Seres Therapeutics Overview

Eric Shaff, Chief Executive Officer

Oppenheimer Fall Healthcare Summit

September 23, 2020

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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, the ability of our clinical trials to support approval, the timing of clinical studies, the timing and ultimate results of the SER-109 safety data, the size of the market for SER-109, 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 July 28, 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.

SER-109 Phase 3 success highlights that the time for microbiome therapeutics is now

Seres' mission: To transform the lives of patients worldwide with revolutionary microbiome therapeutics

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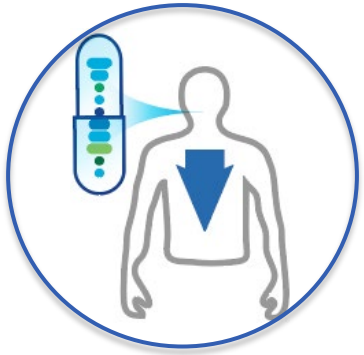
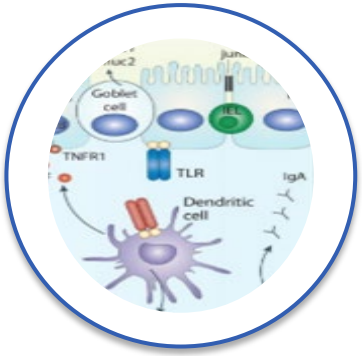
Seres is developing a novel drug modality that modulates the gut microbiome

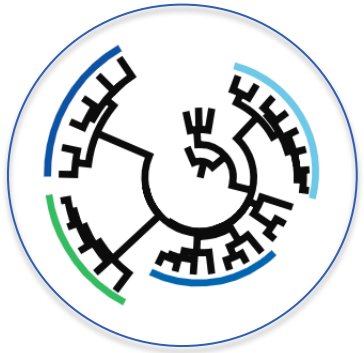
Ecobiotic® microbiome therapeutics are encapsulated consortia of commensal bacteria with specific pharmacologic properties



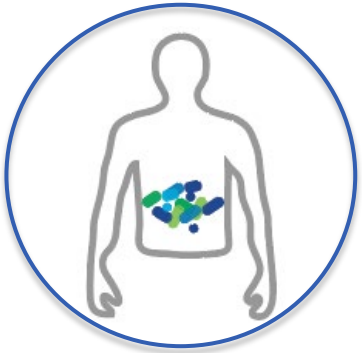
Formulated for **oral delivery** using current Good Manufacturing Practices (cGMP)



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

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Industry-leading, in-house research engine for drug discovery, development & manufacturing

Disease Target Identification → **Hit-to-Lead Identification** → **Lead Optimization & Bioprocess** → **End-to-End GMP Manufacturing**

Microbiome Biomarker Discovery

Clinical sample biorepository

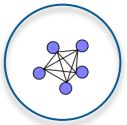
Proprietary genomic & metabolomic analytics

World-class collaborations

Consortia Design

Broad strain library & culturing know-how

Genomic & host function screening



In-silico drug design for functional targets

Pharmacological Properties Validation

Ex vivo & in vivo disease modeling

Fermentation & formulation optimization platforms

Oral formulation

Donor-derived & multi-strain fermentation

Anaerobic, spore & lyophilized technologies

Late clinical stage drug release assays

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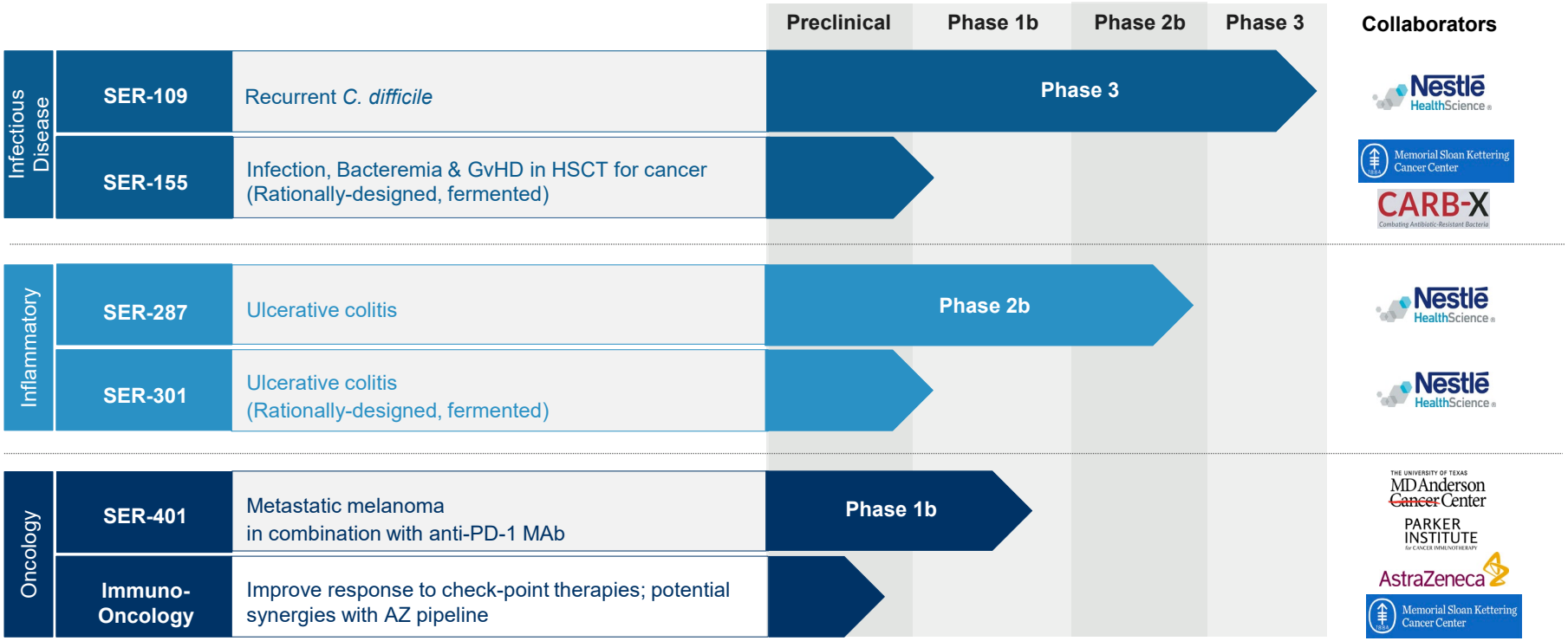
Broad opportunities for microbiome therapeutics



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.

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C. difficile Infection

Overview and SER-109 Phase 3 study

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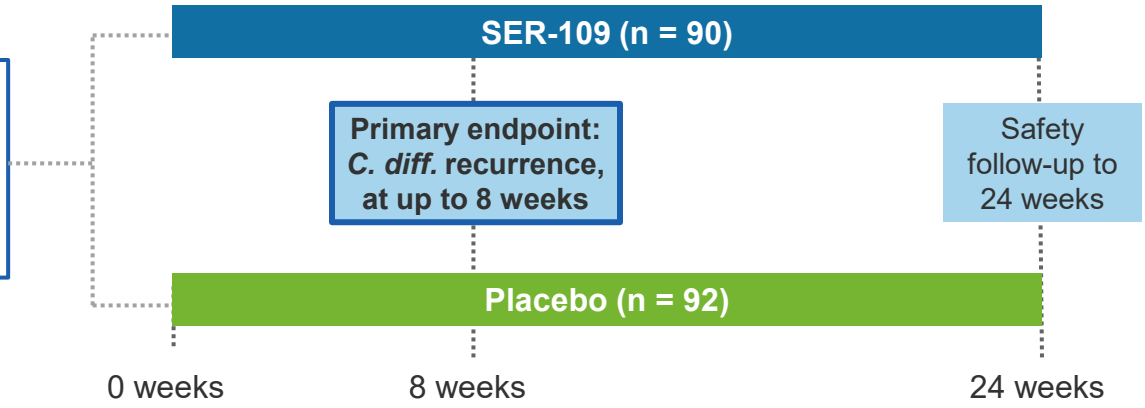
August 2020: Positive ECOSPOR III Phase 3 study read-out

- Multiply recurrent *C. difficile* patients (n=182)
- All subjects treated with standard of care antibiotics



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

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Topline SER-109 Phase 3 study efficacy results

Primary efficacy endpoint results:

Time point	SER-109 (N =90)	Placebo (N =92)	RR (95%CI)	p-Value (p1/p2)
	n (%)	n (%)		
Week 8	10 (11.1)	38 (41.3)	0.27 (0.15, 0.51)	<0.001 / <0.001

- Sustained clinical response rate (i.e., percentage of patients who remain free of CDI at 8 weeks): SER-109 was effective in 88.9% of SER-109 subjects vs. 58.7% of subjects in the placebo arm.
- Results were statistically significant in both age stratified subgroups: 18-64 years old, or 65 and over

- **Highly statistically significant 30.2% absolute reduction in the rate of CDI recurrence compared to placebo**
- **Number needed to treat = approximately 3**

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Favorable safety profile observed in Phase 3

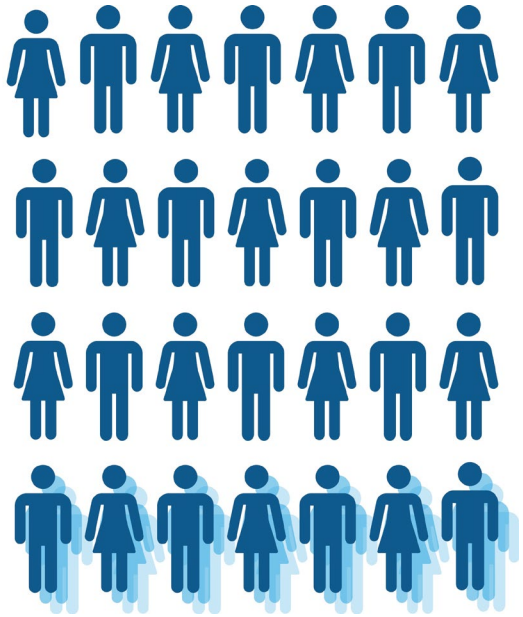
- SER-109 was well tolerated, with **no treatment-related serious adverse events (SAEs) observed in the active arm**, and an adverse event profile similar to placebo
- **Overall incidence of patients who experienced AEs during the eight-week study period was similar** between SER-109 and placebo arms
- Most commonly observed treatment-related AEs were flatulence, abdominal distention and abdominal pain, which were generally mild to moderate in nature, and these were observed at a similar rate in both the SER-109 and placebo arms

Substantial recurrent *C. difficile* infection 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



25% of primary *C. difficile* recur

Over **20,000 deaths** per year

- **Potential broad FDA label covering rCDI patients**

Source: * 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

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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

Since July 2020, the largest U.S. provider of FMT has quarantined supply and halted shipments

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Amplifying efforts for market preparation and launch

Scaling Market Education Efforts

- Medical communications strategy
- KOL mapping
- Develop and deploy payer value proposition

Enhancing Understanding of Commercial Opportunity

- Deeper patient journey analysis
- Pricing analysis
- Customer segmentation
- Identify options for go-to-market model

Building Infrastructure to Launch

- Scale Medical Affairs organization and deploy MSL team
- Hire key commercial leadership roles
- Key external strategic partners on board

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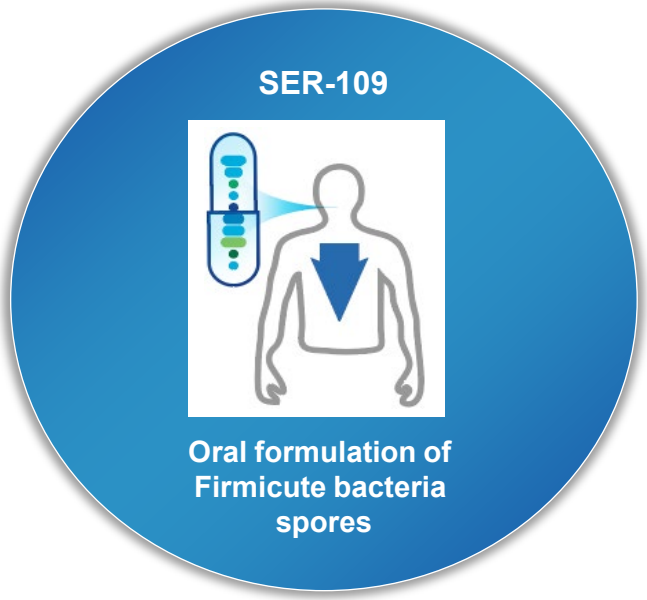
SER-109: Investigational, spore-based therapeutic designed to break the cycle of recurrent *C. difficile* infection



Strong clinical & scientific data

- Dramatic reduction in CDI recurrence rate
- Spore-forming Firmicute bacteria prevent *C. difficile* germination and growth

Oral formulation

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

Favorable safety profile

- Favorable tolerability & safety profile with no imbalance in adverse event
- Spore purification mitigates risk of transmission of known and unknown infectious agents

FDA regulatory designations

- Breakthrough designation
- Orphan drug status

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SER-287 and Ulcerative Colitis

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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

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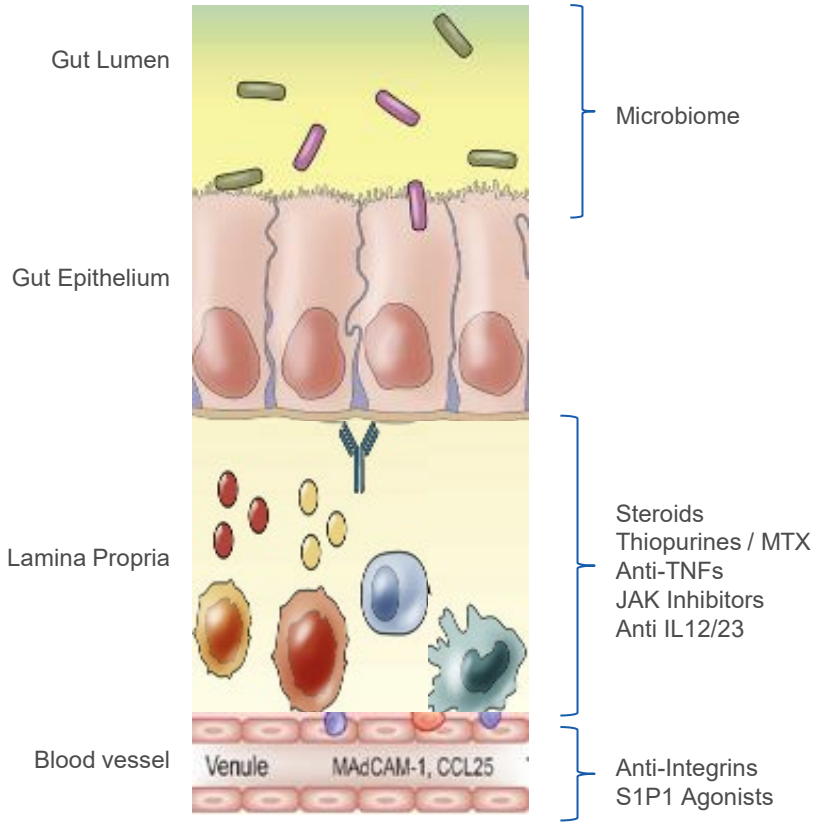
The dysbiotic microbiome may be a trigger of inflammation in ulcerative colitis



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

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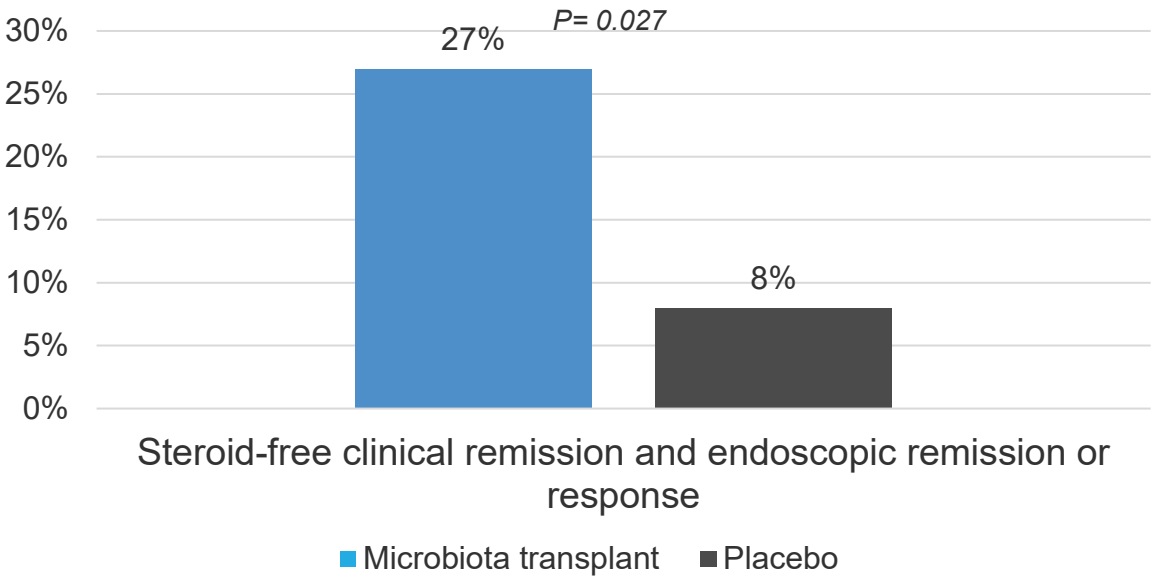
Published study regarding microbiota transplantation provided clinical proof-of-concept in ulcerative colitis

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

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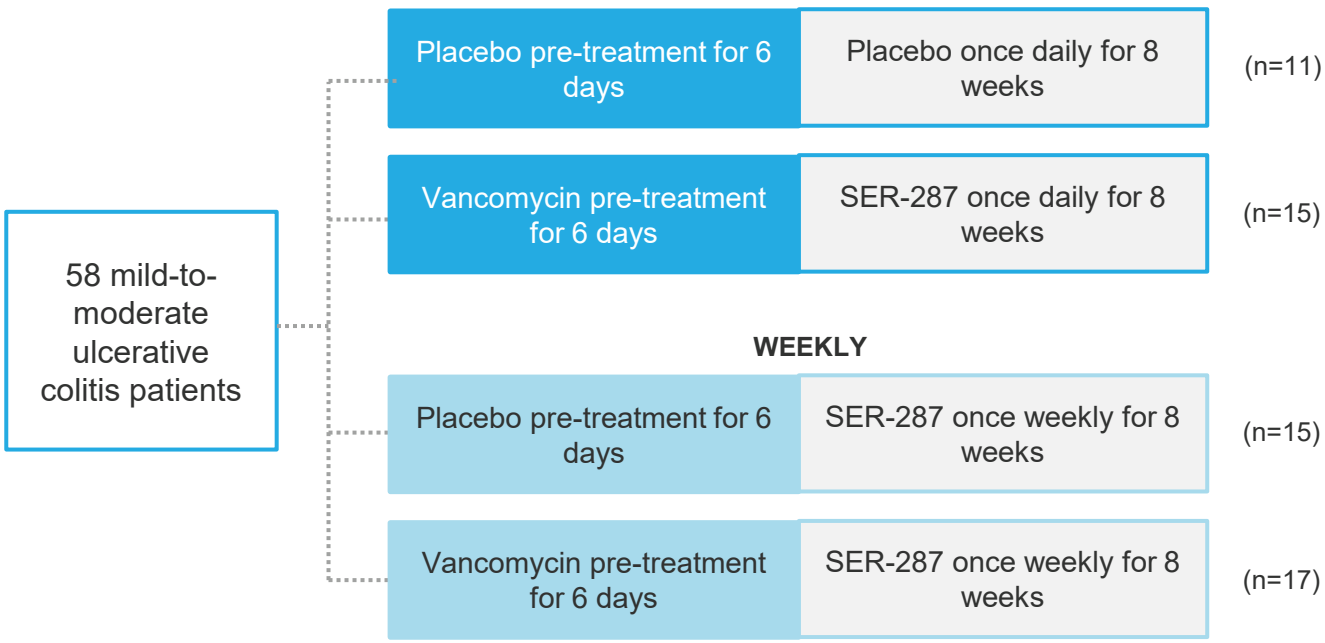
SER-287 Phase 1b ulcerative colitis study



Primary Objectives

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

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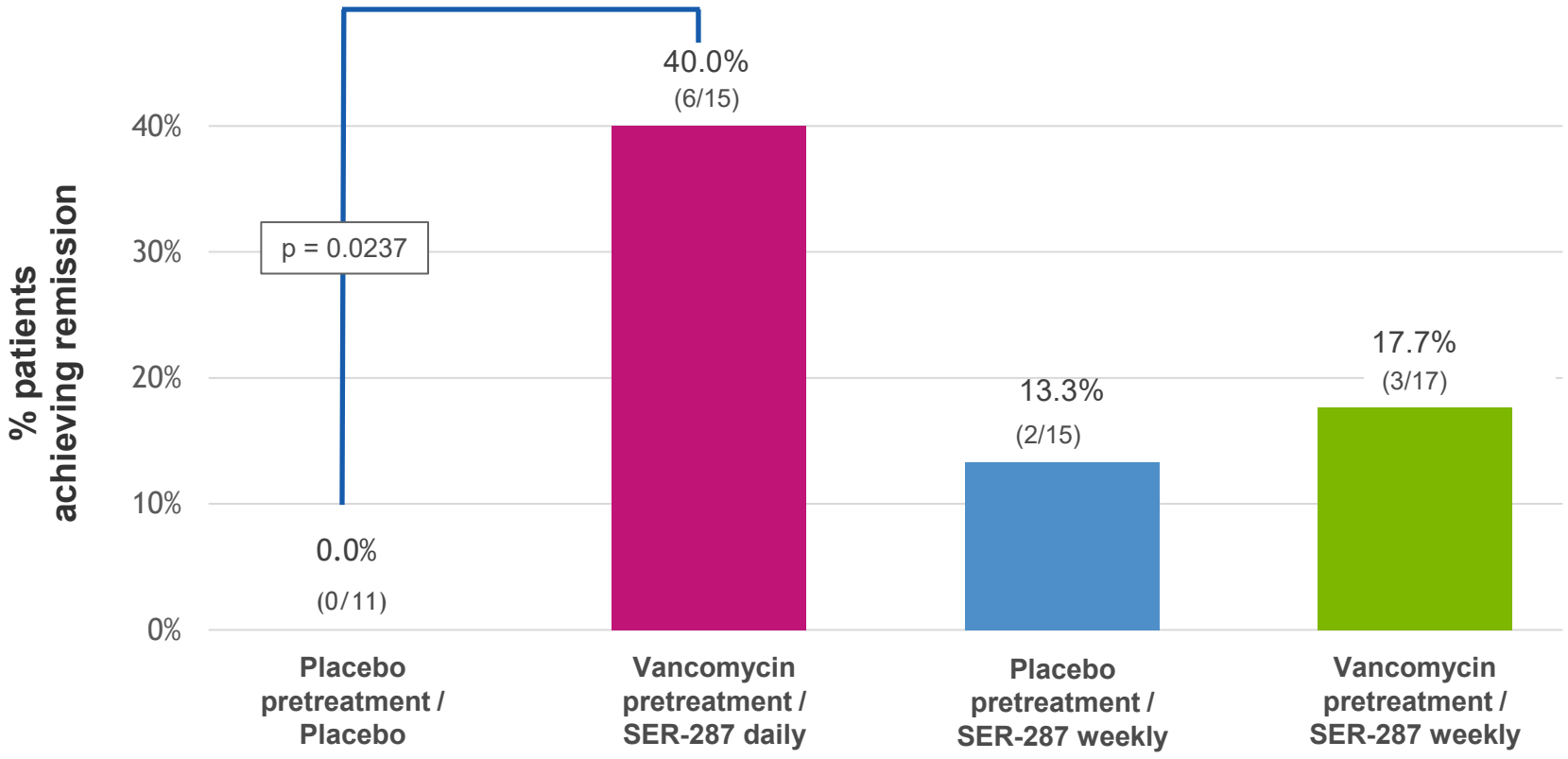
Phase 1b study results – Statistically significant clinical remission improvement observed in Vanco/SER-287 daily treatment arm



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

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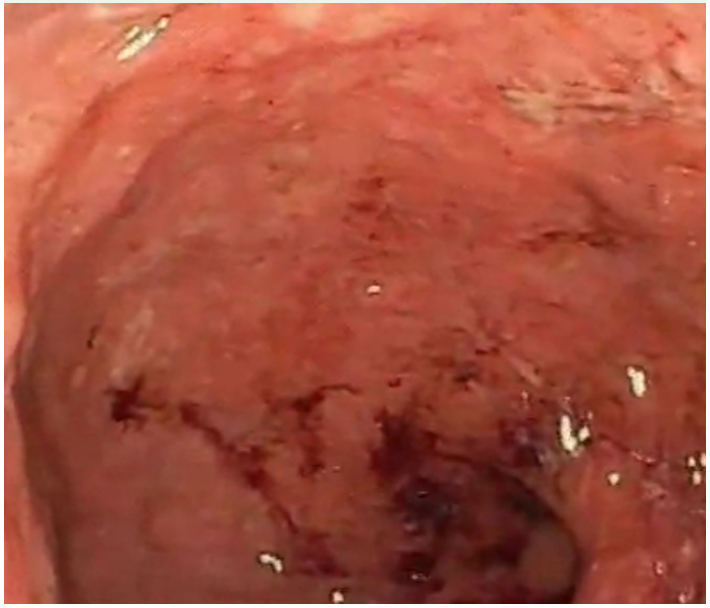
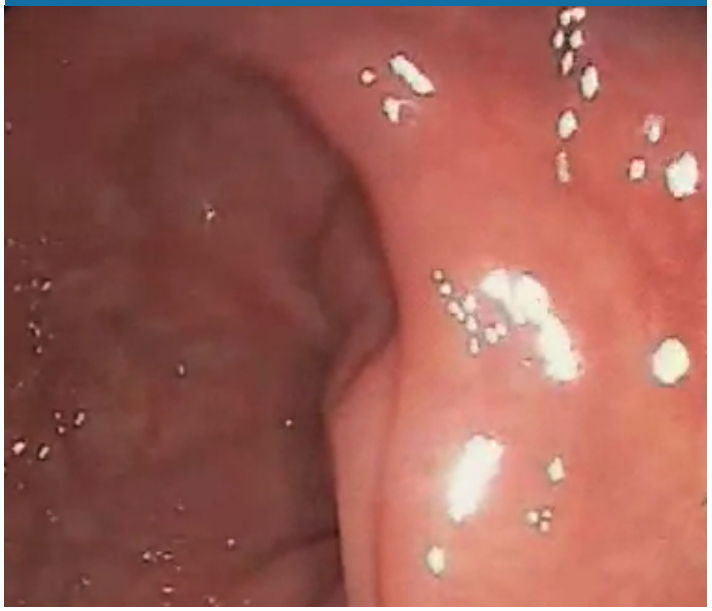
Illustrative endoscopy improvement — Vanco/SER-287 daily treatment

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



Post-treatment day 64 endoscopy



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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%)

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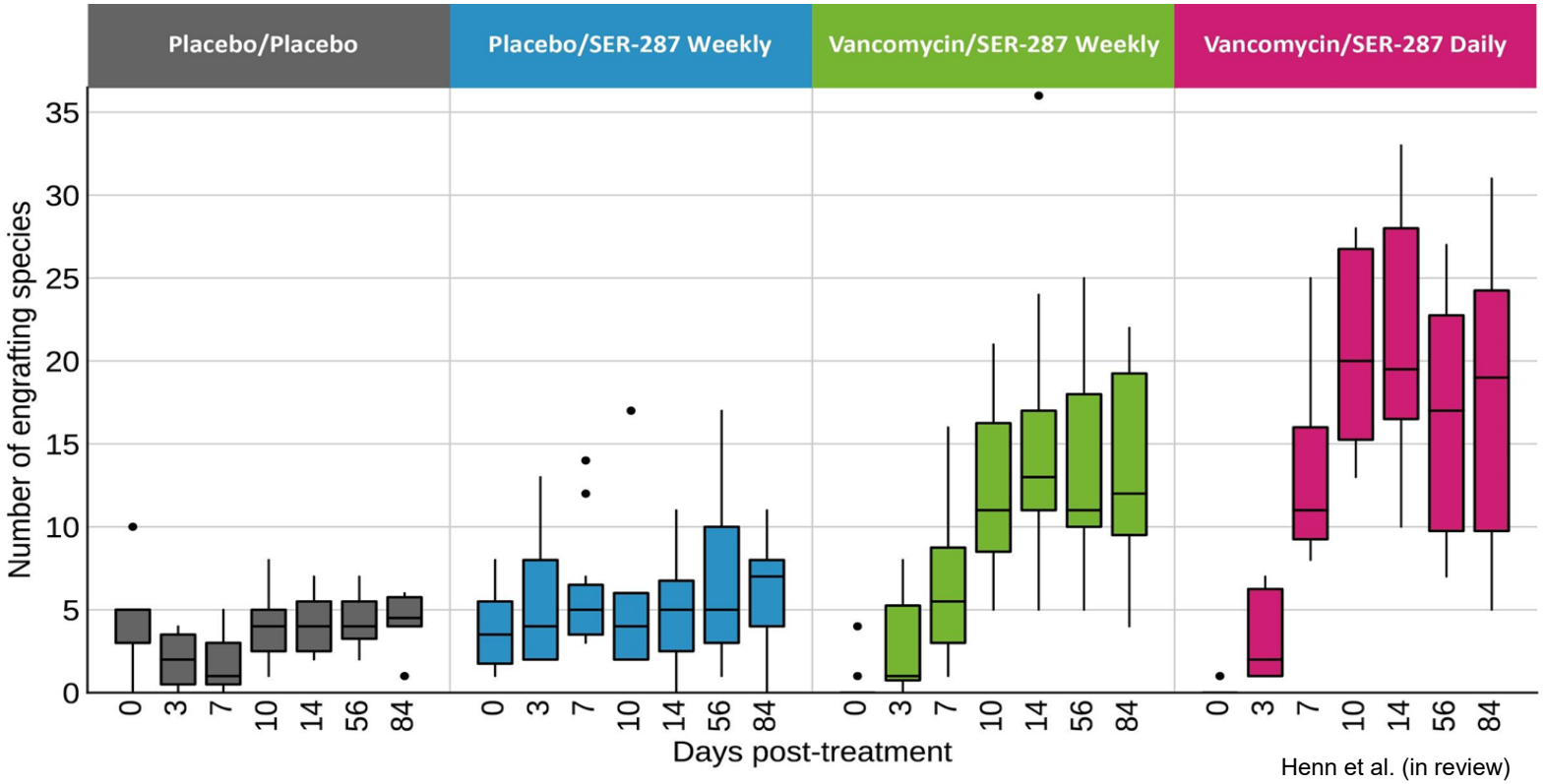
Phase 1b study results – SER-287 bacteria engrafted in subjects and was durable to four weeks after dosing



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)

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SER-287 Phase 1b study results published

Gastroenterology aga American Gastroenterological Association

Gastroenterology. 2020 Aug 4
doi: 10.1053/j.gastro.2020.07.048 [Epub ahead of print]
PMCID: PMC7402096
PMID: 32763240

A Phase 1b safety study of SER-287, a spore-based microbiome therapeutic, for active mild to moderate ulcerative colitis

Matthew R. Henn,[1] Edward J. O'Brien,[1] Liyang Diao,[1] Brian G. Feagan,[2] William J. Sandborn,[3] Curtis Huttenhower,[4] Jennifer R. Wortman,[1] Barbara H. McGovern,[**,1] Sherry Wang-Weigand,[1] David I. Lichter,[1] Meghan Chafee,[1] Chris B. Ford,[1] Patricia Bernardo,[1,*] Peng Zhao,[1,*] Sheri Simmons,[1,*] Amelia Tomlinson,[1,*] David Cook,[1,*] Roger Pomerantz,[1,*] Bharat K. Misra, John G. Auninš,[1] and Michele Trucksis[1,*]

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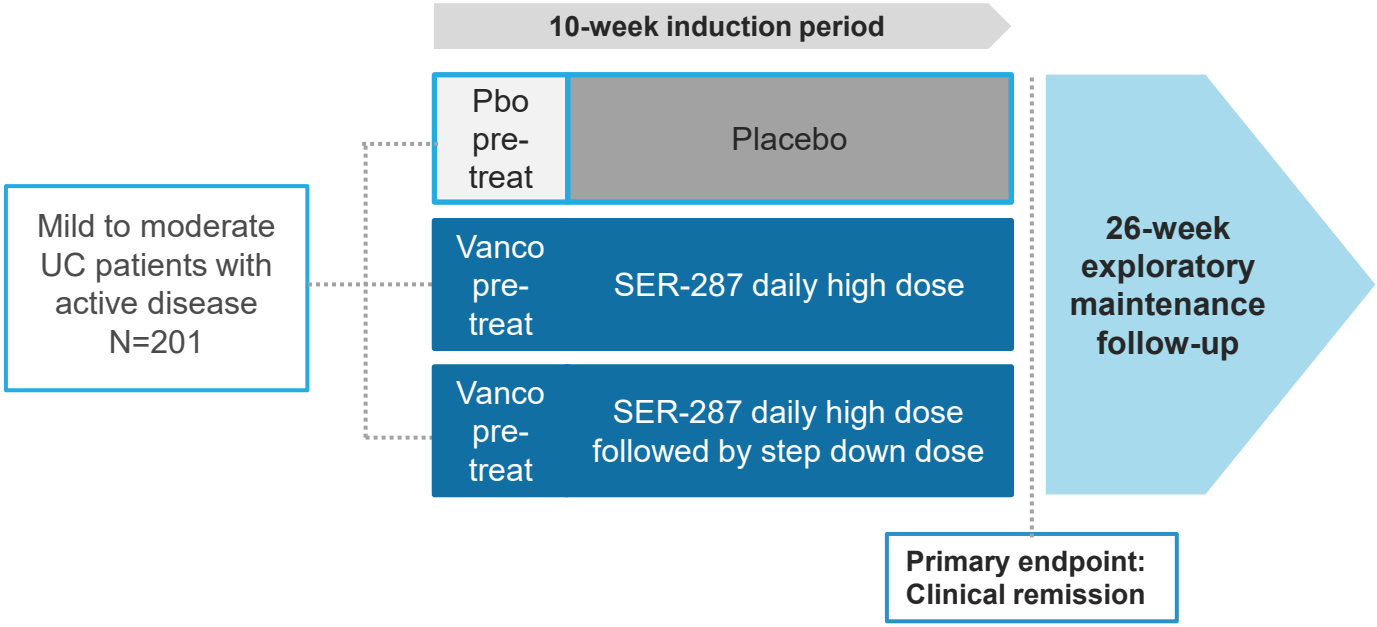
Ongoing SER-287 ECO-RESET Phase 2b study in patients with mild-to-moderate active ulcerative colitis



- **FDA Fast Track designation**
- **FDA feedback: Phase 2b study results, in conjunction with data from a second pivotal study, could support BLA submission**

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

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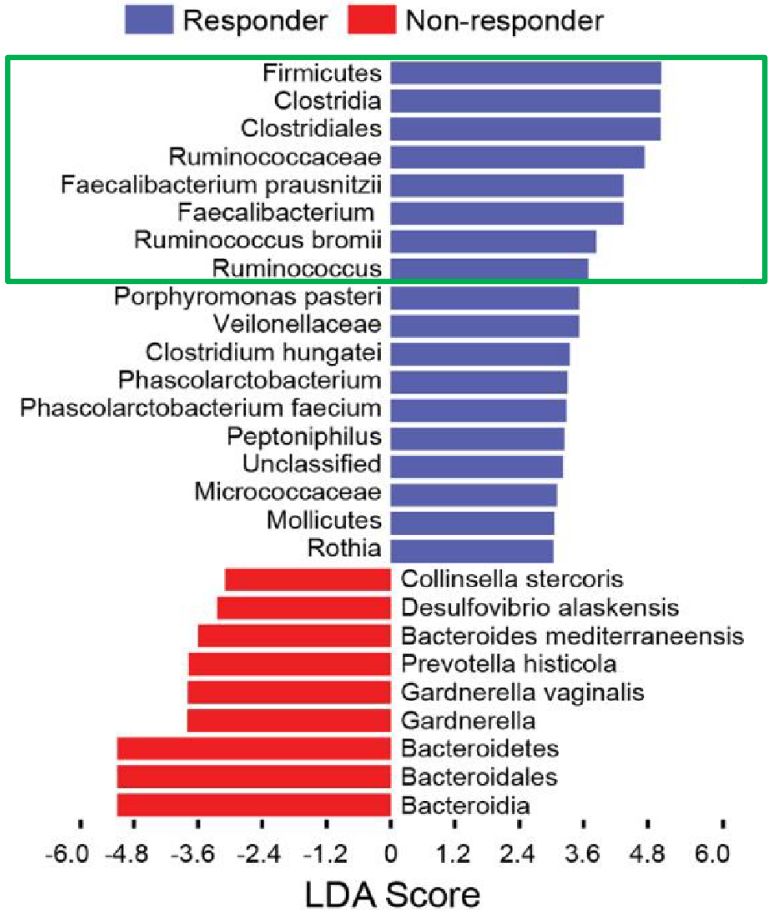
Immuno-oncology - Microbiome signature in melanoma patient responder to anti-PD-1

- 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

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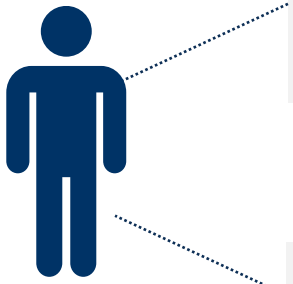
Ongoing SER-401 Phase 1b study



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)

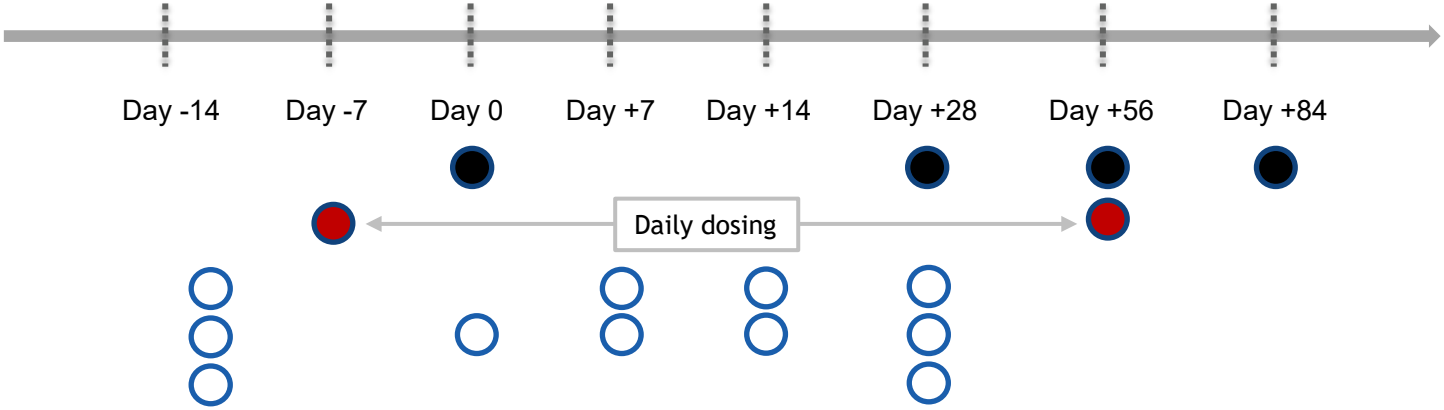
Placebo (n=10)

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

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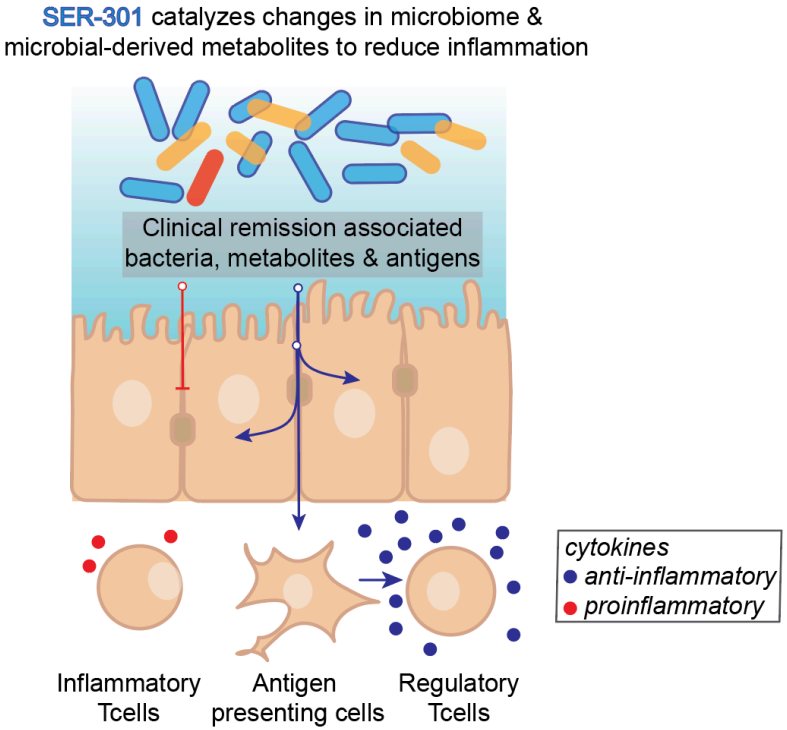
SER-301: Next-generation, rationally designed fermented microbiome therapeutic candidate for ulcerative colitis

- 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



- **Activities to initiate clinical development ongoing**
- **Human Research Ethics Committee approval in Australia**

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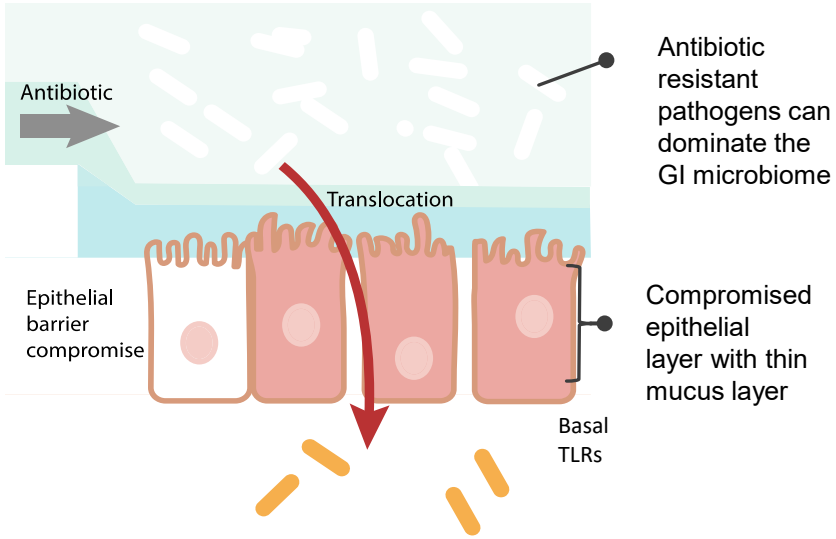
SER-155: Rationally-designed, fermented microbiome therapeutic candidate for infection, bacteremia & GvHD

- 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 nominated**
- **U.S. regulatory submission preparation in process**

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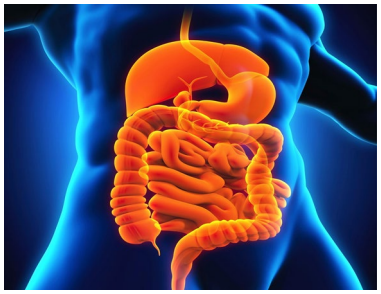
SER-109 success validates our microbiome therapeutic approach, presenting opportunity in multiple additional areas



- Deep understanding of the broad role of the microbiome in health:
  - Resistance to pathogens
  - Gut & systemic inflammation
  - Innate & adaptive immunity
  - Regulation of metabolism
- Novel drug discovery and development platform
- Option to pursue multiple diseases with high unmet need

Highly productive R&D engine pursing multiple promising potential opportunities

- Infectious (e.g. Antibiotic resistant infections)
- Inflammatory (e.g. Crohn's, RA)
- Oncology (e.g. tumor progression & bacteremia)
- Immune modulation & autoimmune disease
- Metabolic & Cardiovascular (e.g. NASH)
- Neurologic & CNS disease

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Differentiated CMC capabilities producing rationally designed fermented products

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

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Broad IP portfolio and regulatory exclusivity

PATENT PORTFOLIO OF OWNED & LICENSED PATENTS AND APPLICATIONS*

- Have 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

15 Nationalized

1 Pending Provisionals

PROJECTED BIOSIMILAR REGULATORY EXCLUSIVITY

12 years for new biological composition

10 years for new drug

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Seres is well positioned to harness core microbiome capabilities advance pipeline

SER-109	Positive ECOSPOR III Phase 3 study results expected to serve as single study to support BLA; Plan to meet with FDA to discuss filing
SER-287	Ulcerative colitis – Phase 2b study ongoing
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
Additional R&D opportunities	Multiple earlier stage programs under consideration as new development opportunities

Strong balance sheet, following August 2020 capital raise of $264 M

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