Seres Therapeutics

Eric Shaff, Chief Executive Officer

39th Annual J.P. Morgan Healthcare Conference
January 14, 2021

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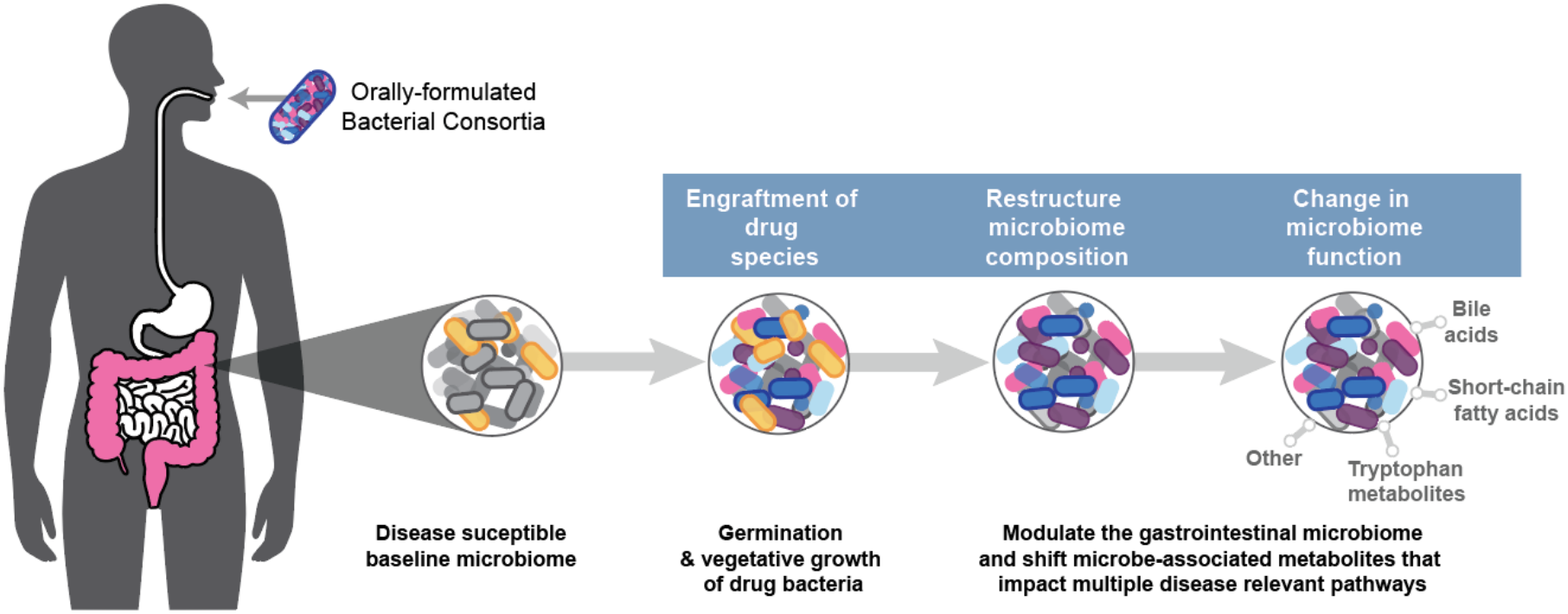
Forward looking statements

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 November 9, 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.

Pioneering the development of microbiome therapeutics

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



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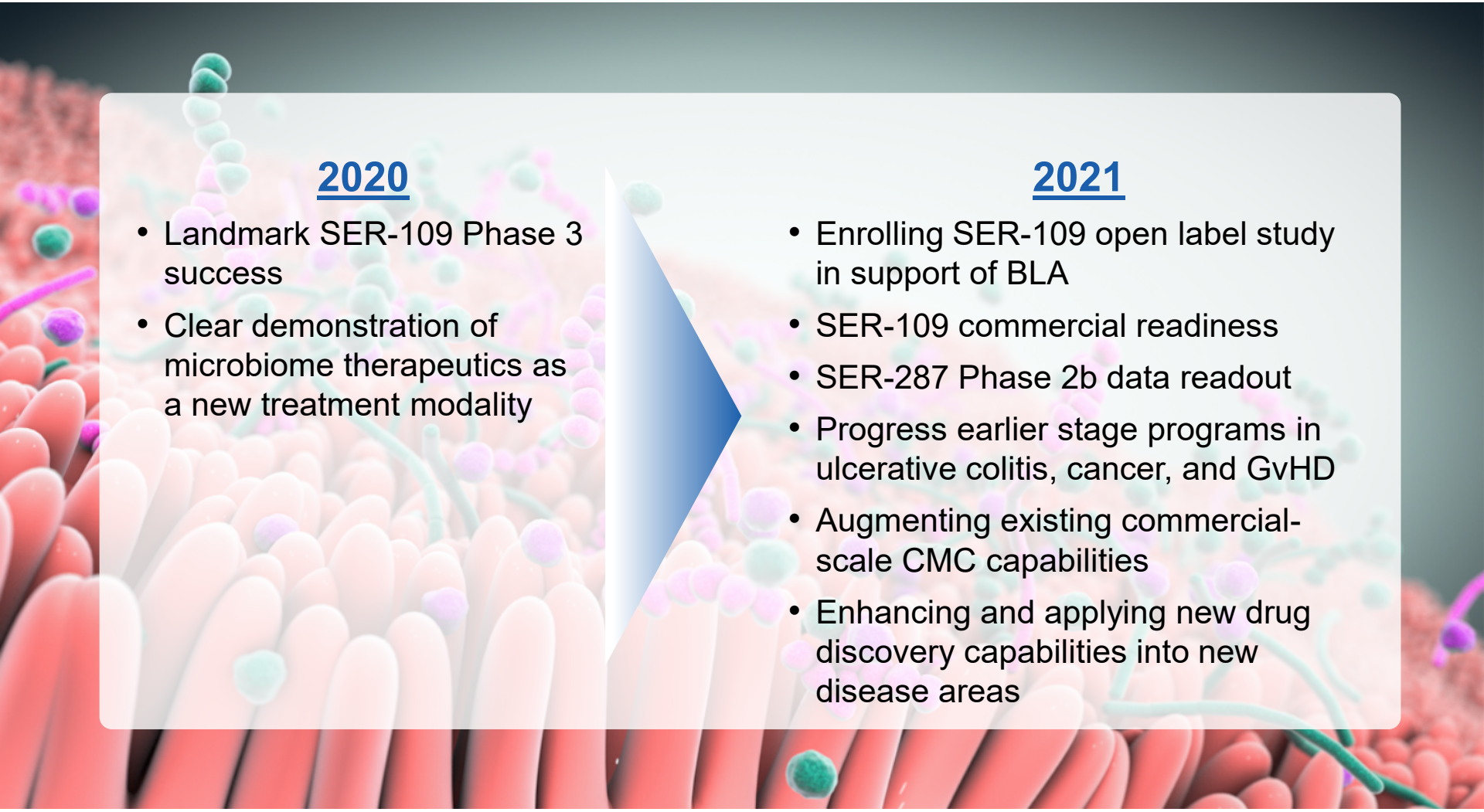
Building on microbiome therapeutic leader position



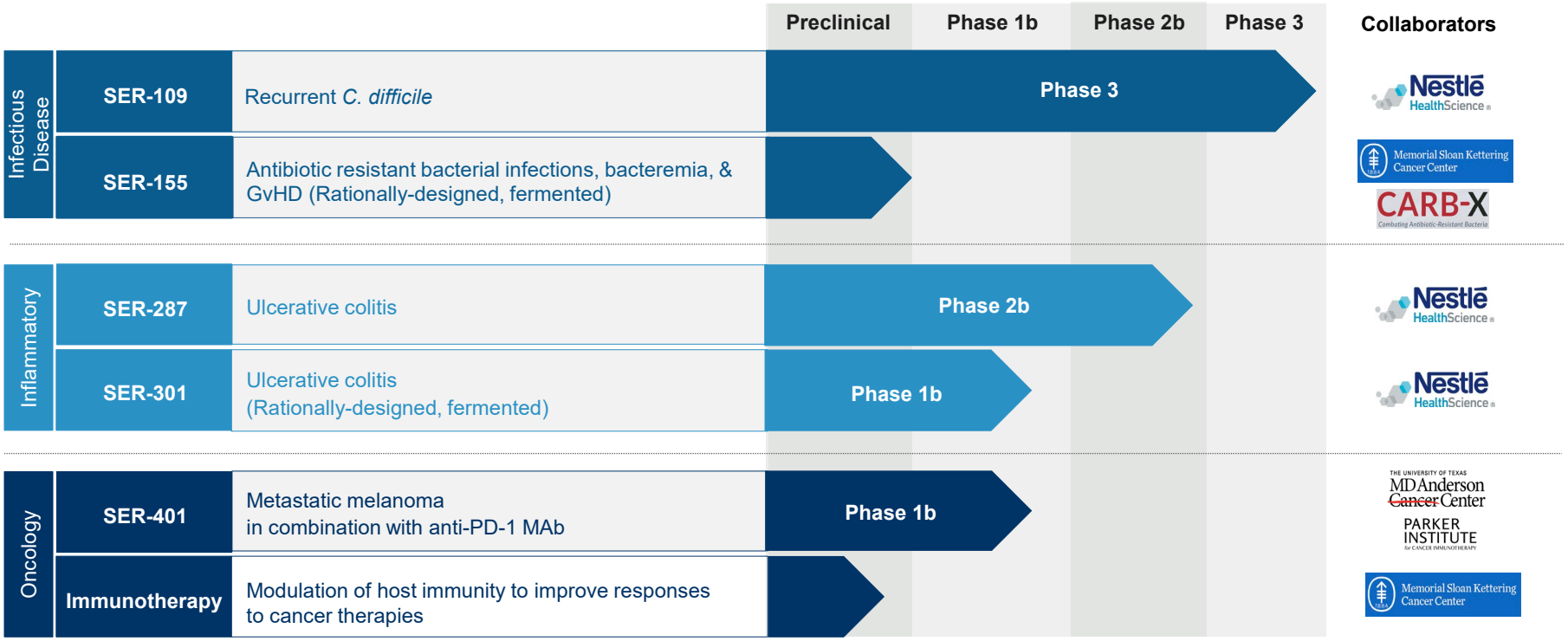
2020

- 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
- SER-109 commercial readiness
- SER-287 Phase 2b data readout
- Progress earlier stage programs in ulcerative colitis, cancer, and GvHD
- Augmenting existing commercial-scale CMC capabilities
- Enhancing and applying new drug discovery capabilities into new disease areas

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.

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C. difficile Infection

Overview and SER-109 Phase 3 study

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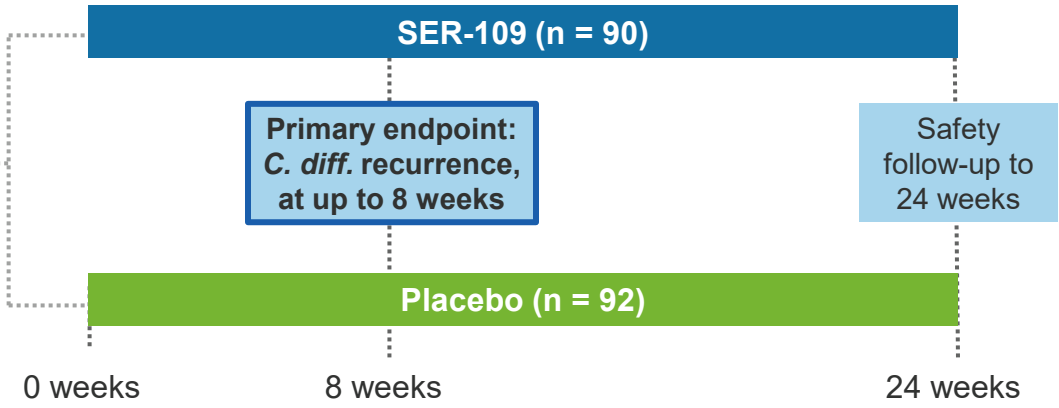
Positive ECOSPOR III Phase 3 study readout

Topline results announced August 2020

- 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+
- Sustained patient benefit maintained at 12 weeks with a highly statistically significant 31.1% absolute reduction in the rate of *C. difficile* infection recurrence compared to placebo

- **Highly statistically significant 30.2% absolute reduction in the rate of CDI recurrence compared to placebo at 8 weeks**
- **Number needed to treat = approximately 3**

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Favorable safety profile observed in Phase 3

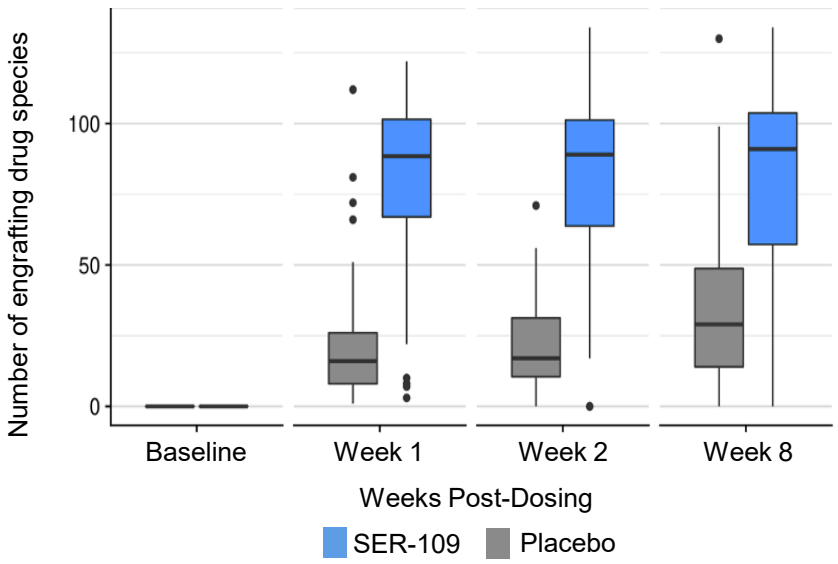
- SER-109 was well tolerated, with **no treatment-related serious adverse events (SAEs) observed in the active arm**, and an adverse event profile comparable to placebo
- **Overall incidence of patients who experienced AEs during the eight-week study period was similar** between SER-109 and placebo arms
- 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

Phase 3 mechanism of action data support clinical outcome

New Study Results

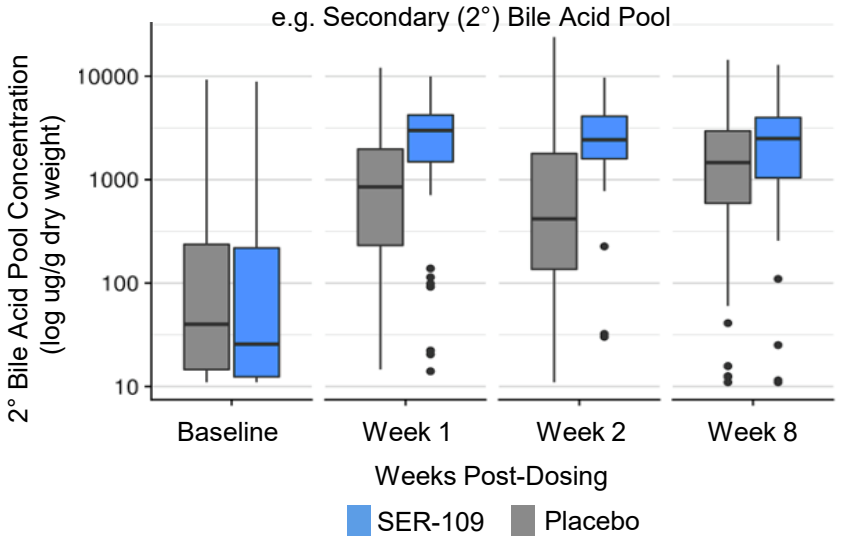
Pharmacokinetics:

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



1° Bile Acids: Germinant for *C. difficile* spores
2° Bile Acids: Inhibit *C. difficile* vegetative growth

Data to be presented on Jan 20, 2021

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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 is ongoing in a SER-109 open-label study in recurrent CDI patients, including those with a first recurrence of disease

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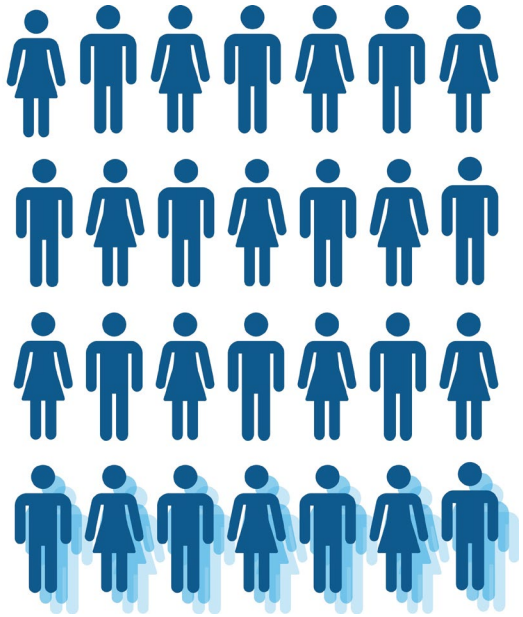
Substantial recurrent *C. difficile* infection market opportunity

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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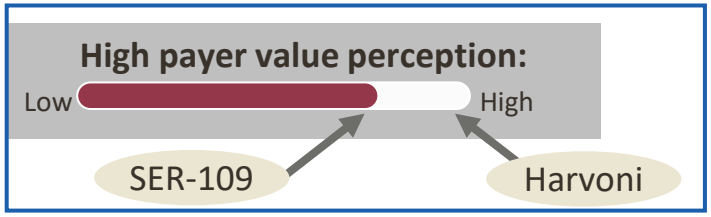
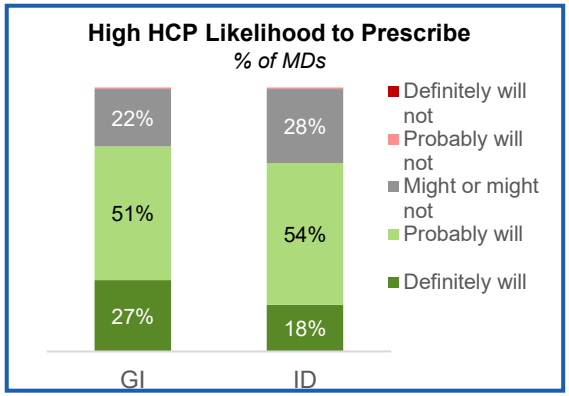
SER-109 is potential first and best-in-class microbiome therapeutic to transform care for patients with rCDI

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

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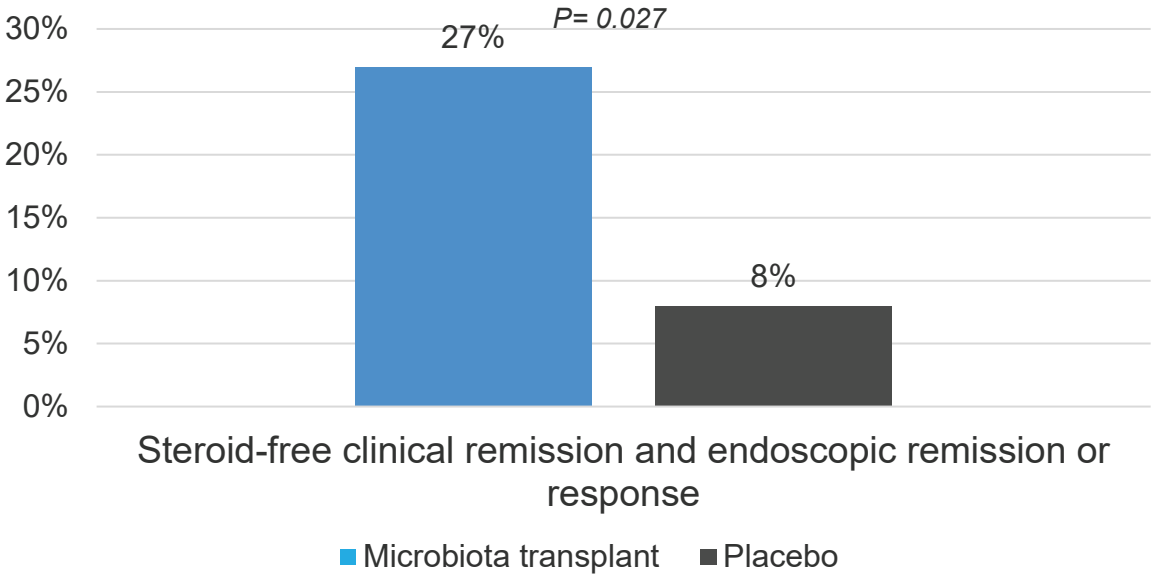
Published study evaluating microbiota transplantation provided clinical proof-of-concept in ulcerative colitis

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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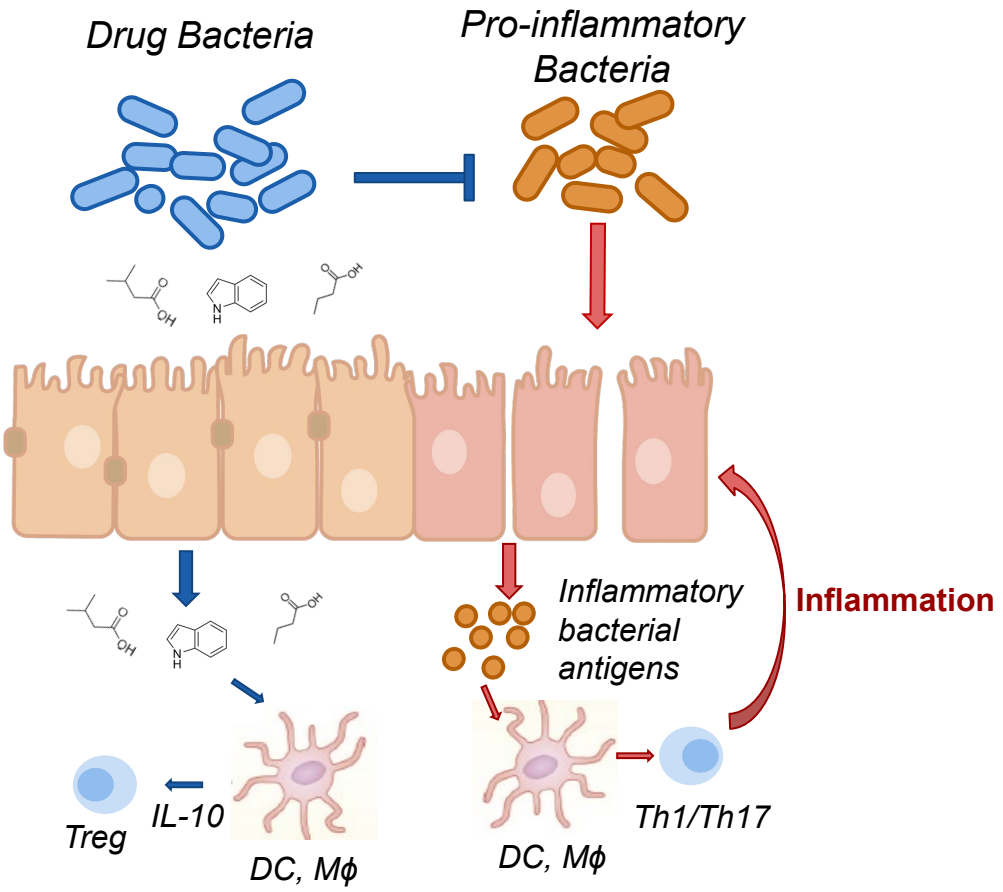
Seres' therapeutic candidates have the potential to target multiple triggers of ulcerative colitis pathology

Reduce the abundance of pro-inflammatory bacteria and epithelial cell inflammation

Produce immunomodulatory metabolites that improve epithelial barrier integrity

Decrease cytokine-induced inflammation and modulate T cell populations



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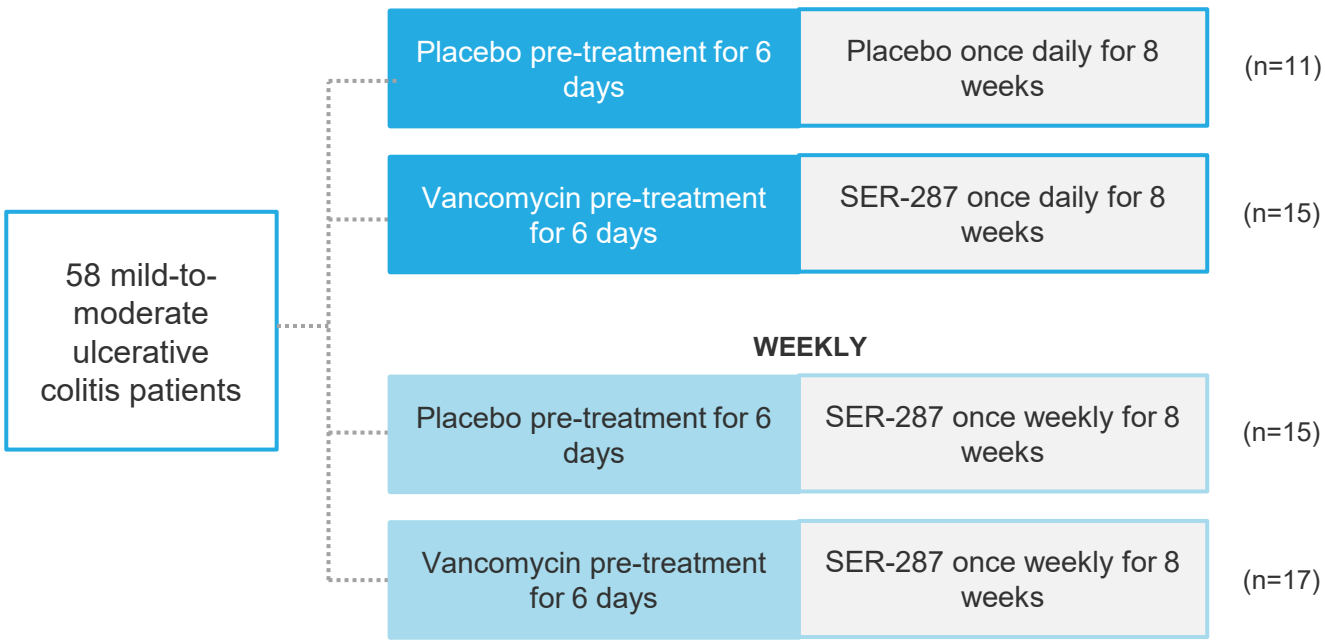
SER-287 Phase 1b ulcerative colitis study



Primary Objectives

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

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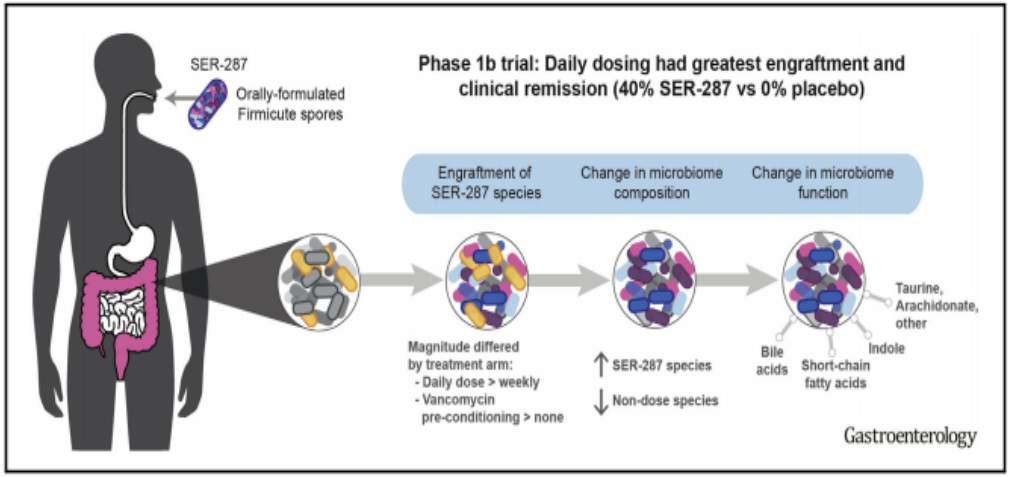
SER-287 Phase 1b study results published January 2021

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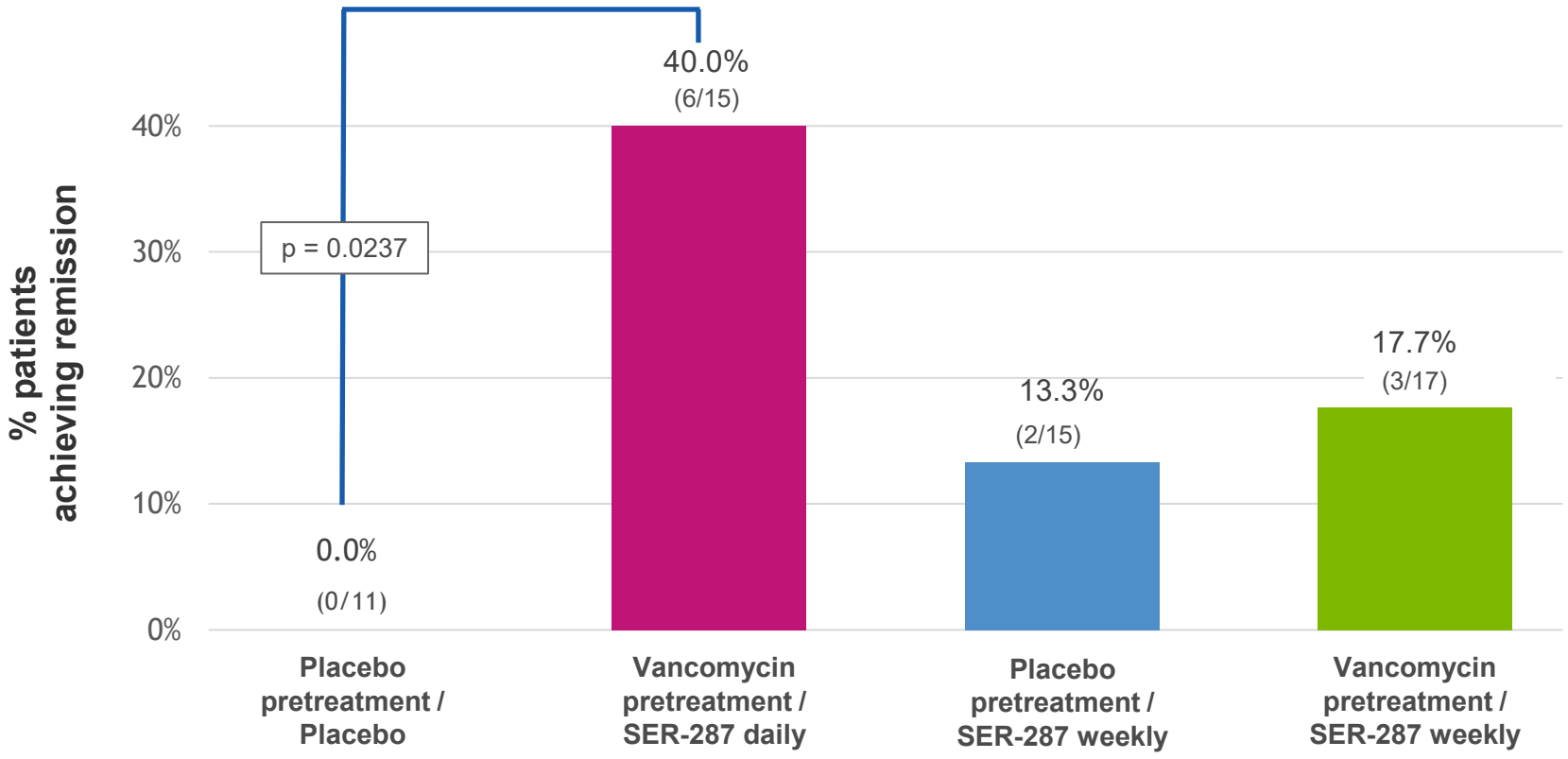
Phase 1b study results – Statistically significant clinical remission improvement observed in SER-287 daily treatment arm



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 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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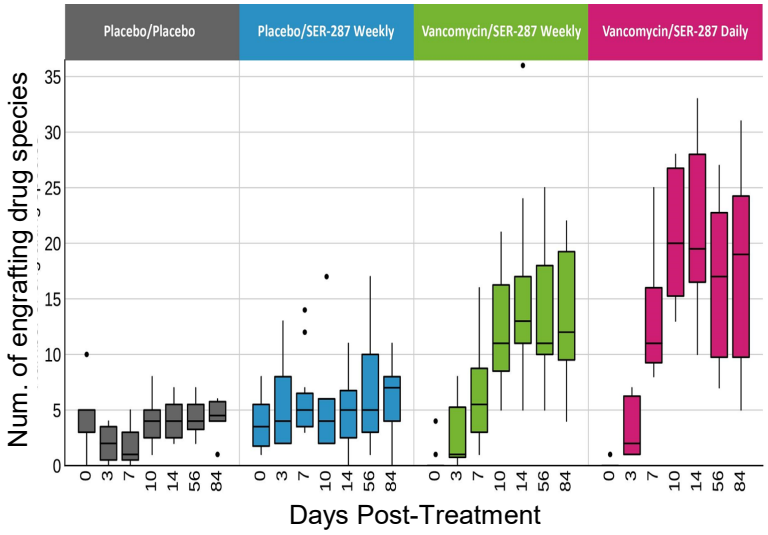
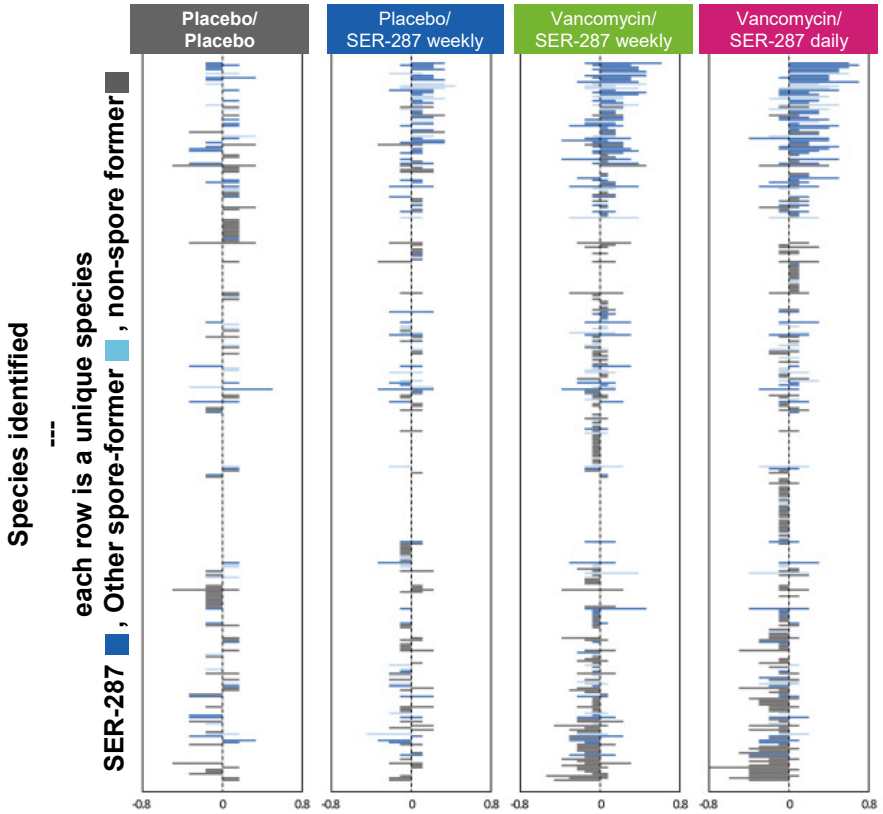
Phase 1b – High resolution microbiome biomarker analytics inform drug pharmacokinetics & pharmacodynamics

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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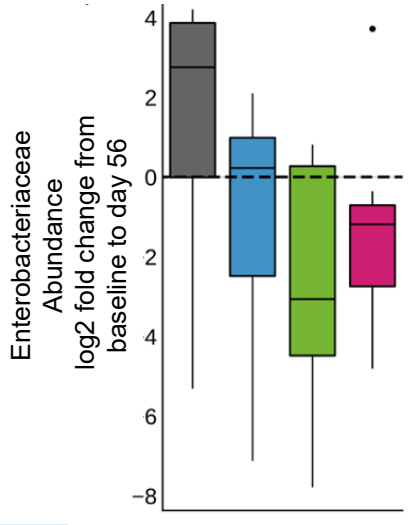
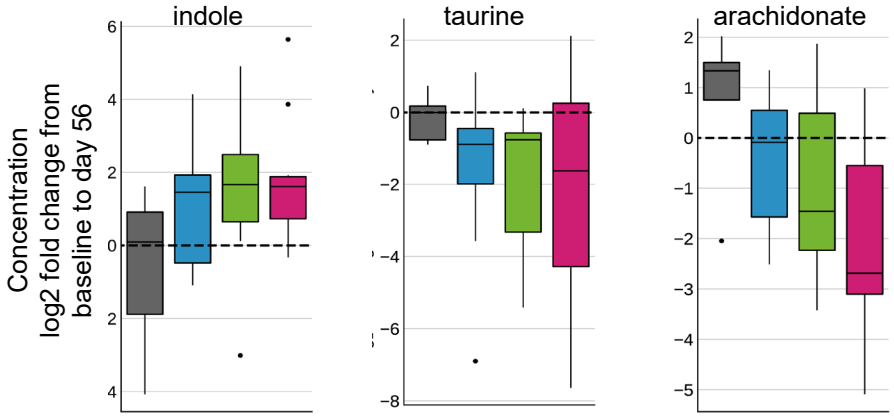
Phase 1b PD – Clinical remission is significantly associated with changes in microbiome and microbe-associated metabolism

Decrease in pro-inflammatory Enterobacteriaceae bacteria post-treatment is associated with SER-287 treatment & clinical remission



Microbially-mediated metabolites that modulate host inflammation & barrier integrity are significantly associated with SER-287 treatment & clinical remission



38 metabolites associated with both SER-287 & clinical remission

Henn et al. 2021. Gastroenterology

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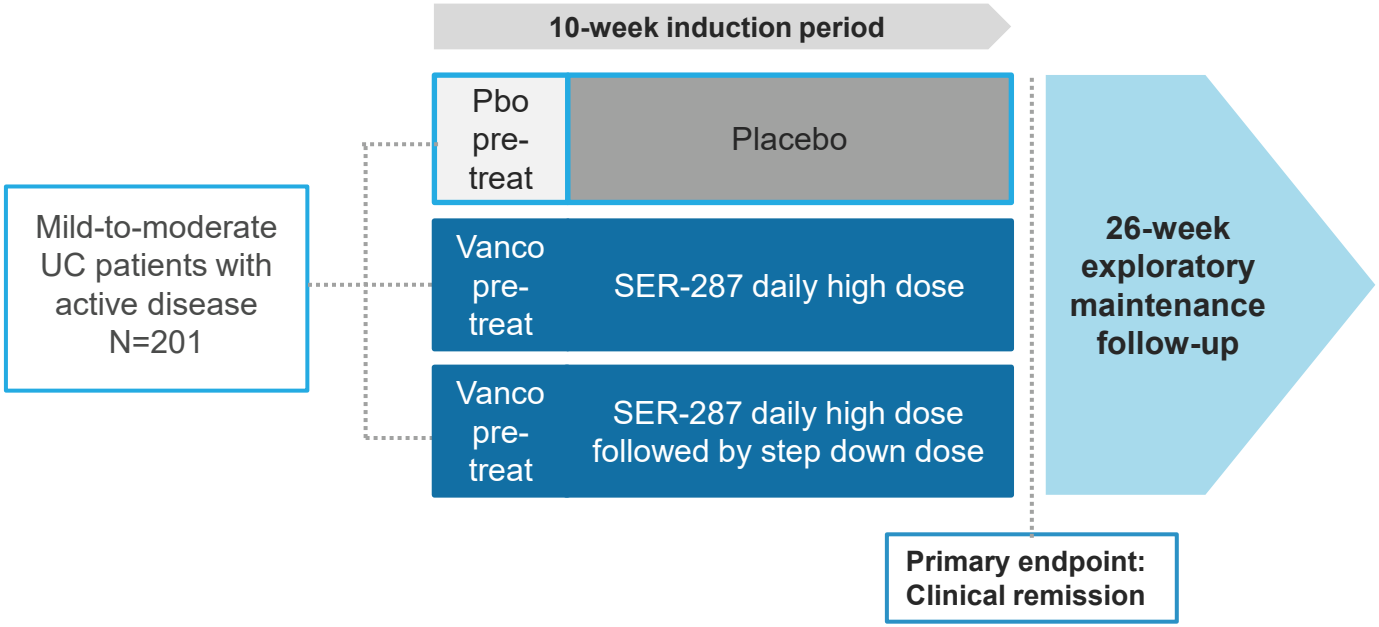
Ongoing SER-287 ECO-RESET Phase 2b study in patients with mild-to-moderate active ulcerative colitis



- **FDA Fast Track designation**
- **FDA feedback: Phase 2b study results, in conjunction with data from a second pivotal study, could support BLA submission**
- **Nearly 90% enrolled (as of Jan. 14, 2021)**
- **Topline results anticipated in H2 2021**

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Earlier stage development programs

	SER-301	SER-401	SER-155
Microbiome drug type	Rationally designed, fermented product; spore + vegetative species	Biologically sourced; composition selected to match I-O therapy responder profile	Rationally designed, fermented product; spore + vegetative species
Stage	Phase 1b	Phase 1b	Approaching Phase 1b
Indication	Mild-to-moderate ulcerative colitis	Metastatic melanoma in combination with anti-PD-1	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	• Modulate microbiome to increase abundance of bacteria associated with systemic immune responses and improved checkpoint therapy efficacy • Increase activated CD8 T cell infiltration in tumors • Upregulation of anti-tumoral cytokines	• 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	The University of Texas MD Anderson Cancer Center; Parker Institute for Cancer Immunotherapy	Memorial Sloan Kettering Cancer Center; CARB-X Combating Antibiotic-Resistant Bacteria

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Opportunity for microbiome therapeutics in multiple 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

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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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; Open-label study enrollment ongoing
SER-287	Ulcerative colitis – Phase 2b ongoing; Topline results anticipated H2 ’21
SER-401	Metastatic melanoma – Phase 1b ongoing
SER-301	Ulcerative colitis – Phase 1b ongoing
SER-155	Antibiotic resistant bacterial infections, bacteremia, & GvHD – Initiate clinical development H1 ’21
Additional R&D opportunities	Additional programs under consideration

- **As of Sept. 30, 2020: $320M in cash, cash equivalents and short and long-term investments**

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