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THERAPEUTICS

Eric Shaff

Chief Executive Officer

Jefferies Virtual Healthcare Conference

June 1, 2021

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 and results 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 May 4, 2021, 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.

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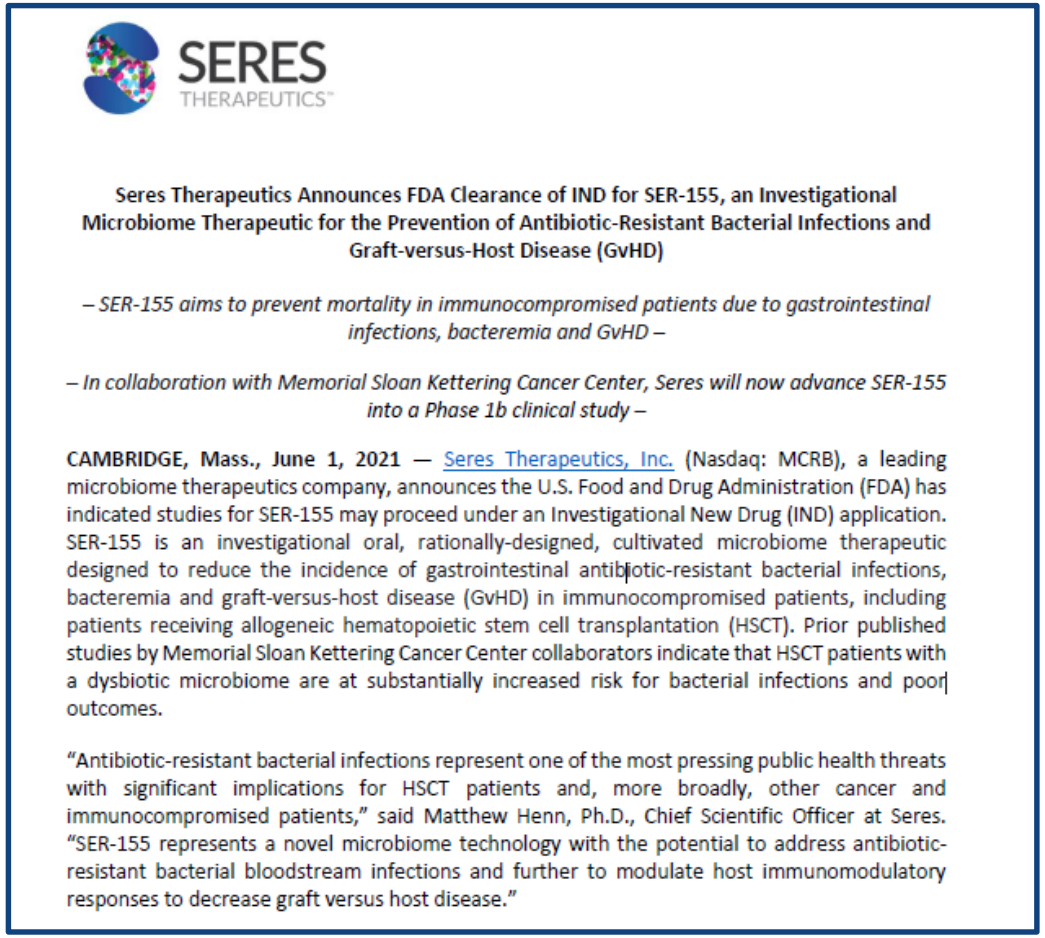
SER-155 IND Clearance

Rationally-designed investigational microbiome therapeutic designed prevent mortality in immunocompromised patients due to gastrointestinal infections, bacteremia and GvHD



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Seres Therapeutics Announces FDA Clearance of IND for SER-155, an Investigational Microbiome Therapeutic for the Prevention of Antibiotic-Resistant Bacterial Infections and Graft-versus-Host Disease (GvHD)

– SER-155 aims to prevent mortality in immunocompromised patients due to gastrointestinal infections, bacteremia and GvHD –

– In collaboration with Memorial Sloan Kettering Cancer Center, Seres will now advance SER-155 into a Phase 1b clinical study –

CAMBRIDGE, Mass., June 1, 2021 — Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, announces the U.S. Food and Drug Administration (FDA) has indicated studies for SER-155 may proceed under an Investigational New Drug (IND) application. SER-155 is an investigational oral, rationally-designed, cultivated microbiome therapeutic designed to reduce the incidence of gastrointestinal antibiotic-resistant bacterial infections, bacteremia and graft-versus-host disease (GvHD) in immunocompromised patients, including patients receiving allogeneic hematopoietic stem cell transplantation (HSCT). Prior published studies by Memorial Sloan Kettering Cancer Center collaborators indicate that HSCT patients with a dysbiotic microbiome are at substantially increased risk for bacterial infections and poor outcomes.

"Antibiotic-resistant bacterial infections represent one of the most pressing public health threats with significant implications for HSCT patients and, more broadly, other cancer and immunocompromised patients," said Matthew Henn, Ph.D., Chief Scientific Officer at Seres. "SER-155 represents a novel microbiome technology with the potential to address antibiotic-resistant bacterial bloodstream infections and further to modulate host immunomodulatory responses to decrease graft versus host disease."

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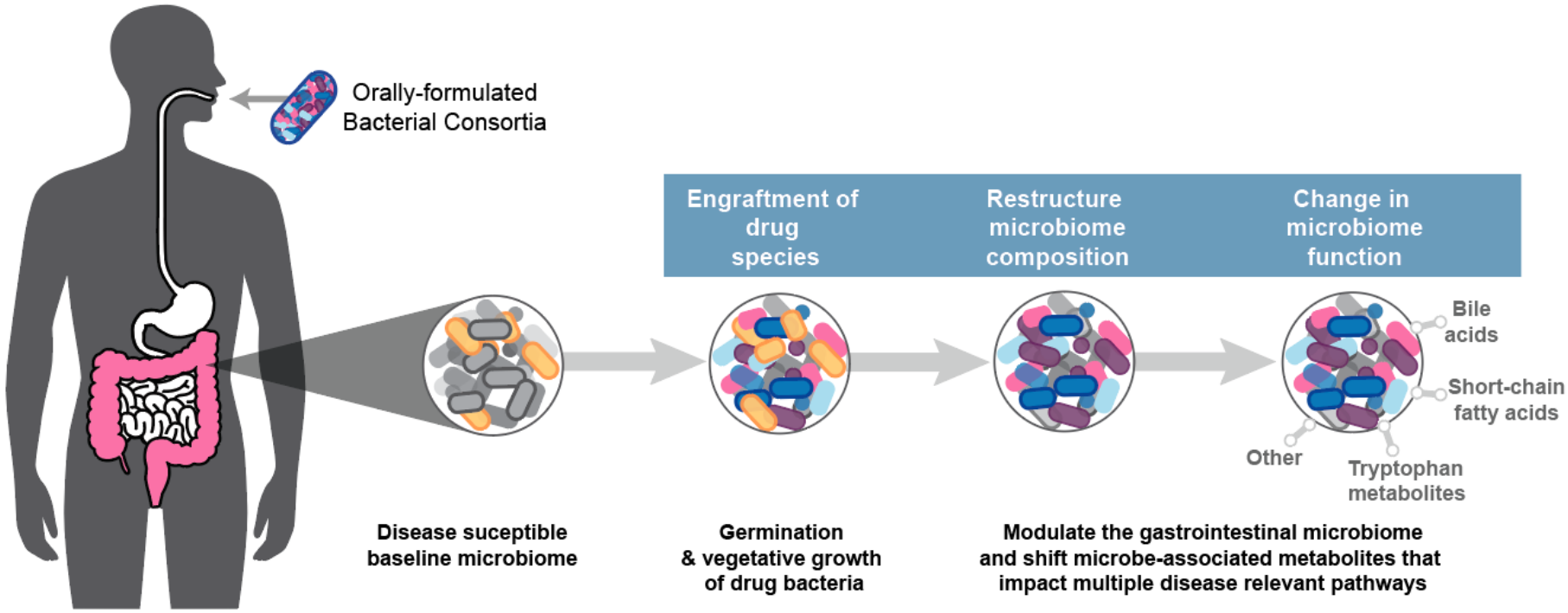
Pioneering the Development of Microbiome Therapeutics

Encapsulated consortia of commensal bacteria designed to target multiple disease-relevant pathways simultaneously



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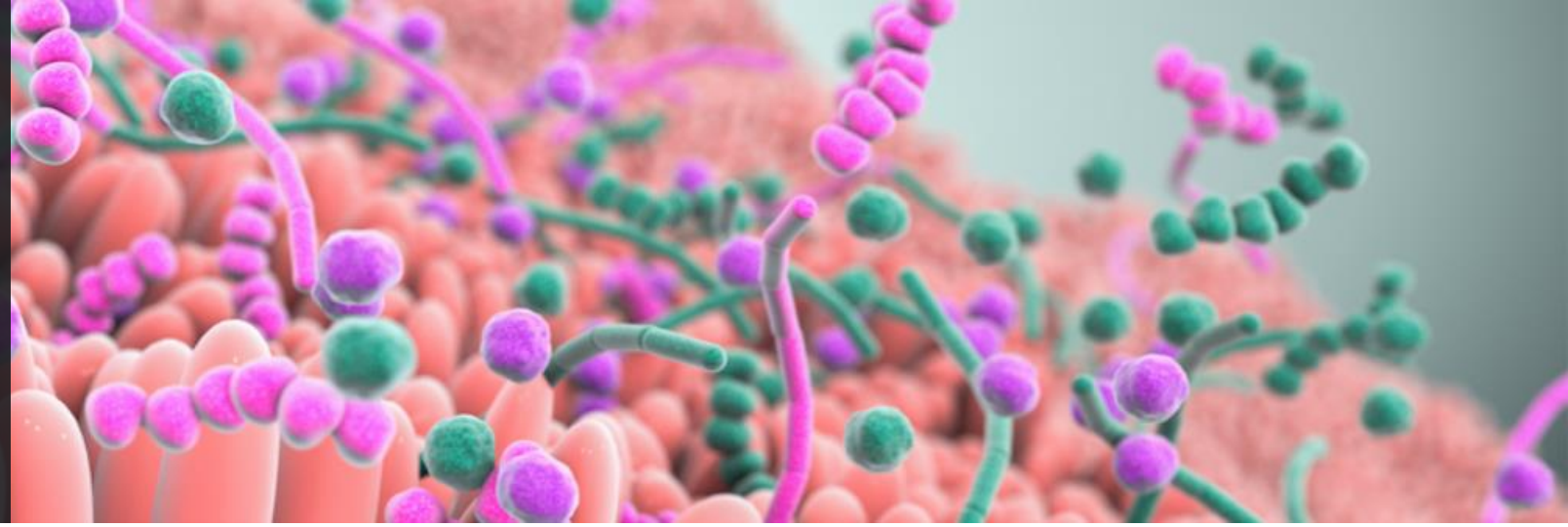
Building on microbiome therapeutic leadership position



2020

- Landmark SER-109 Phase 3 success
- Clear demonstration of microbiome therapeutics as a new treatment modality

2021

- Enrolling SER-109 open label study in support of BLA; anticipate achieving target enrollment in Q3 2021
- SER-109 commercial readiness
- SER-287 Phase 2b clinical data readout mid-2021
- Advancing earlier stage pipeline candidates
  - SER-155 IND cleared
  - SER-301 Phase 1b enrollment ongoing
- Augmenting existing commercial-scale CMC capabilities
- Enhancing and applying new drug discovery capabilities into new disease areas

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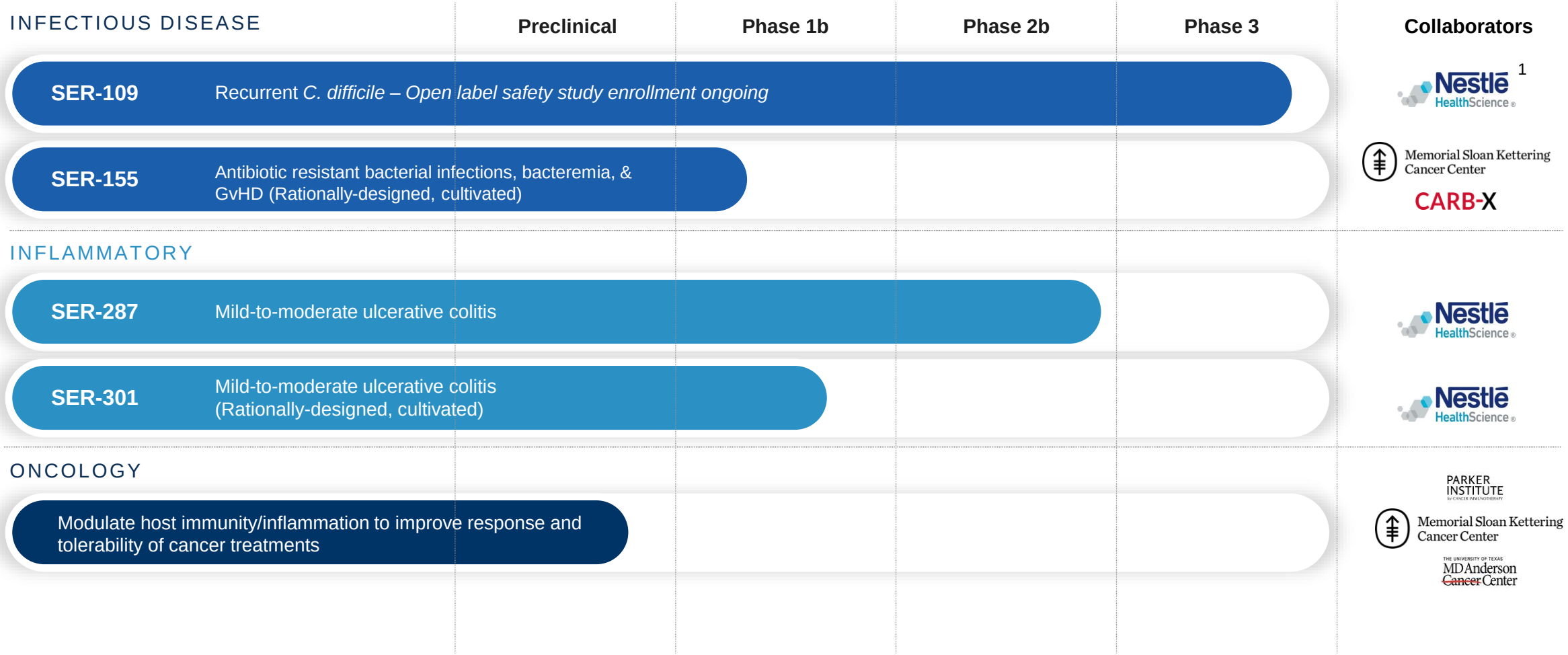
Broad Opportunities for Microbiome Therapeutics



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

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C. difficile Infection

Overview and SER-109 Phase 3 study

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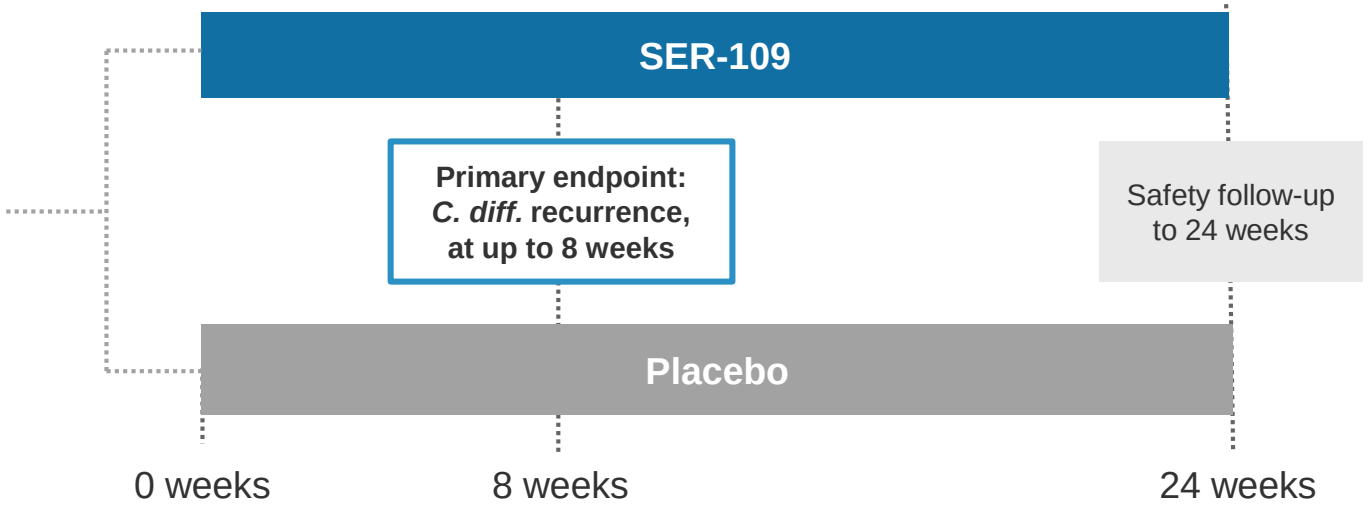
Positive ECOSPOR III Phase 3 Study Readout

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



Topline SER-109 Phase 3 Study Efficacy Results

PRIMARY EFFICACY ENDPOINT RESULTS:

Time point	SER-109 (N =89)	Placebo (N =93)	RR (95%CI)	p-Value (p1/p2)
	n (%) of recurrences	n (%) of recurrences		
Week 8	**11** (12.4)	**37** (39.8)	**0.32** (0.18-0.58)	**<0.001 / <0.001**

- Highly statistically significant treatment effect compared to placebo at 8 weeks
- Absolute reduction in risk of 27%
- Results were statistically significant in both age-stratified subgroups: 18-64 years old, or 65+
- Sustained patient benefit maintained at 12 weeks

Approximately 88% sustained clinical response rate

(percentage of patients who remain free of CDI at 8 weeks)

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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 comparable 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

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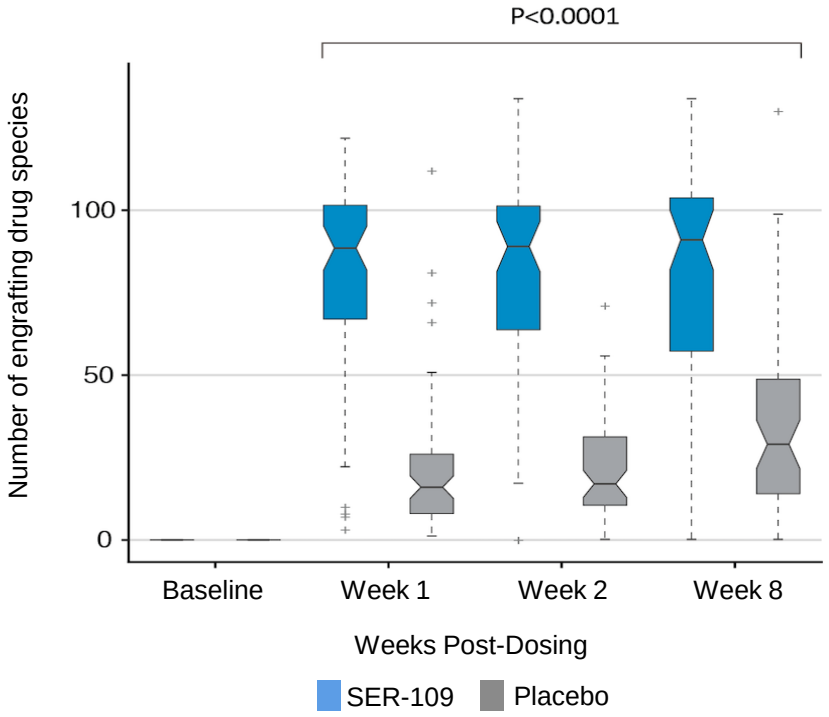
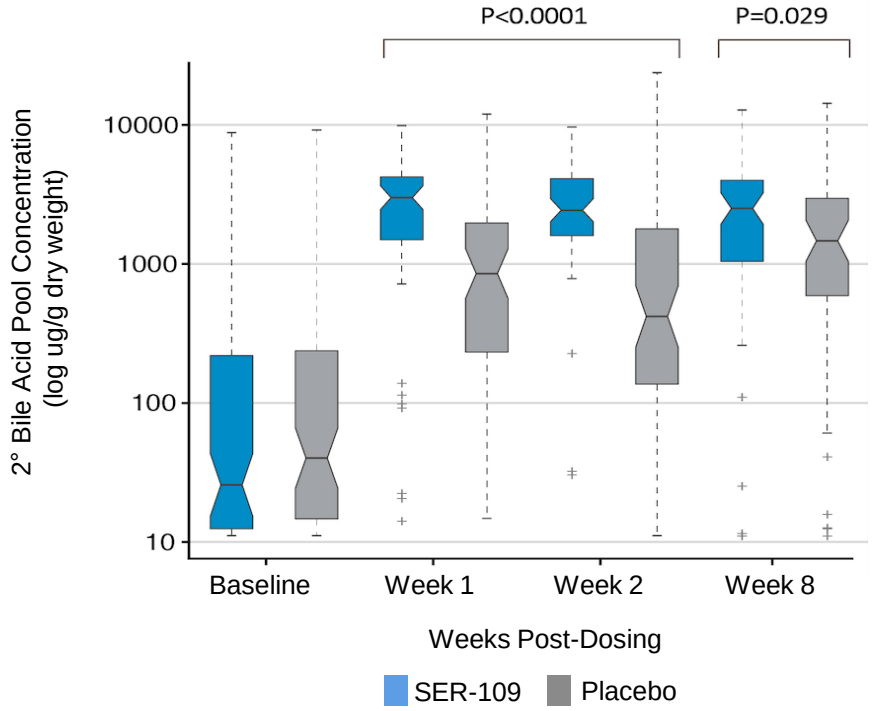
Phase 3 Mechanism of Action Data Support Clinical Outcome

Pharmacokinetics:
SER-109 bacteria engrafted rapidly in subjects & significantly greater engraftment was durable at all timepoints post dosing



Pharmacodynamics:
SER-109 administration broadly modulated the gut microbiome and rapidly shifted metabolic landscape of the gut significantly decreasing 1° bile acids and increasing 2° bile acids



e.g. Secondary (2°) Bile Acid Pool

1° Bile Acids: Germinant for *C. difficile* spores

2° Bile Acids: Inhibit *C. difficile* vegetative growth

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SER-109 Open-label Study Enrollment Ongoing

- FDA has indicated that ECOSPOR III efficacy results should support BLA filing as a single pivotal trial
- Per FDA, the SER-109 safety database should include at least 300 treated subjects
- Enrollment ongoing in SER-109 open-label study in recurrent CDI patients, including those with a first recurrence of disease
- Anticipate achieving target enrollment in Q3 2021

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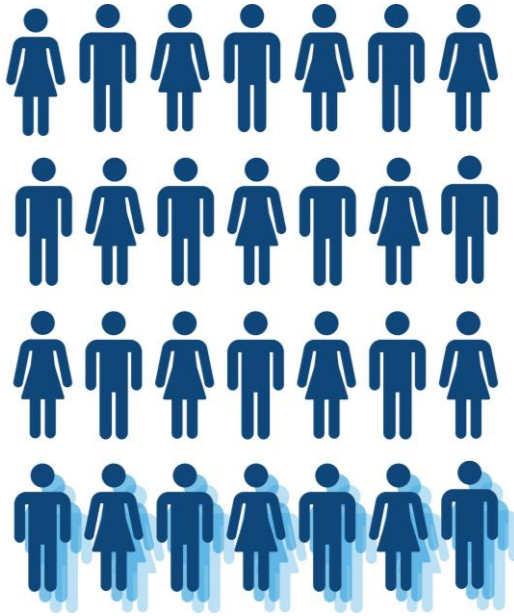
Substantial Recurrent *C. difficile* Infection Market Opportunity

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

Sources: 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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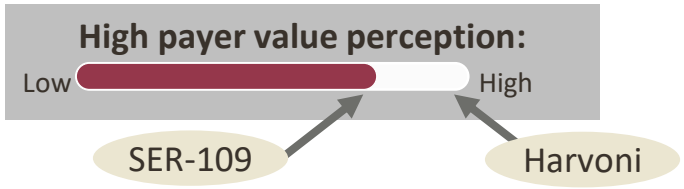
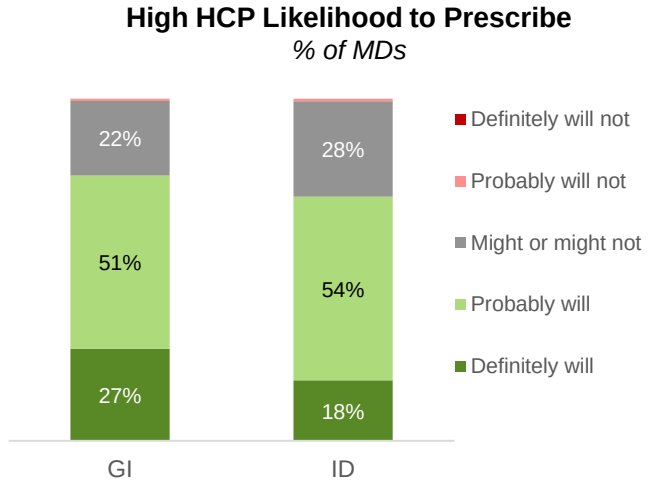
SER-109 is Potential First and Best-in-class Microbiome Therapeutic to Transform Care for Patients with rCDI

- **External stakeholder feedback on SER-109 is resoundingly positive**
  - Highly appealing addition to the current armamentarium for rCDI
  - Combination of efficacy and safety profile delivered in a short course oral regimen





- **SER-109 has potential to become the cornerstone of treatment**

- **Success is breaking the vicious cycle of recurrence that is the current hallmark of this disease**
  - Relieving patients of their fear and frustration
  - Providing HCPs for the first time a proven, highly effective option for sustained clinical response
  - Potentially transforming care for tens of thousands of patients across the US annually

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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 deployed MSL team
- Hire key commercial leadership roles
- Key external strategic partners on board

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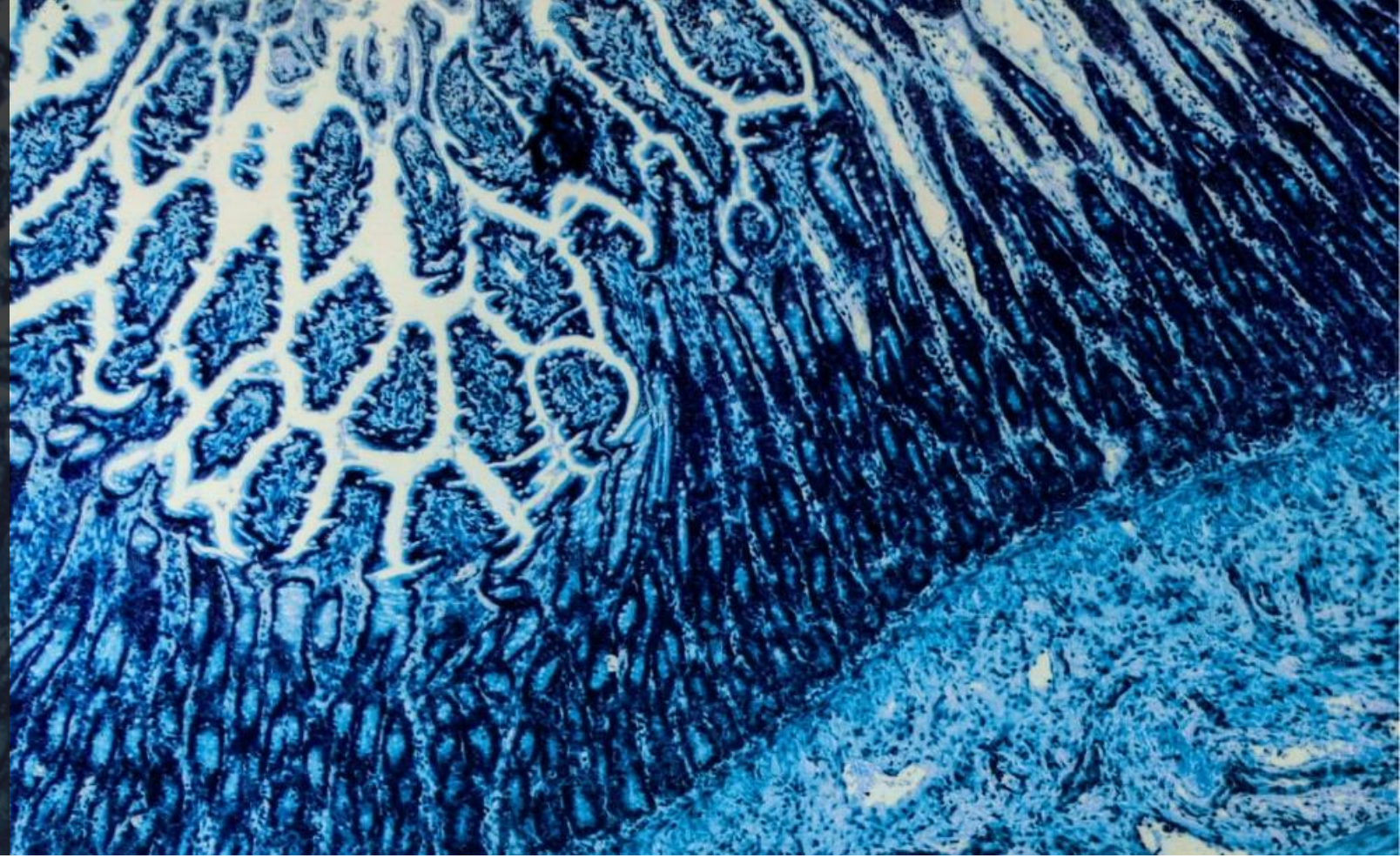
SER-287 and Ulcerative Colitis



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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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SER-287 Phase 1b Ulcerative Colitis Study

58 mild-to-moderate ulcerative colitis patients

DAILY

Placebo pre-treatment for 6 days	Placebo once daily for 8 weeks	(n=11)
Vancomycin pre-treatment for 6 days	SER-287 once daily for 8 weeks	(n=15)

WEEKLY

Placebo pre-treatment for 6 days	SER-287 once weekly for 8 weeks	(n=15)
Vancomycin pre-treatment for 6 days	SER-287 once weekly for 8 weeks	(n=17)

Primary Objectives

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

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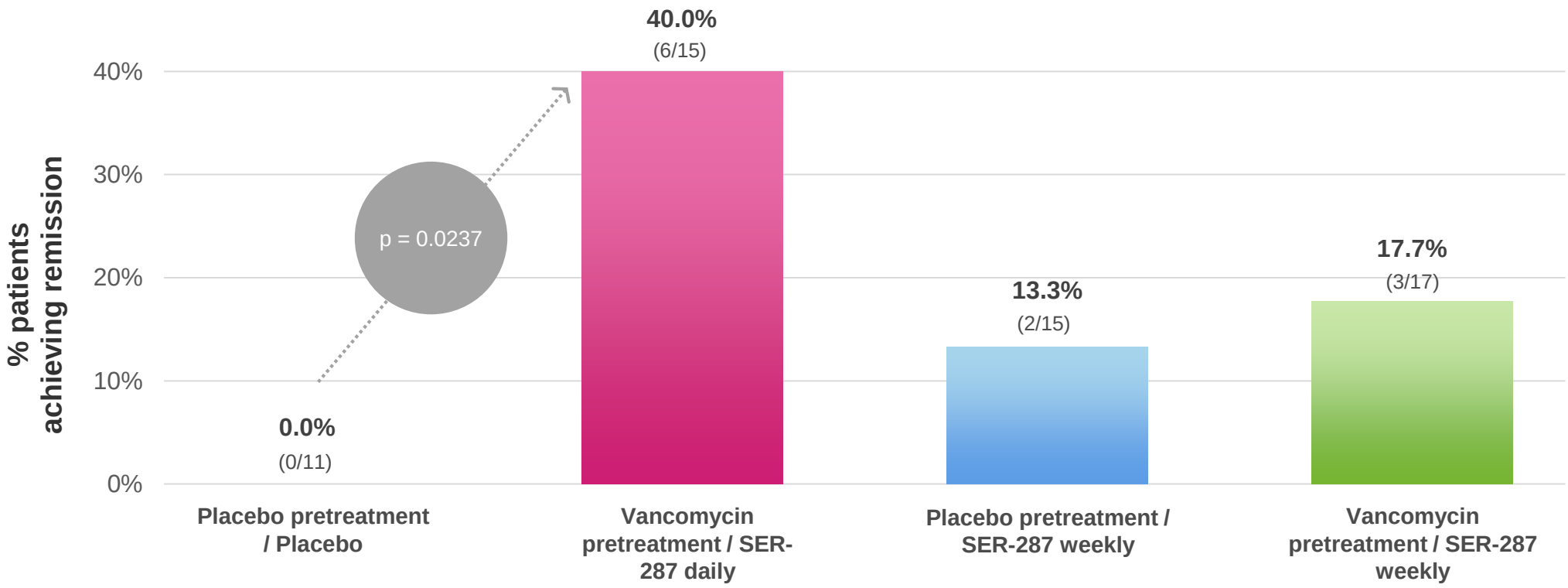
Phase 1b Study Results – Statistically Significant Improvement in Clinical Remission Observed in SER-287 Daily Treatment Arm



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

Henn et al. 2021. Gastroenterology

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SER-287 Phase 1b 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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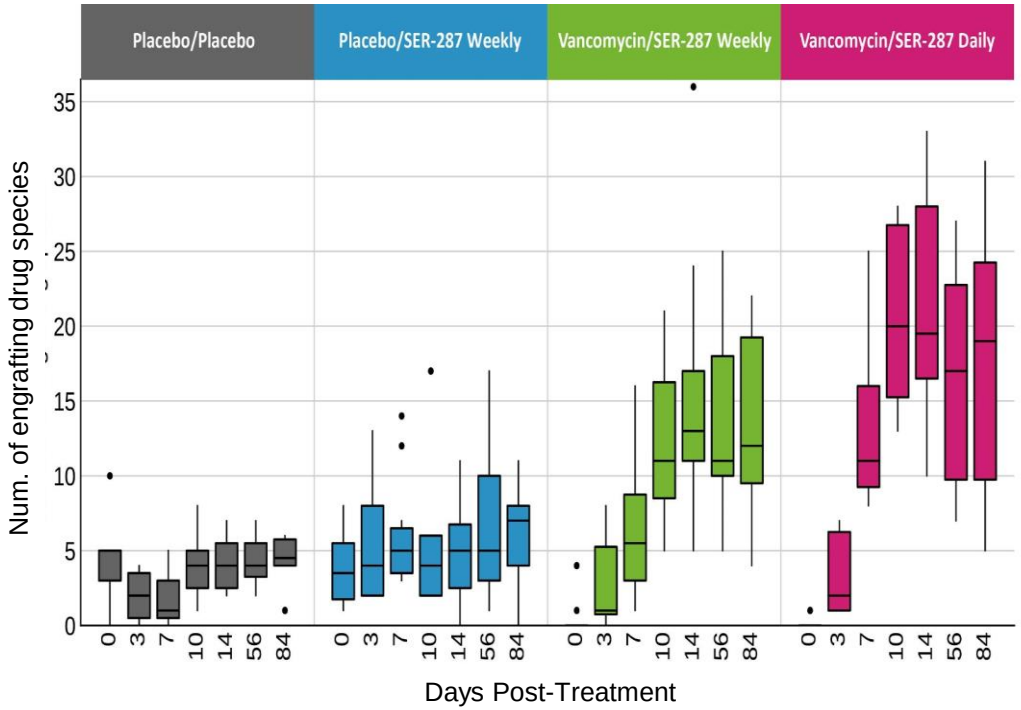
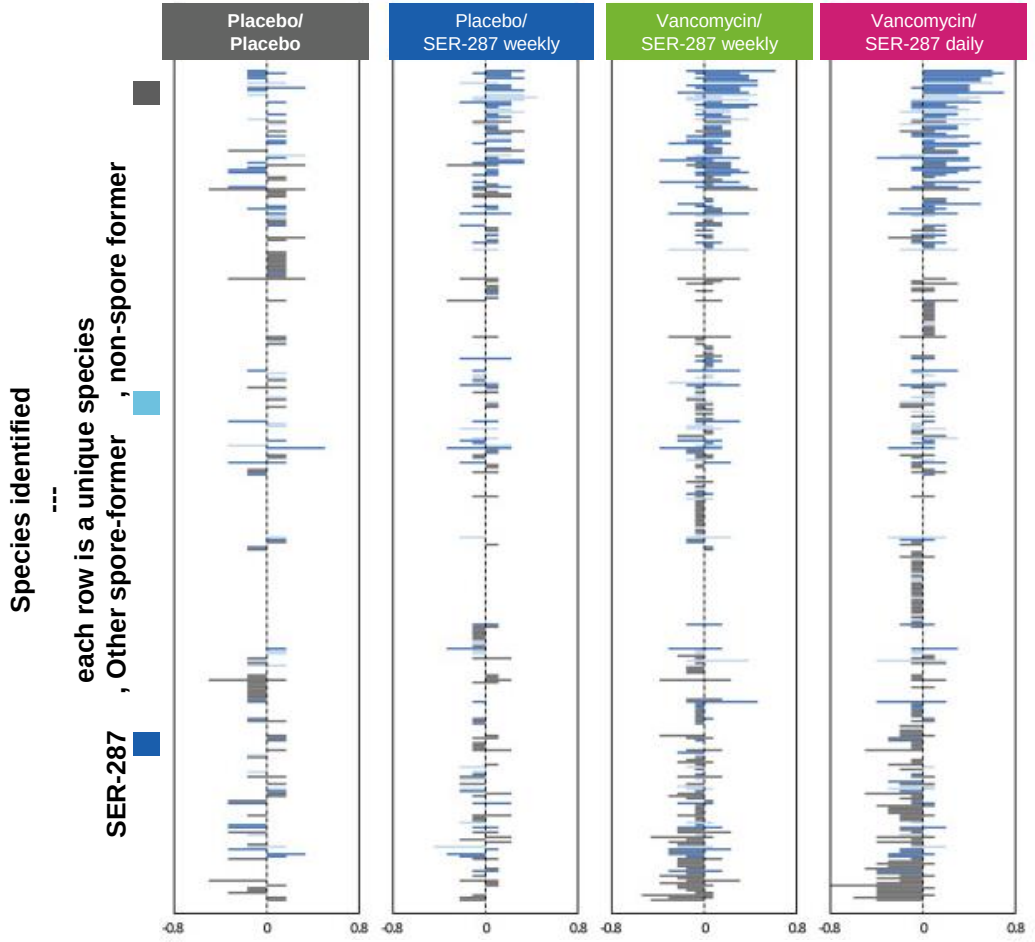
Phase 1b – High Resolution Microbiome Biomarker Analytics

SER-287 bacteria engrafted in subjects, was durable post-dosing, and was significantly greater in daily dosing arm



SER-287 treatment results in a broad shift in the overall composition of spore & non-spore gut species by 8 weeks post-treatment



Henn et al. 2021. Gastroenterology

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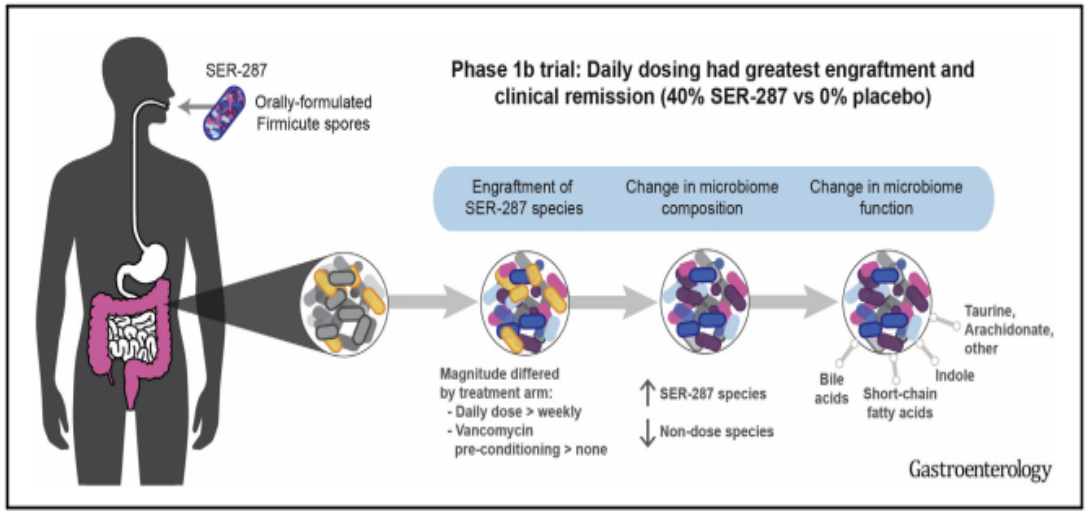
SER-287 Phase 1b Study Results Published January 2021

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] Christopher B. Ford,[1] Patricia Bernardo,[1] Peng Zhao,[1] Sheri Simmons,[1] Amelia D. Tomlinson,[1] David N. Cook,[1] Roger J. Pomerantz,[1] Bharat K. Misra,[5] John G. Auniņš,[1] and Michele Trucksis[1]

[1]Seres Therapeutics, Cambridge, Massachusetts; [2] Robarts Research Institute, London, Ontario, Canada; [3]University of California San Diego, La Jolla, California; [4]Harvard T.H. Chan School of Public Health, Boston, Massachusetts; and [5]Borland Groover Clinic, Jacksonville, Florida



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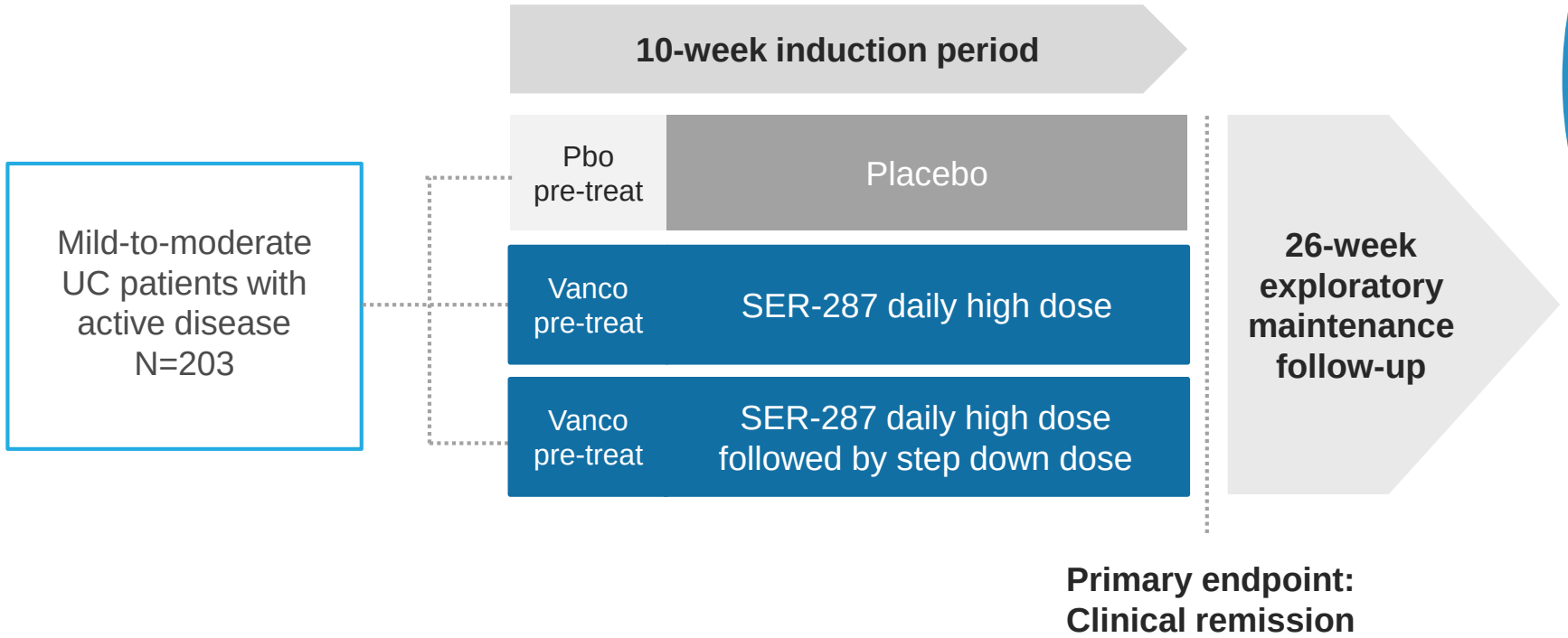
Ongoing SER-287 ECO-RESET Phase 2b Study in Patients with Mild-to-moderate Active Ulcerative Colitis



- FDA Fast Track designation
- FDA feedback: Phase 2b study results, in conjunction with data from a second pivotal study, could support BLA submission
- Announced target enrollment achieved in March 2021
- Topline clinical results anticipated in mid 2021; microbiome biomarker data in H2 2021

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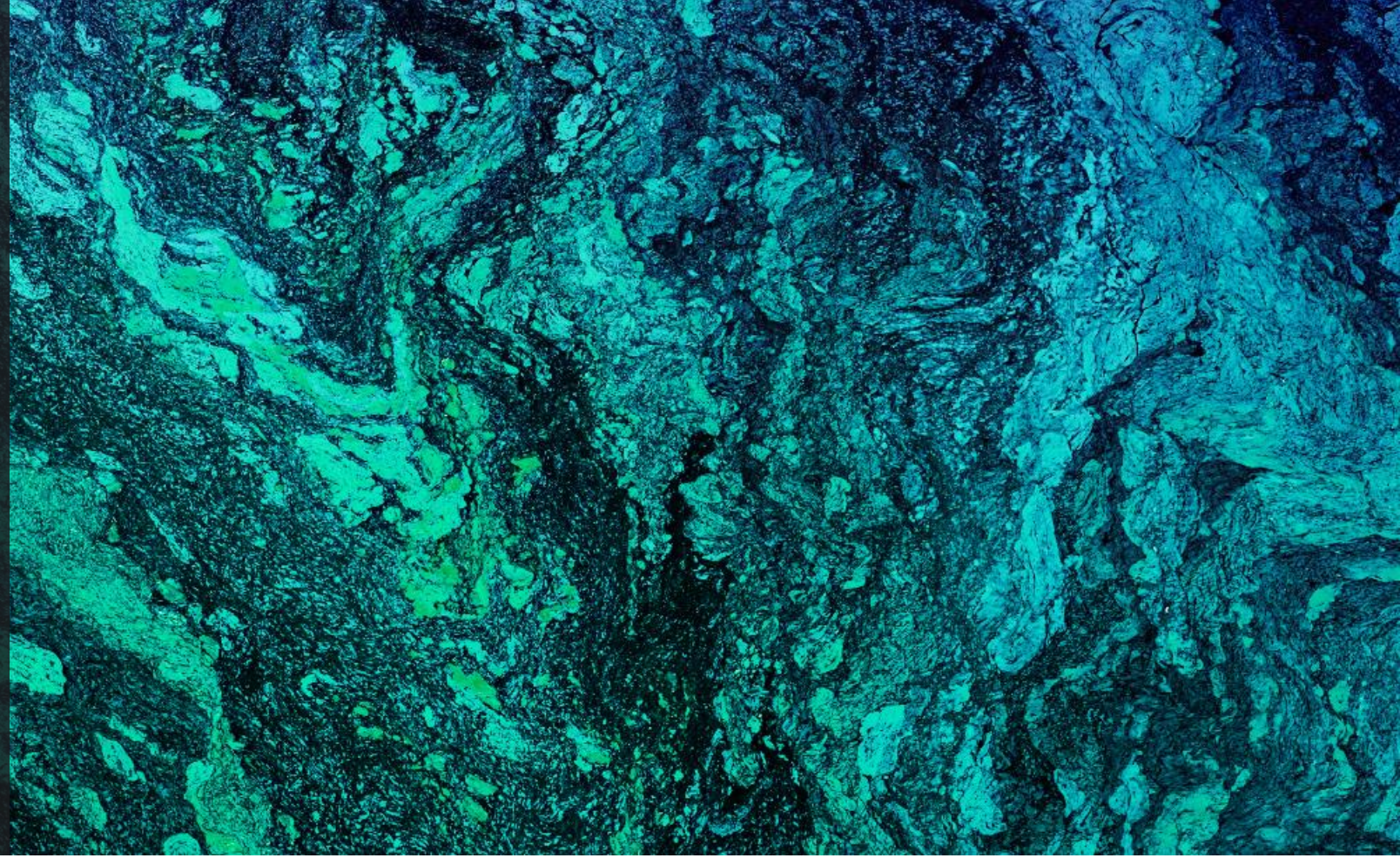
Additional Pipeline Opportunities



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Earlier Stage Clinical Development Programs

	SER-301	SER-155
Microbiome drug type	Rationally designed, cultivated product; spore + vegetative species	Rationally designed, cultivated product; spore + vegetative species
Stage	Phase 1b	IND clearance obtained; plan to initiate Phase 1b
Indication	Mild-to-moderate ulcerative colitis	Infection, bacteremia & GvHD in HSCT for cancer
Designed mechanisms of action	• Reduce induction of pro-inflammatory activity • Improve epithelial barrier integrity & TNF-α driven inflammation in intestinal epithelial cells • Modulate UC-relevant anti-inflammatory, innate & adaptive immune pathways	• Decrease infection by antibiotic-resistant bacteria in the GI • Enhance epithelial barrier integrity to prevent bacterial translocation • Modulate local and systemic immunomodulatory responses to decrease graft versus host disease
Collaborations	Nestlé HealthScience®	Memorial Sloan Kettering Cancer Center; CARB-X Combating Antibiotic-Resistant Bacteria

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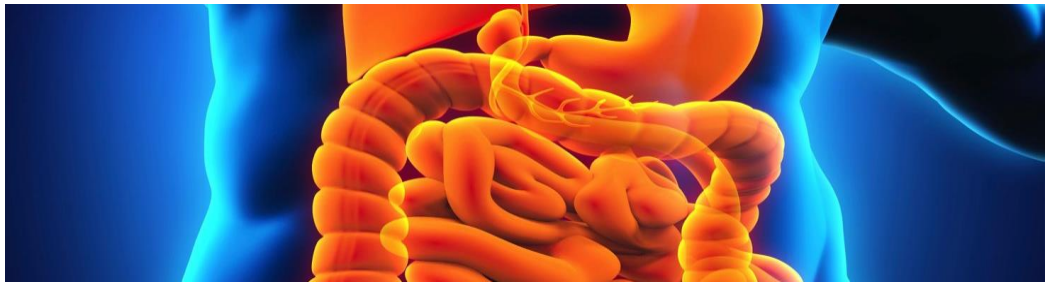
Opportunity for Microbiome Therapeutics in Additional Therapeutic Areas



- Deep understanding of the sweeping 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 pursuing 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 diseases
- Metabolic & cardiovascular (e.g. NASH)
- Neurologic & CNS diseases

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Differentiated CMC Capabilities

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
- Cultivated approach enables efficient and highly scalable manufacturing process to serve large markets

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Well capitalized to Extend Microbiome Therapeutic Leadership

SER-109	Positive ECOSPOR III Phase 3 study results expected to serve as single study to support BLA; Anticipate target enrollment in Q3 2021
SER-287	Ulcerative colitis – Topline clinical results anticipated mid-2021
SER-301	Ulcerative colitis – Phase 1b ongoing
SER-155	Antibiotic resistant bacterial infections, bacteremia, & GvHD; IND clearance obtained
Additional R&D opportunities	Additional programs under consideration

As of Mar. 31, 2021: $272.5M in cash, cash equivalents and short and long-term investments

SER-287 webcast investor event – June 21, 2021

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Thank You