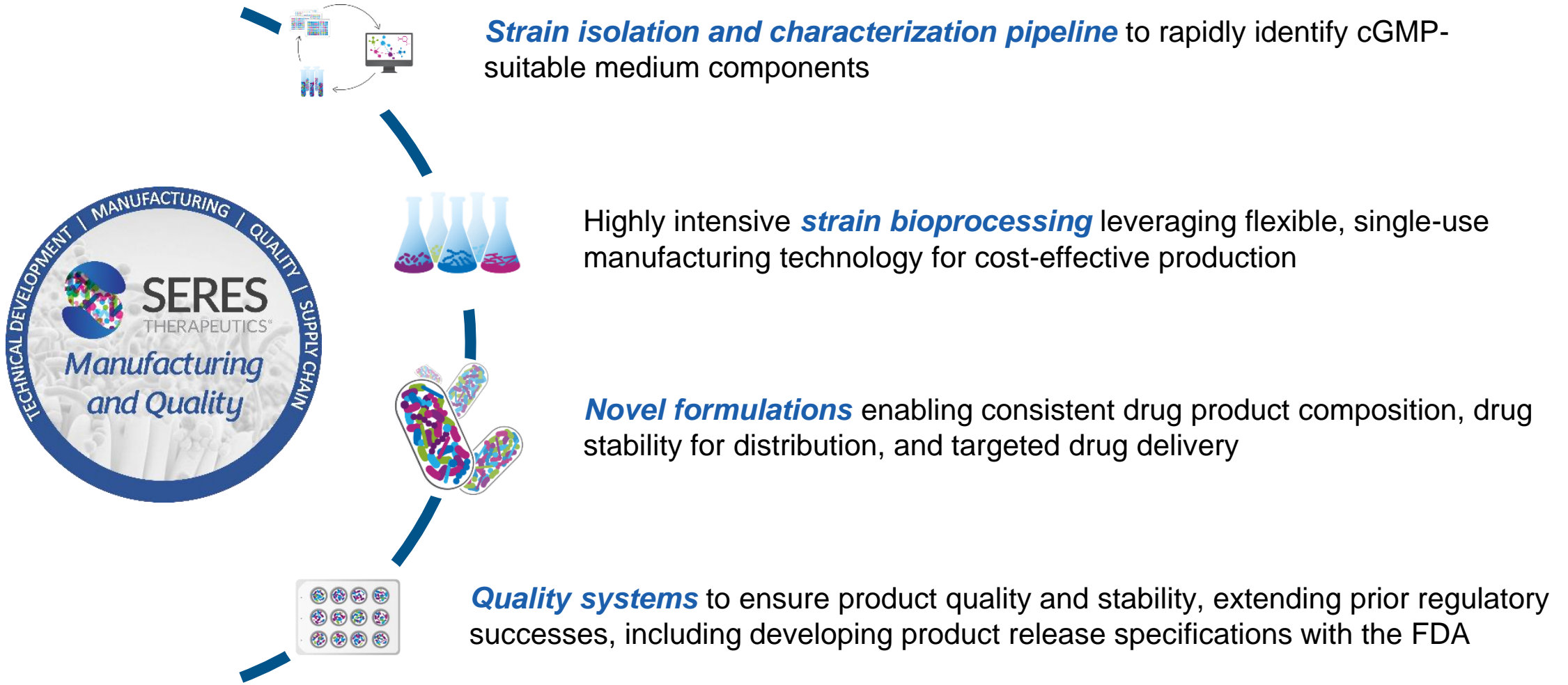
SER-147 is an investigational live oral biotherapeutic designed to reduce pathogens causing gut-seeded SBP and BSIs in liver disease patients

Example: 1-3 log reduction of *E. coli* in *in vitro* models, plus reduction of other pathogens

Declining *E. coli* titers



Manufacturing platform delivers defined consortia in oral formulation using cost-effective production



Maximizing opportunity of live biotherapeutics going forward

Additional Opportunities

- Prevent life-threatening bacterial infections, including antimicrobial resistant infections in additional populations
- Treat immune-related diseases (e.g., IBD, GvHD, checkpoint colitis)

SER-147

- **Infections in Chronic liver disease:** Progressing towards IND readiness
- **Indication expansion** (e.g., radiation enteritis, ICU and long-term care patients, organ transplant)

SER-155

- **Bloodstream infections in Allo-HSCT:** Engaging with FDA to accelerate; received Breakthrough Therapy designation and filed for Orphan Drug designation
- **Evaluate** in additional cancer treatment populations with high risk of serious bacterial infections

VOWST

- **rCDI:** Proven clinical and regulatory success; asset sale to Nestlé; Seres to participate in future milestones

Summary and path forward

Developing a pipeline of novel live biotherapeutics in areas of high unmet need

- SER-155 Phase 1b placebo-controlled clinical efficacy data further support Seres' strategy
- Pipeline aims to bring transformative medicines to a wider set of patients, led by SER-155 while advancing SER-147
- VOWST approval validates using live biotherapeutics to prevent life-threatening infections

SER-155 Phase 1b placebo-controlled clinical results promising

- Administration associated with 77% relative risk reduction for BSIs, significant reduction in systemic antibiotic exposure and lower incidence of febrile neutropenia vs placebo; Exploratory biomarker data support epithelial barrier integrity and the potential role for Seres' platform to provide clinical benefit to patients with inflammatory and immune diseases, such as IBD, including ulcerative colitis and Crohns disease
- FDA Breakthrough Designation obtained
- Company pursuing SER-155 strategic partnership to accelerate next study in allo-HSCT and expand to multiple target populations

VOWST asset sale strengthens financial position

- ~\$31M in cash/cash equivalents at Dec 31, 2024; cash runway projected into Q1 2026
- Fully retired debt
- VOWST asset sale closed in Sept 2024; \$50M expected to be received in January 2025 and \$25M (less ~\$1.5M in employment-related payments) due in July 2025 + \$275M potential future milestones