Seres Therapeutics Overview

Jefferies Virtual Healthcare Conference

June 3, 2020

Eric Shaff, Chief Executive Officer

SERES THERAPEUTICS™

Forward looking statements

Some of the statements in this presentation constitute “forward looking statements” under the Private Securities Litigation Reform Act of 1995, including, but not limited to, our development plans, the promise and potential impact of any of our microbiome therapeutics or clinical trial data, the ability of our clinical trials to support approval, the timing of clinical studies, the sufficiency of cash to fund operations, and the potential benefits of Seres’ collaborations. Such statements are subject to important factors, risks and uncertainties, such as those discussed under the caption "Risk Factors" in the Company’s Quarterly Report on Form 10-Q filed on May 7, 2020, and its other filings with the SEC, that may cause actual results to differ materially from those expressed or implied by such forward looking statements. Any forward looking statements included herein represent our views as of today only. We may update these statements, but we disclaim any obligation to do so.

Seres Therapeutics Overview

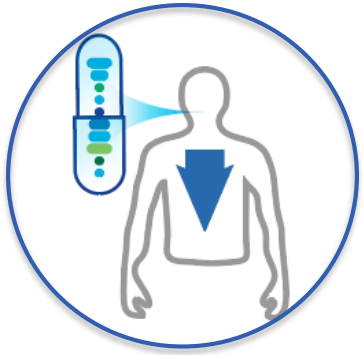
Platform	Leader in microbiome drug development with differentiated drug discovery, manufacturing and clinical capabilities
Focus	Prioritized pipeline in *C. difficile* infection, ulcerative colitis, oncology
Pipeline	• **SER-109 for *C. difficile* infection; Phase 3 top-line data in mid 2020** • SER-287 for ulcerative colitis in Phase 2b • SER-401 for metastatic melanoma in Phase 1b • SER-301 for ulcerative colitis; clinical development initiated • SER-155 for infection, bacteremia & GvHD in HSCT for cancer; clinical development initiated
Team	Experienced, highly accomplished leadership team

Based on the Company's current operating plan, cash resources are expected to fund operations into Q2 2021

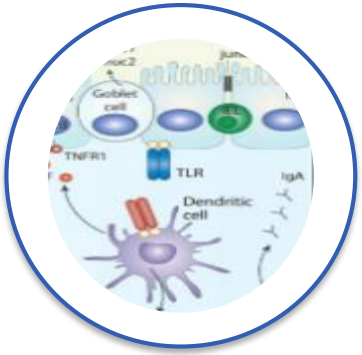
SERES THERAPEUTICS™

Seres is developing a novel drug modality that modulates the gut microbiome

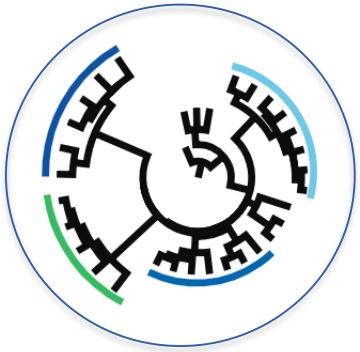
Ecobiotic® microbiome therapeutics are encapsulated consortia of commensal bacteria with specific pharmacologic properties



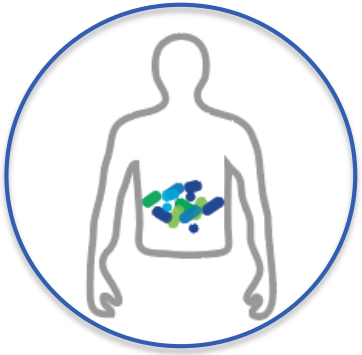
Formulated for **oral delivery** using current Good Manufacturing Practices (cGMP)



Designed to **target inflammatory & immunological** disease pathways simultaneously



Consortia capture **breadth of biological & functional diversity**



Mechanisms includes microbial **engraftment in GI tract** to restructure the microbiome

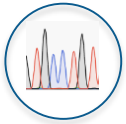
SERES THERAPEUTICS™

Industry-leading, in-house drug discovery, development & manufacturing platforms

Disease Target Identification

Microbiome Biomarker Discovery

Clinical sample biorepository



Proprietary genomic & metabolomic analytics

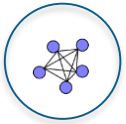
World-class collaborations

Hit-to-Lead Identification

Consortia Design

Broad strain library & culturing know-how

Genomic & host function screening



In-silico drug design for functional targets

Lead Optimization & Bioprocess

Pharmacological Properties Validation

Ex vivo & in vivo disease modeling

Fermentation & formulation optimization platforms

End-to-End GMP Manufacturing

Oral formulation

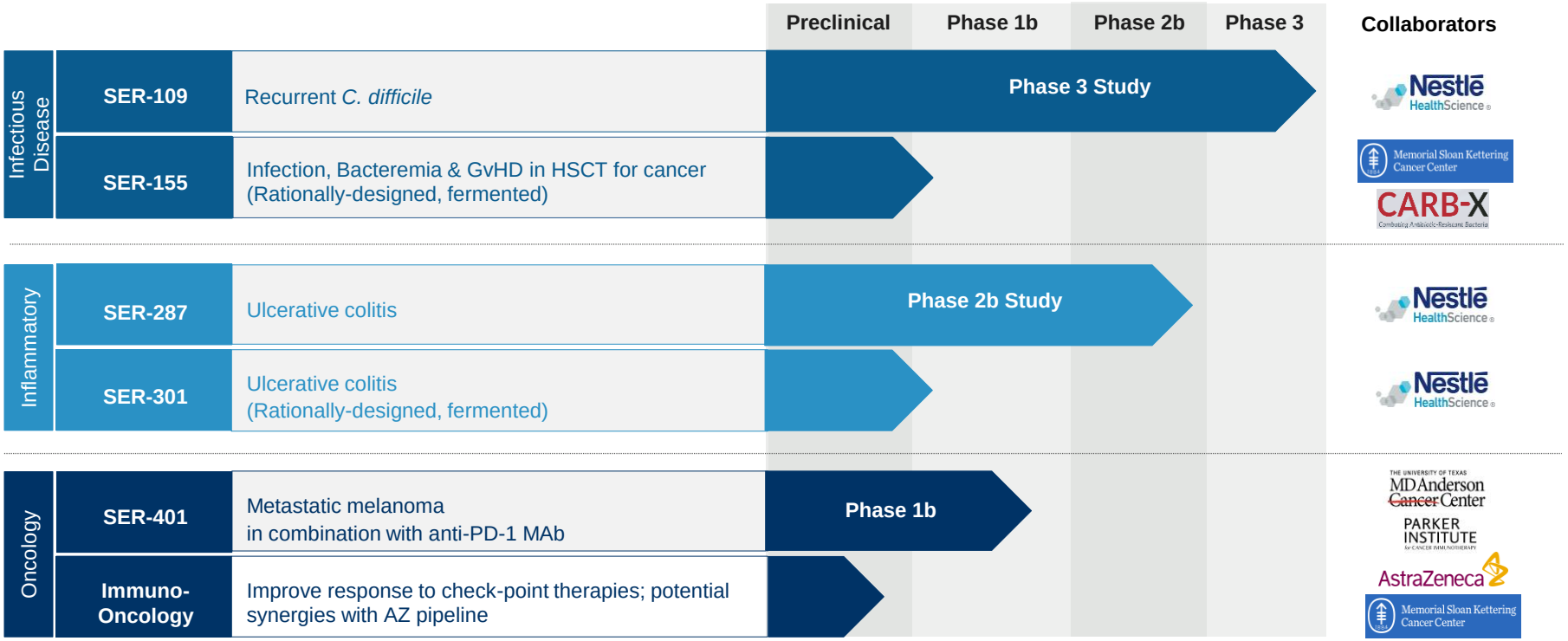
Donor-derived & multi-strain fermentation

Anaerobic, spore & lyophilized technologies

Late clinical stage drug release assays

SERES THERAPEUTICS™

Promising microbiome therapeutic pipeline



1. Collaboration with Nestlé Health Science, announced Jan. 11, 2016, regarding *C. difficile* and IBD programs for markets outside of North America

2. Collaboration with University of Texas MD Anderson Cancer Center and the Parker Institute for Cancer Immunotherapy, announced Nov. 14, 2017, regarding evaluation of microbiome therapies to improve the outcomes of cancer patients treated with immunotherapy. The Parker Institute is the IND application holder for SER-401.

3. Collaboration with AstraZeneca, announced Mar. 11, 2019, regarding advancing mechanistic understanding of the microbiome in augmenting the efficacy of cancer immunotherapy, including potential synergy with AstraZeneca compounds.

SERES THERAPEUTICS™

C. difficile Infection

Overview and SER-109 Phase 3 study

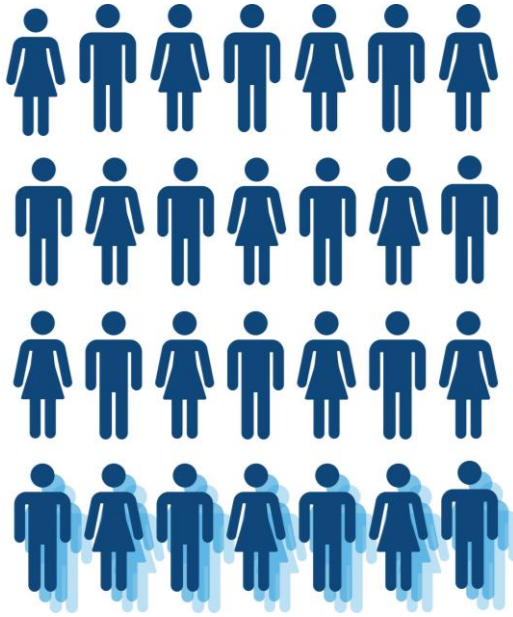
SERES THERAPEUTICS™

C. difficile infection overview and market opportunity

Infectious disease caused by toxin-producing bacteria, resulting in diarrhea, abdominal pain, fever and nausea

Leading cause of hospital-acquired infection in the U.S.

- ~ 453K cases of primary CDI within the U.S. each year
- ~ 170K episodes per year (100K episodes of first recurrence; ~ 73K episodes of 2+ recurrences)
- Estimated ~ $5B in healthcare burden each year
- Unregulated FMT is viewed as effective, but inconvenient treatment given its invasive route of administration, high unmet medical need for FDA approved treatment options



25% of primary *C. difficile* recur

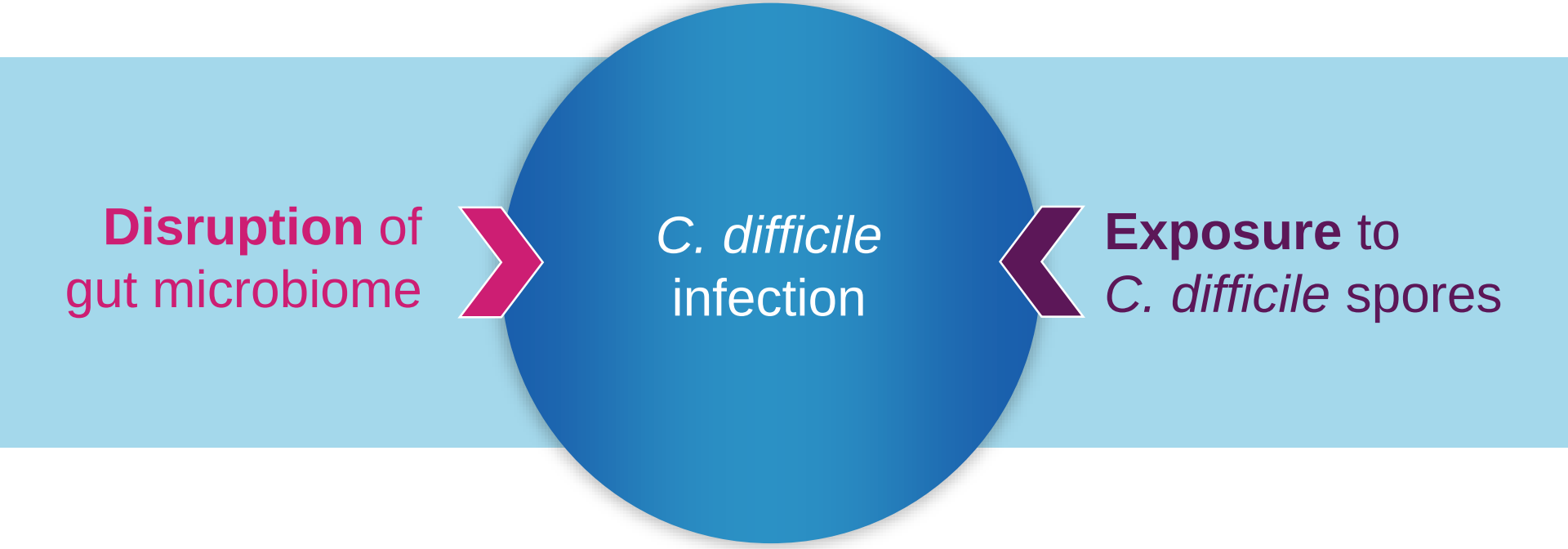
Over **20,000 deaths** per year

Source: L.E.K. analysis of interviews, survey, and secondary research; * Desai et al., Epidemiological and economic burden of *Clostridium difficile* in the United States: estimates from a modeling approach, BMC Infectious Diseases (2016) 16:303; Guh AY et al. NEJM 2020

SERES THERAPEUTICS™

C. difficile pathogenesis is a two-hit process: Disruption and Exposure

Leading risk factor for *C. difficile* infection - exposure to antibiotics, which disrupt the microbiome



McGovern *Clin Infect Dis* 2020; Theriot *Ann Review Micro* 2015

Current treatment options for *C. difficile* are suboptimal

Primary *C. difficile* infection:

- Vancomycin or fidaxomicin associated with rapid recurrence in 25% within 1 to 3 weeks of antibiotic completion

Multiply recurrent disease:

- Treatment options are limited with high rates of recurrence: 42-74%

Unapproved fecal microbiota transplant (FMT) provides proof-of-concept, and is used for recurrent disease, but has important limitations:

- Invasive route of administration
- Poorly characterized clinical profile
- Safety, including risk of transmissible disease

FMT safety concerns highlight the need for improved, FDA-approved treatment options for *C. difficile* infection

FDA U.S. FOOD & DRUG ADMINISTRATION

Important Safety Alert Regarding Use of Fecal Microbiota for Transplantation and Risk of Serious Adverse Reactions Due to Transmission of Multi-Drug Resistant Organisms

June 13, 2019

The Food and Drug Administration (FDA) is informing health care providers and patients of the potential risk of serious or life-threatening infections with the use of fecal microbiota for transplantation (FMT). The agency is now aware of bacterial infections caused by multi-drug resistant organisms (MDROs) that have occurred due to transmission of a MDRO from use of investigational FMT.

FDA U.S. FOOD & DRUG ADMINISTRATION

Safety Alert Regarding Use of Fecal Microbiota for Transplantation and Risk of Serious Adverse Events Likely Due to Transmission of Pathogenic Organisms

March 12, 2020

The Food and Drug Administration (FDA) is informing health care providers and patients of the potential risk of serious or life-threatening infections with the use of fecal microbiota for transplantation (FMT). The agency is now aware of infections caused by enteropathogenic *Escherichia coli* (EPEC) and Shigatoxin-producing *Escherichia coli* (STEC) that have occurred following investigational use of FMT that it suspects are due to transmission of these pathogenic organisms from FMT product supplied by a stool bank company based in the United States. The stool bank provides FMT product manufactured from pre-screened donors to healthcare providers and researchers.

FDA U.S. FOOD & DRUG ADMINISTRATION

Safety Alert Regarding Use of Fecal Microbiota for Transplantation and Additional Safety Protections Pertaining to SARS-CoV-2 and COVID-19

March 23, 2020

The global public health community is responding to a rapidly evolving pandemic of respiratory disease caused by a novel coronavirus that was first detected in China. The virus has been named "SARS-CoV-2" and the disease it causes has been named "COVID-19."

The Food and Drug Administration (FDA) is informing health care providers and patients of the potential risk of transmission of SARS-CoV-2 virus by the use of fecal microbiota for transplantation (FMT) and that FDA has determined that additional safety protections are needed.

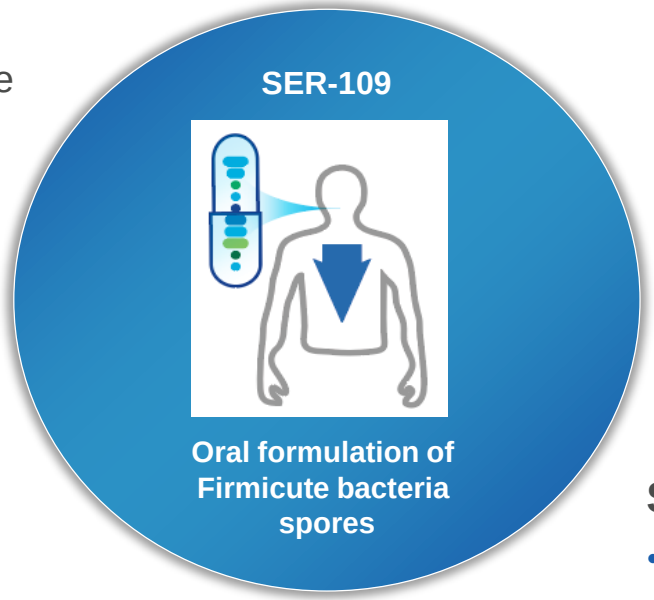
- In contrast to FMT, SER-109 is comprised of a highly purified consortia of spore-based bacteria manufactured under GMP conditions to ensure product quality and consistency
- Unique manufacturing process to inactivate potential pathogens
- Process inactivates many emerging potential pathogens where diagnostic assays may not yet be widely available, such as SARS-CoV-2

SERES THERAPEUTICS™

SER-109: Investigational, spore-based therapeutic designed to break the cycle of recurrent *C. difficile* infection

Strong Scientific Rationale

- Spore-forming Firmicute bacteria prevent *C. difficile* germination and growth
- Restructure disease susceptible microbiome and shift metabolic state to prevent *C. difficile* recurrence



Oral Formulation

- Spores are resistant to gastric acid, facilitating oral delivery to gastrointestinal tract

Granted FDA Status

- Obtained FDA Breakthrough & Orphan Drug designations

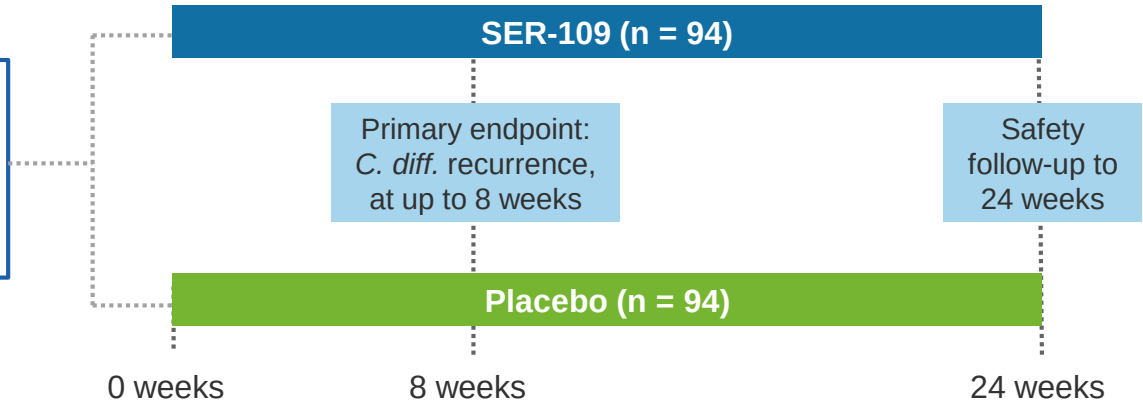
Safety

- Prior clinical studies demonstrate favorable tolerability & safety
- Spore purification mitigates risk of transmission of known and unknown infectious agents

SERES THERAPEUTICS™

ECOSPOR III Phase 3: Top-line results expected in mid-2020

- Multiply recurrent *C. difficile* patients
- All subjects treated with standard of care antibiotics



Features:

Toxin testing to ensure inclusion of subjects with active rCDI, and for accuracy of endpoint	Substantially higher dose vs. Phase 2 designed to result in greater and earlier microbiome restoration	Placebo arm to provide invaluable safety and efficacy data that cannot be obtained in open-label trials

SERES THERAPEUTICS™

* Recruitment completed in April 2020;182 patients were enrolled

Looking ahead to ECOSPOR-III study results

Seeking to demonstrate efficacy and safety in patients with true *C. difficile* infection

- Clinically compelling data with statistically significant delta between placebo and SER-109
- Safety and tolerability consistent with Ph1 and Ph2 trials

With favorable Phase 3 data, plan to engage with FDA regarding path to approval

- ECOSPOR III has potential to be a single pivotal study to support SER-109 product registration, though additional safety data may be required
- SER-109 Breakthrough and Orphan Drug Designations

SER-287 and Ulcerative Colitis

SERES THERAPEUTICS™

Ulcerative colitis overview

Serious chronic condition characterized by inflammation of the colon and rectum resulting in abdominal pain, bowel urgency and diarrhea

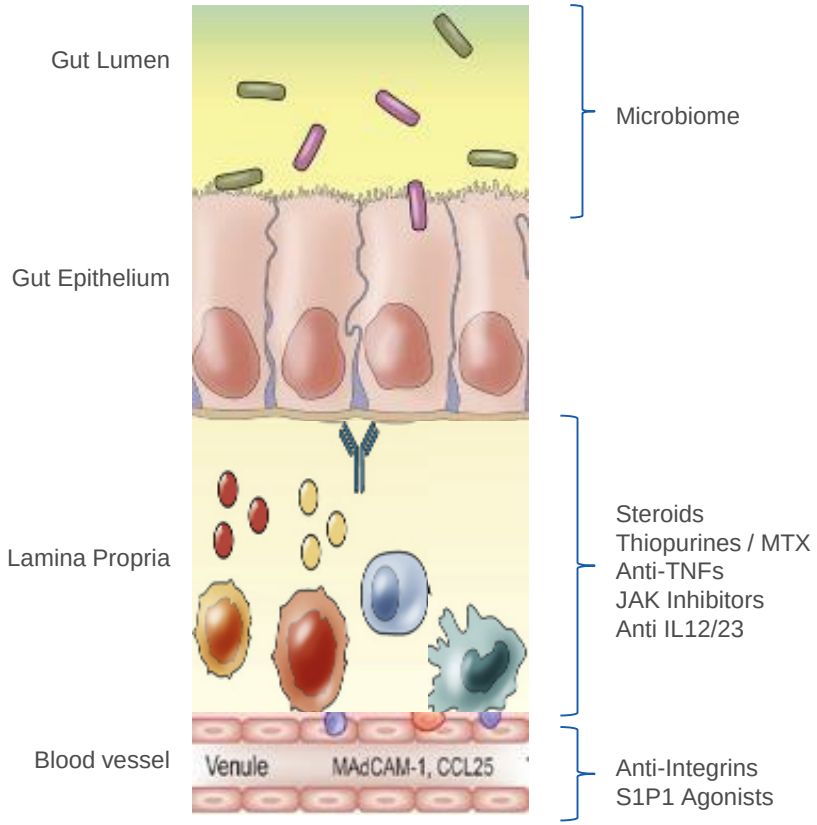
Significant need for improved therapies - Many drugs are immunosuppressive, limiting use to more severe patients

~700K in the United States

Only ~1/3 achieve remission

SERES THERAPEUTICS™

The dysbiotic microbiome may be a trigger of inflammation in ulcerative colitis



Microbiome therapeutics may drive therapeutic benefit

- May address drivers of inflammation, barrier integrity, innate immune activation, and adaptive immune education and cell trafficking
- Effector molecules may include short chain fatty acids, secondary bile acids, tryptophan metabolites, and TLR ligands

Microbial consortia can likely target multiple pathways simultaneously

Opportunity to develop both first-line and combination therapies

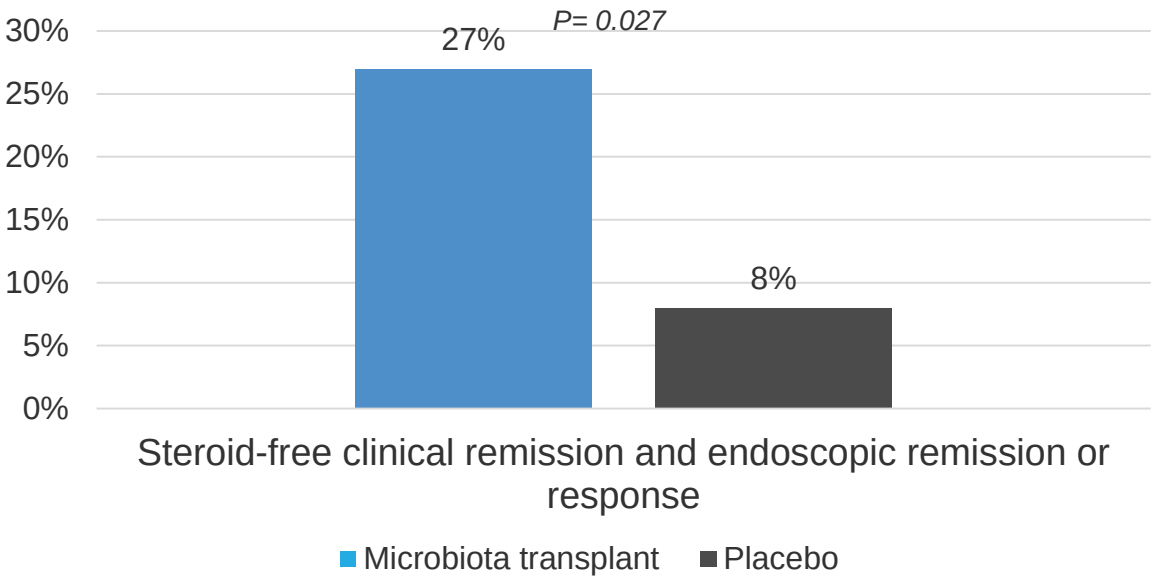
SERES THERAPEUTICS™

Published study regarding microbiota transplantation provided clinical proof-of-concept in ulcerative colitis

THE LANCET

Multidonor intensive faecal microbiota transplantation for active ulcerative colitis: a randomised placebo-controlled trial

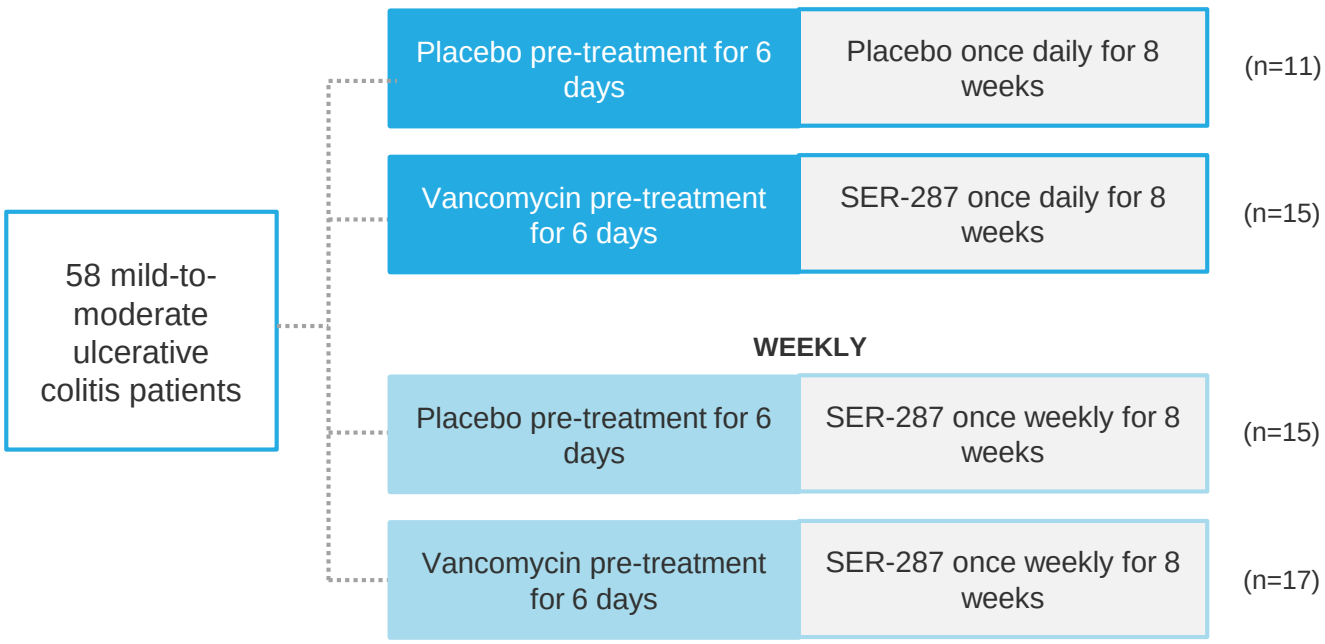
Sudarshan Paramsothy, Michael A Kamm, Nadeem O Kaakoush, Alissa J Walsh, Johan van den Bogaerde, Douglas Samuel, Rupert W L Leong, Susan Connor, Watson Ng, Ramesh Paramsothy, Wei Xuan, Enmoore Lin, Hazel M Mitchell, Thomas J Borody



Note: SER-287 was not involved in this study

SERES THERAPEUTICS™

SER-287 Phase 1b ulcerative colitis study

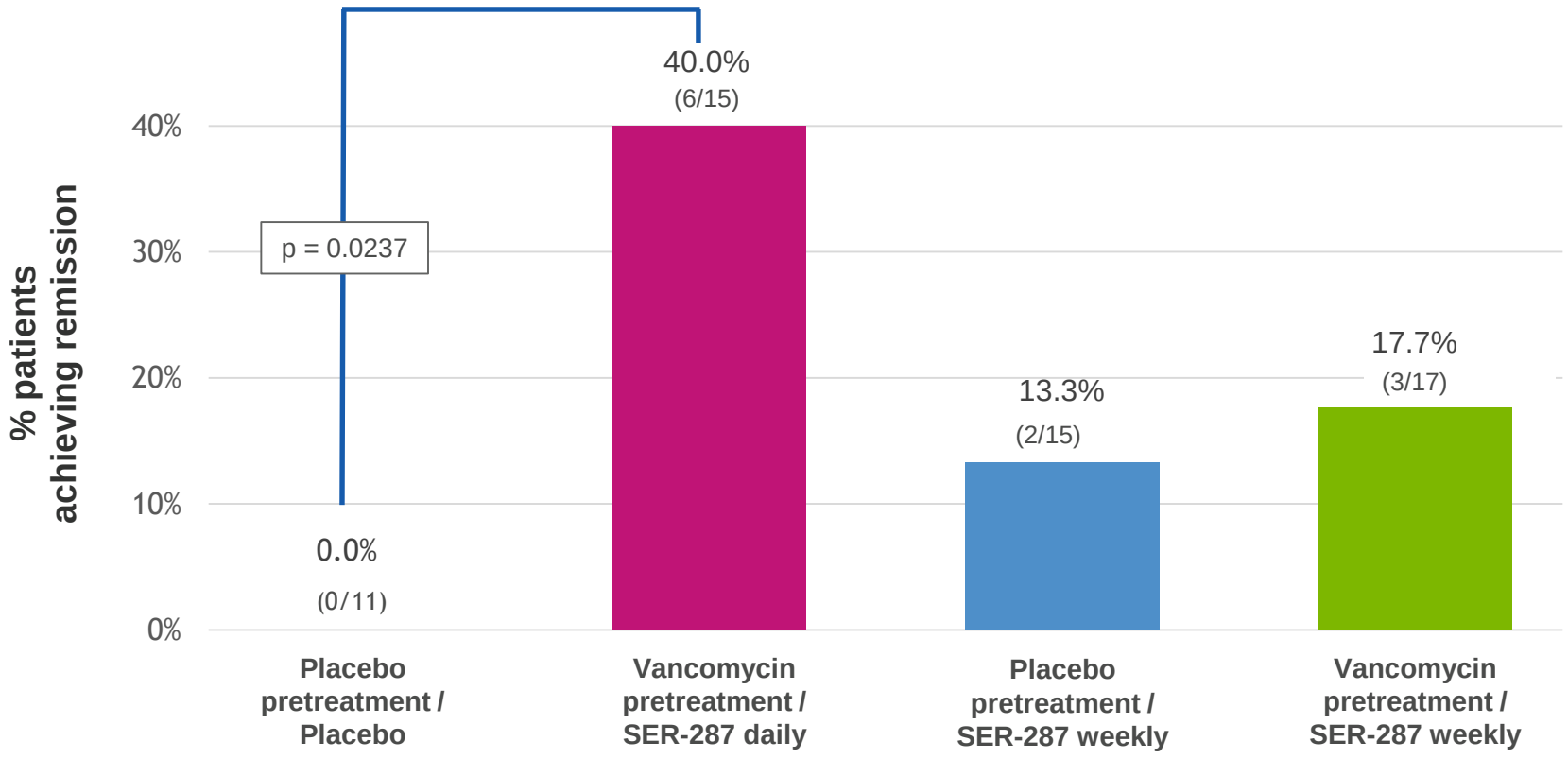


Primary Objectives

- Safety and tolerability
- Change in composition of intestinal microbiome at 8 weeks

SERES THERAPEUTICS™

Phase 1b study results – Statistically significant clinical remission improvement observed in Vanco/SER-287 daily treatment arm

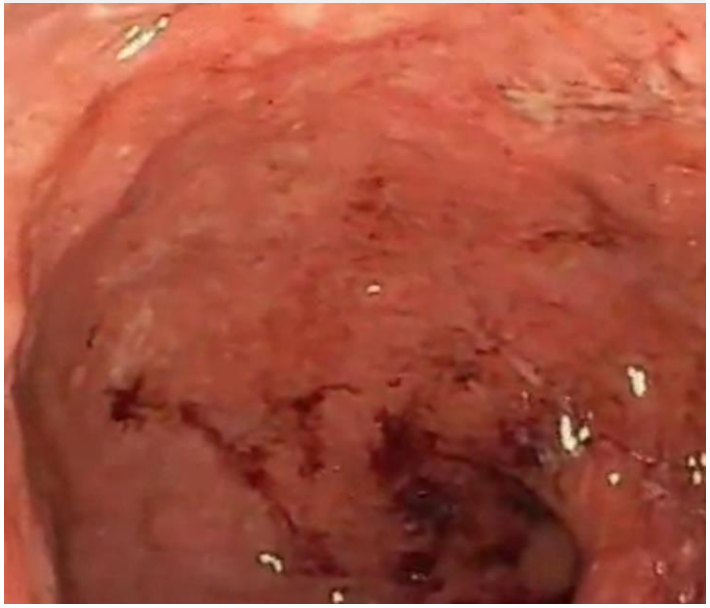


Remission = Total Modified Mayo score ≤ 2 AND endoscopic subscore ≤ 1
Note: Missing data treated as failure; statistical significance not found in SER-287 weekly arms

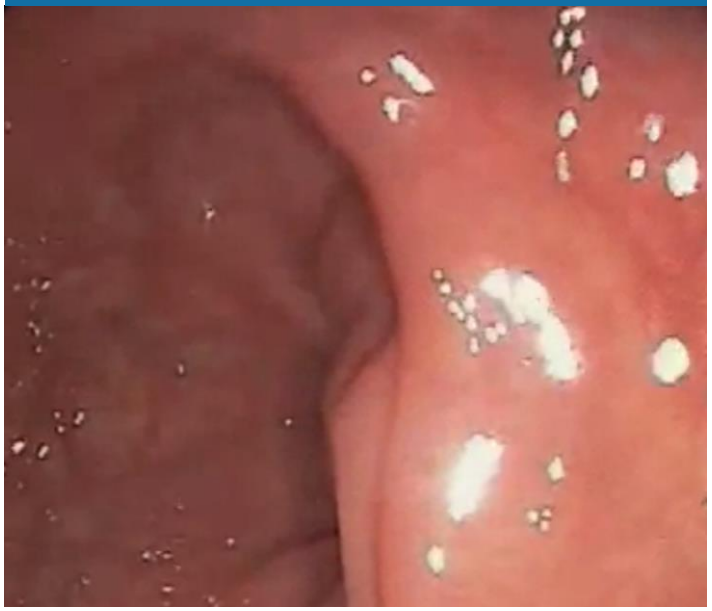
SERES THERAPEUTICS™

Illustrative endoscopy improvement — Vanco/SER-287 daily treatment

Pre-treatment endoscopy showing the sigmoid colon with spontaneous bleeding and ulceration



Post-treatment day 64 endoscopy



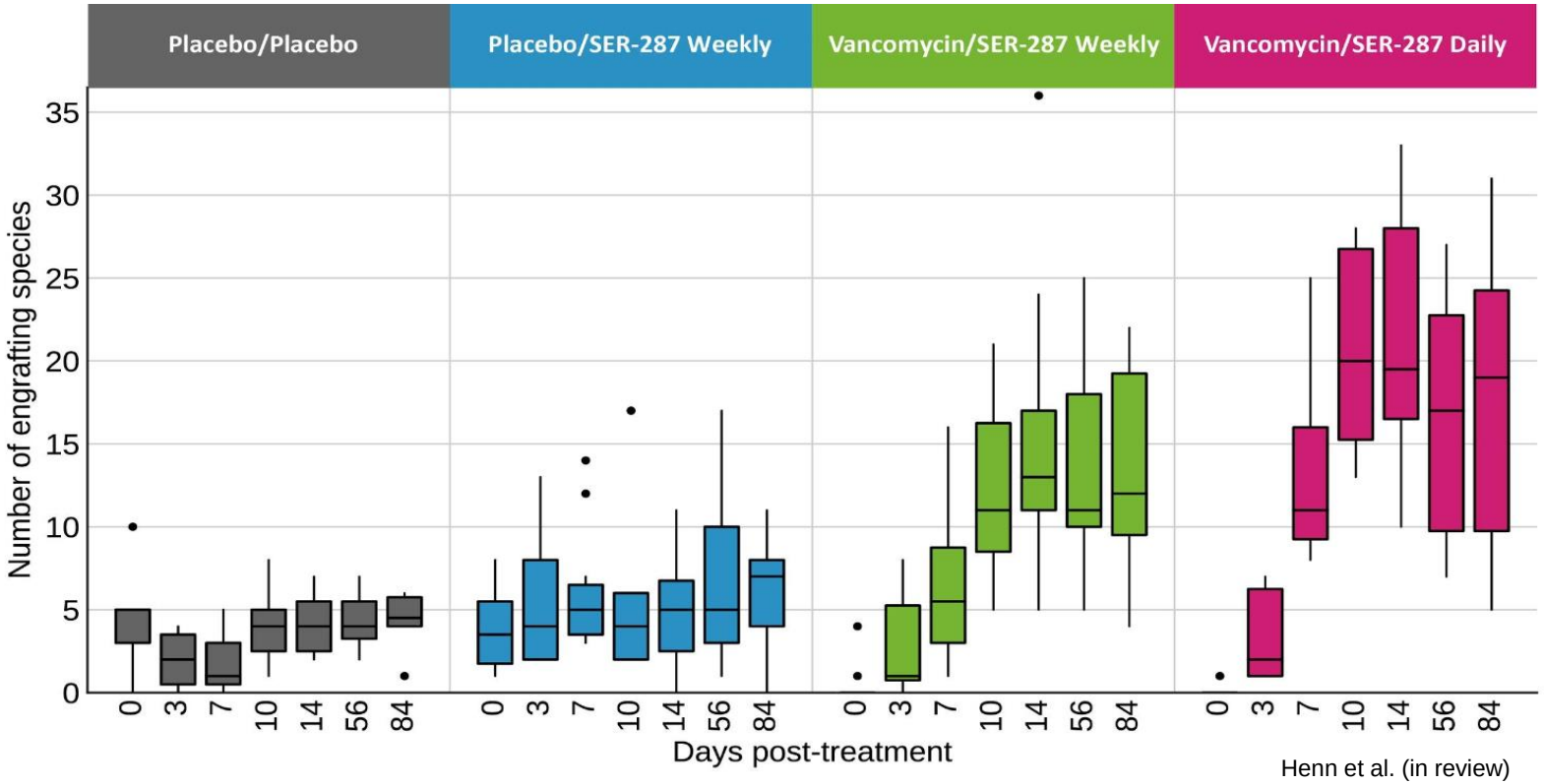
SERES THERAPEUTICS™

SER-287 Phase 1b safety results show safety profile comparable to placebo

- SER-287 daily arm demonstrated a similar safety profile to placebo
- No serious drug-related adverse events
- Reduced gastrointestinal adverse events provide an independent assessment of efficacy as the GI adverse events likely reflect ulcerative colitis disease activity
  - SER-287 daily arm GI AEs: 2/15 (13.3%) vs. placebo arm: 5/11 (45.5%)

SERES THERAPEUTICS™

Phase 1b study results – SER-287 bacteria engrafted in subjects and was durable to four weeks after dosing

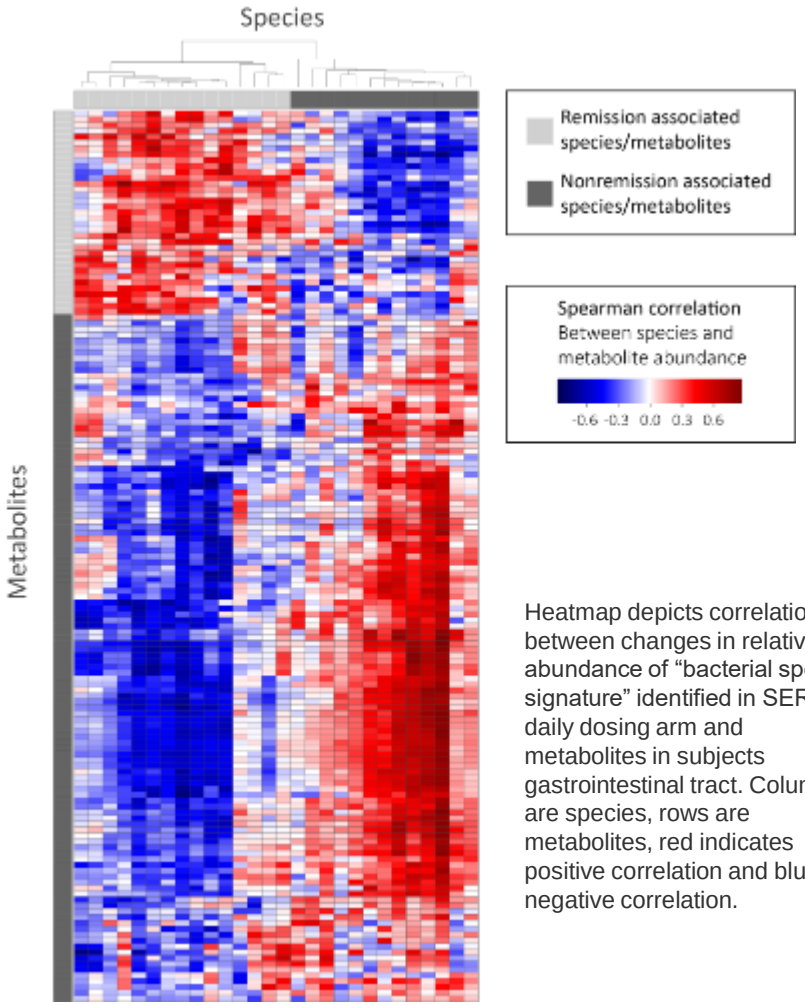


Henn et al. (in review)

- Significant engraftment observed starting one week post-dosing
- Engraftment is significantly higher in arms with vancomycin pre-conditioning
- Engraftment in vancomycin arms is dose-dependent; significantly greater in daily dosing arm (arm with greatest efficacy)

SERES THERAPEUTICS™

Microbiome signature of remission strongly correlated with metabolite shifts in patients administered SER-287

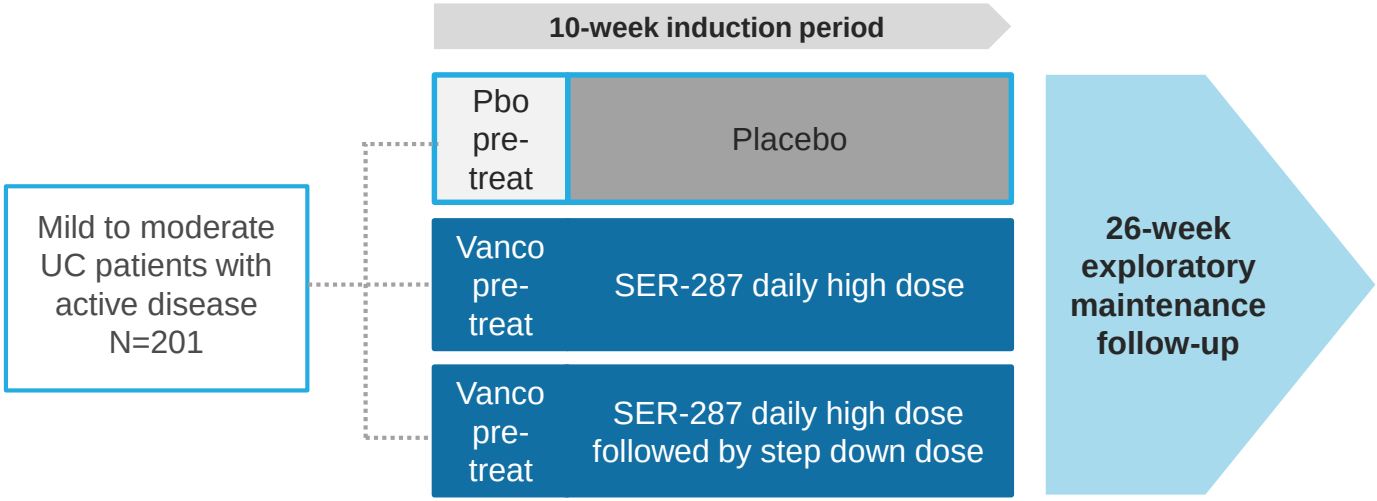


Heatmap depicts correlation between changes in relative abundance of "bacterial species signature" identified in SER-287 daily dosing arm and metabolites in subjects gastrointestinal tract. Columns are species, rows are metabolites, red indicates positive correlation and blue negative correlation.

- Strong correlation between signature species and stool metabolites that predict clinical remission
- Metabolomic signature of clinical remission represents diverse functional pathways
- Many pathways identified are implicated in IBD and immune dysregulation
- Colonic biopsy transcriptional data support SER-287 is associated with modulation of multiple disease relevant host inflammation & immune pathways

SERES THERAPEUTICS™

Ongoing SER-287 ECO-RESET Phase 2b study in patients with mild-to-moderate active ulcerative colitis



- FDA Fast Track designation
- FDA feedback: Phase 2b study results, in conjunction with data from a second pivotal study, could support BLA submission
- As of March 30, 2020, ~60% enrolled based on 201 patient target size
    - Seres is evaluating potential SER-287 study design modifications with the goal of obtaining high quality, clinically interpretable study results

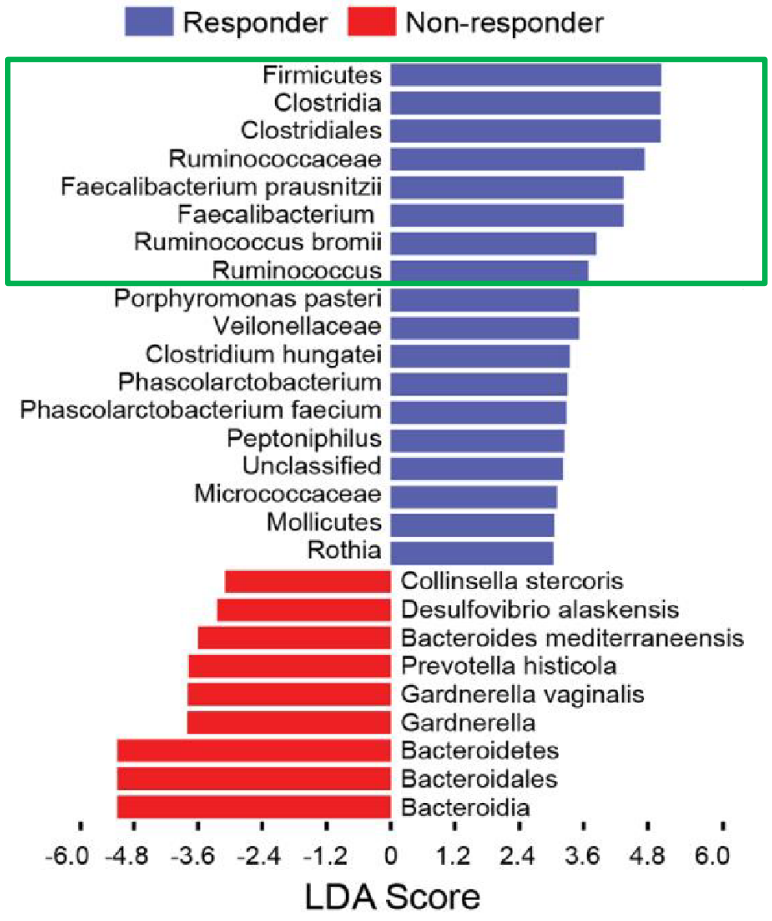
SERES THERAPEUTICS™

Earlier clinical stage development programs: SER-401, SER-301, SER-155

SERES THERAPEUTICS™

Immuno-oncology - Microbiome signature in melanoma patient responder to anti-PD-1

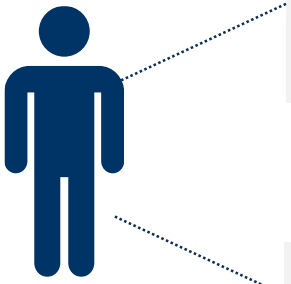
- SER-401 composition driven by bacteria consistent with responder profile
- All spore formers that leverage deep Seres expertise in the biology and manufacturing of these organisms



Gopalakrishnan et al, Science 2017

SERES THERAPEUTICS™

Ongoing SER-401 Phase 1b study



Patients with metastatic melanoma treated with anti-PD-1 (nivolumab)

SER-401; biologically sourced product to match microbiome signature of anti-PD-1 responders (n=20)

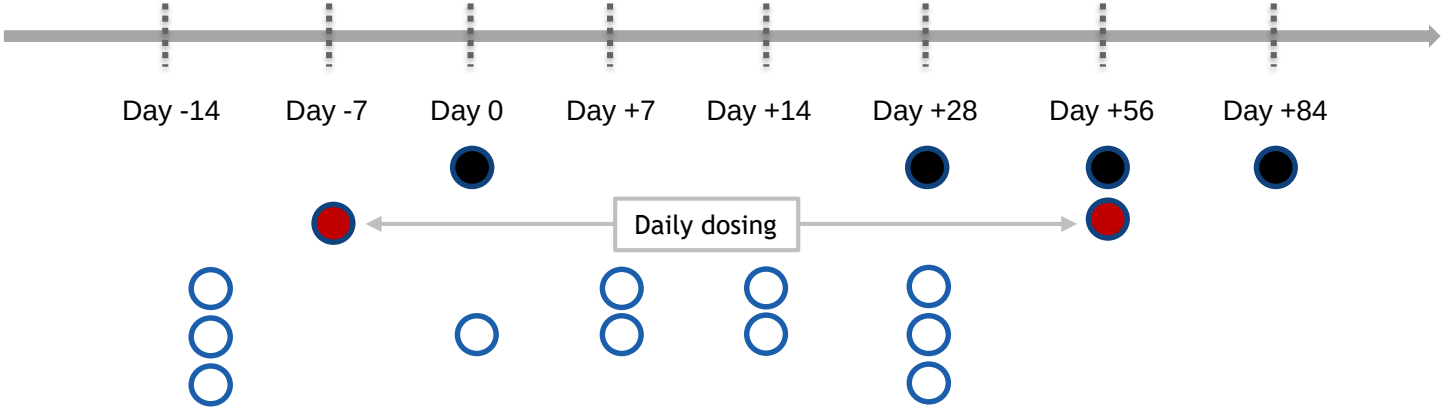
Placebo (n=10)

Study Objectives

Primary endpoint = safety and tolerability

All patients = CT scans with RECIST week 12

Secondary endpoints = engraftment, response and correlative studies (immune correlates in blood and tumor, metabolites)



Additional study arm may be added including fecal microbiota obtained from responders

SERES THERAPEUTICS™

Rationally designed fermented products (SER-301, SER-155) may provide important advantages

Seres in-house GMP manufacturing and quality control capabilities

Cell banking & inoculum

Drug substance

Drug product

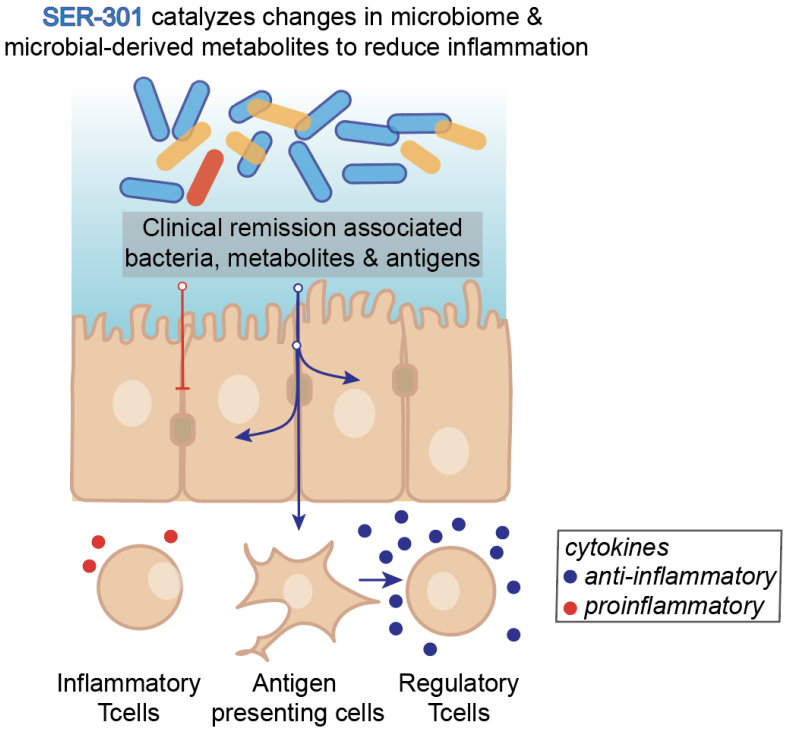
Quality control

- Potential best-in-class clinical profile based on species specific properties
- Fermented approach enables efficient and highly scalable manufacturing process to serve large markets

SERES THERAPEUTICS™

SER-301: Next-generation, rationally designed fermented microbiome therapeutic candidate for ulcerative colitis

- Reduces induction of pro-inflammatory activity
- Improves epithelial barrier integrity & TNF-α driven inflammation in IECs
- Modulates UC-relevant anti-inflammatory, innate & adaptive immune pathways



- **Lead candidate designated**
- **Activities to initiate clinical development ongoing**

SERES THERAPEUTICS™

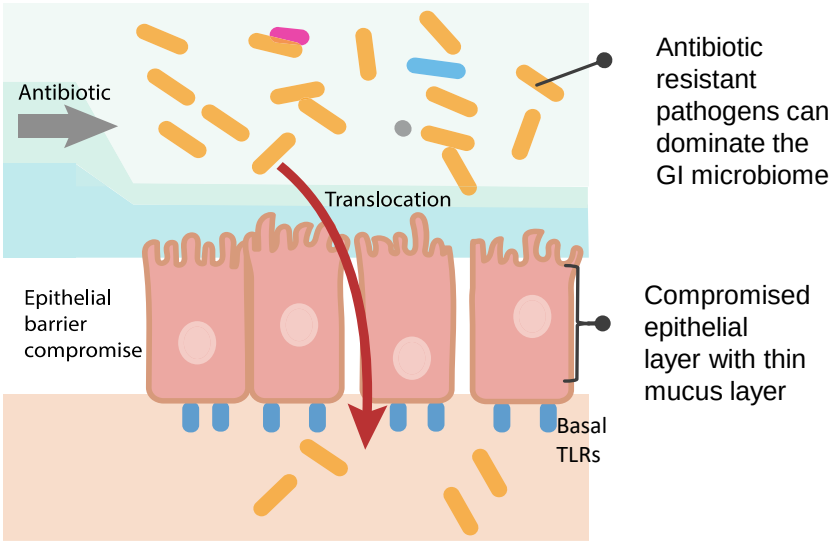
SER-155: Rationally-designed, fermented microbiome therapeutic candidate for infection, bacteremia & GvHD

- Decreases infection by antibiotic resistant bacteria in the gastrointestinal tract that lead to bacteremia
- Enhances epithelial barrier integrity to prevent bacterial translocation to the blood stream
- Modulates local and systemic immunomodulatory responses to decrease graft versus host disease
- Collaboration with:

Memorial Sloan Kettering Cancer Center

CARB-X
Combating Antibiotic-Resistant Bacteria

Catalyzes changes in the microbiome & microbe-derived metabolites to prevent bacteremia



- **Lead candidate designated**
- **Activities to initiate clinical development ongoing**

SERES THERAPEUTICS™

Broad IP portfolio and regulatory exclusivity

PATENT PORTFOLIO OF OWNED & LICENSED PATENTS AND APPLICATIONS*

- Obtained issued patents in the US, demonstrating that rationally designed ecologies of spores and microbes are patentable
- Portfolio includes composition of matter and method claims, including option to license foundational IP from MD Anderson related to the use of bacteria in combination with checkpoint inhibitors. Portfolio also includes exclusive licenses to Memorial Sloan Kettering Cancer Center IP related to use of bacteria to treat gastrointestinal disorders and cancer relapse.
- Issued claims related to SER-109/ *C. difficile & SER-287 / ulcerative colitis* lead candidates extend through **2033**
- 13 Issued US Patents obtained

21	**Families of Applications**
13	**Nationalized**
1	**Pending Provisionals**

PROJECTED BIOSIMILAR REGULATORY EXCLUSIVITY

12 years for new biological composition

10 years for new drug

SERES THERAPEUTICS™

Significant value drivers anticipated

SER-109	Recurrent *C. difficile* infection – Phase 3 enrollment complete; top-line data in mid 2020
SER-287	Ulcerative colitis – Phase 2b study ongoing; ~60% enrolled as of March 30, 2020; study design modifications are under evaluation
SER-401	Metastatic melanoma – Phase 1b study ongoing
SER-301	Rationally designed fermented composition; Activities to initiate clinical development ongoing
SER-155	Rationally designed fermented composition; Plan to initiate development to prevent infections and GvHD

Balance Sheet	As of end of Q1 2020
Cash, cash equivalents and investments	$75.1M

Based on the Company's current operating plan, cash resources are expected to fund operations into Q2 2021

SERES THERAPEUTICS™