Corporate Overview

Eric Shaff, President and Chief Executive Officer

June 5, 2019

Jefferies Healthcare Conference

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 ability of ECOSPOR III to support SER-109 approval, the promise and potential impact of any of our microbiome therapeutics or clinical trial data, timing of clinical studies of SER-287 and SER-401, timing of SER-301 entering clinical development, the timing and results of any clinical studies, and the potential benefits of Seres’ collaboration with AstraZeneca. Such statements are subject to important factors, risks and uncertainties (such as those discussed under the caption "Risk Factors" in the Company’s Report on Form 10-Q filed on May 2, 2019 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 investor highlights

Platform

Leader in microbiome drug development with differentiated drug discovery, manufacturing, and clinical capabilities

Focus

Prioritized pipeline in ulcerative colitis, *C. difficile* infection, oncology

Opportunity

Four anticipated pipeline milestones during 2020:

- SER-287 Phase 2b completion of enrollment by mid-2020; Top-line data in Q3 2020
- SER-109 Phase 3 completion of enrollment by end-2019; Top-line data in early 2020
- SER-401 Phase 1b preliminary results in 2020
- SER-301 initiate clinic development by early 2020

Team

Experienced, highly accomplished leadership team

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Significant corporate progress in recent months to advance strategy of rapidly driving toward meaningful clinical milestones

- ✓ Appointment of Eric Shaff as President and CEO
- ✓ Prioritization of pipeline and reduction in corporate cost structure
- ✓ Initiation of SER-287 Phase 2b in ulcerative colitis
- ✓ Initiation of SER-401 Phase 1b study in metastatic melanoma
- ✓ Immuno-oncology collaboration with AstraZeneca
- ✓ Modification of SER-109 Phase 3 study with the goal of expediting availability of efficacy results

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The microbiome is essential to human health

- Human gastrointestinal microbiome is a vast interacting network of organisms
- Microbial ecology provides essential functions for the host:
  - Modulation of immune system
  - Colonization resistance against potential pathogens
  - Regulation of host metabolism
  - Synthesis of certain vitamins
  - Breakdown of carbohydrates

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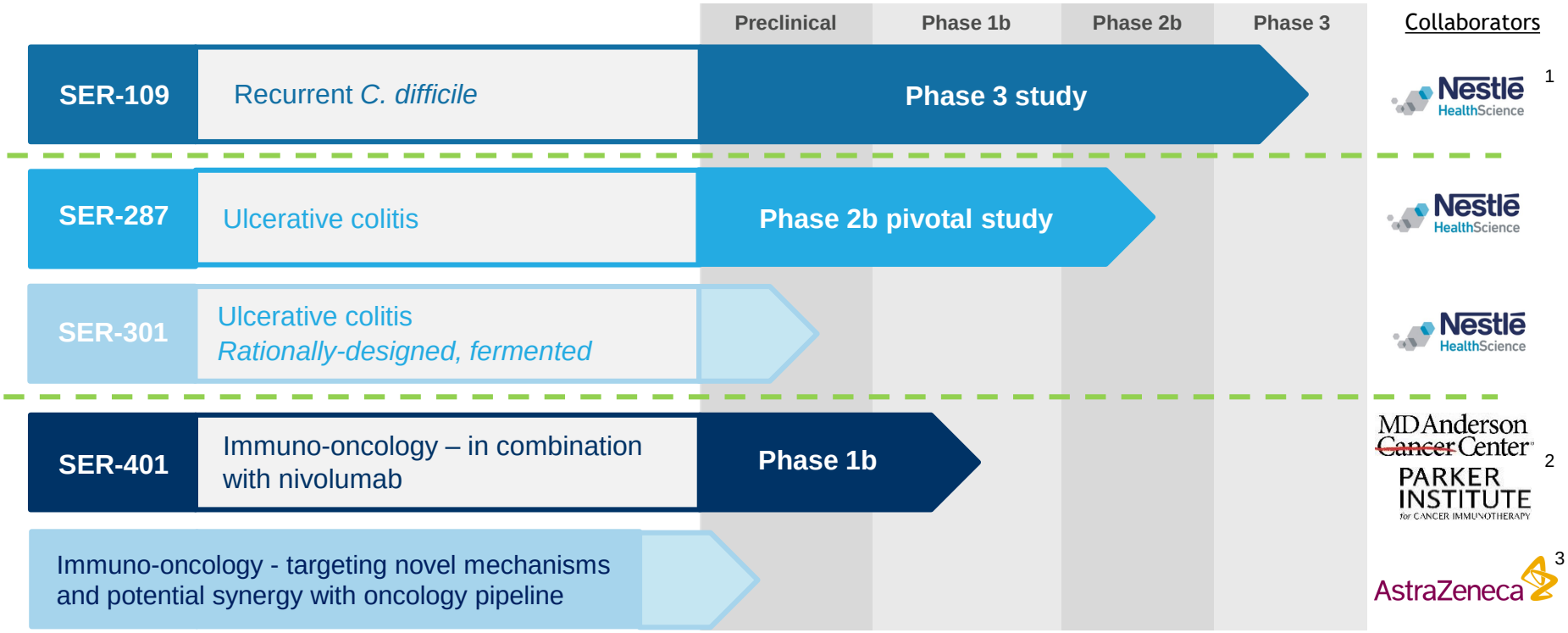
Two pronged strategy

Expeditiously advance prioritized clinical programs to meaningful data read-outs	Advance next generation technology: Rationally designed, fermented microbiome therapeutics
SER-287 Ph 2b for ulcerative colitis	Lead program - SER-301 for UC
SER-109 Ph 3 for *C. difficile* infection	
SER-401 Ph 1b for immuno-oncology	

Prioritized 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.

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SER-287 and Ulcerative Colitis

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Ulcerative colitis overview

A serious chronic condition characterized by inflammation of the colon and rectum that results in abdominal pain, bowel urgency and diarrhea

Significant need for improved therapies

- Large US population: ~700K ulcerative colitis
- Fewer than ~1/3 of patients achieve remission with current therapies
- Many therapies are immunosuppressive

~700K in the United States

<1/3 achieve remission

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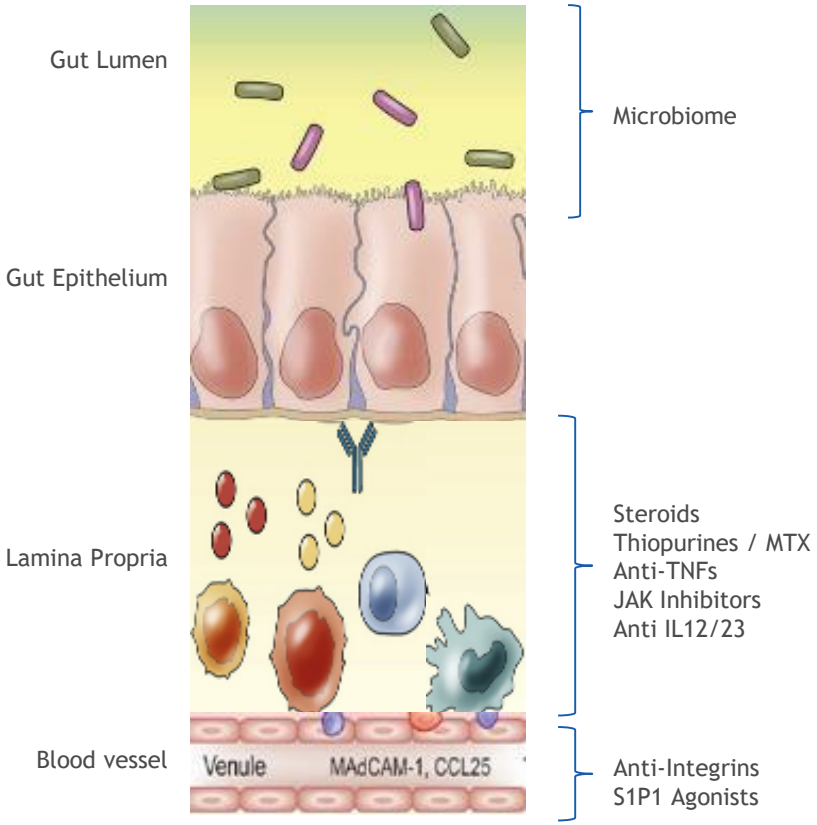
Modulation of the microbiome is an attractive therapeutic target for ulcerative colitis



Microbiome impact on inflammatory and immunological tone

- 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

Potential opportunity to develop both first-line and combination therapies

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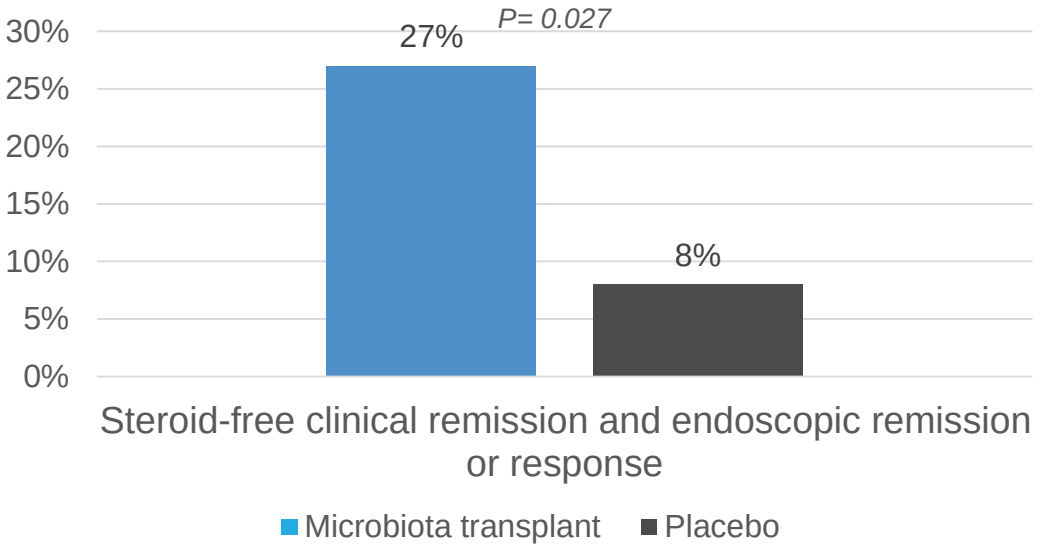
Published study regarding microbiota transplantation provided clinical proof-of-concept in ulcerative colitis

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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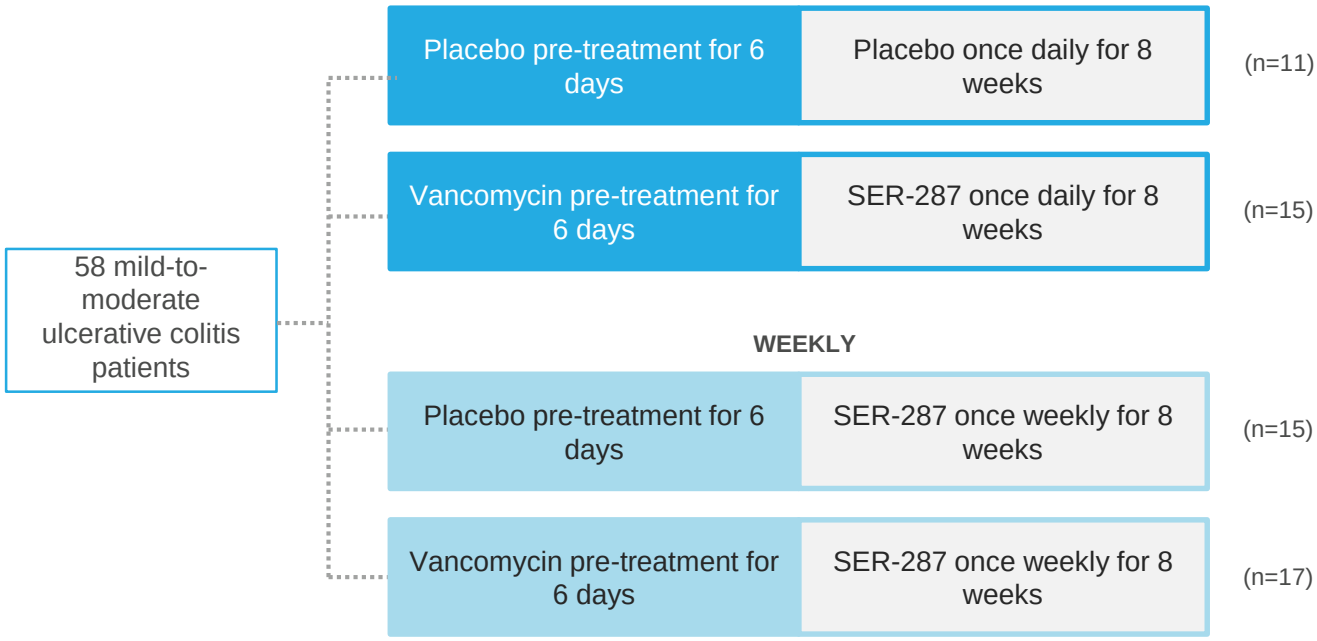
SER-287 Phase 1b ulcerative colitis study



Primary Objectives

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

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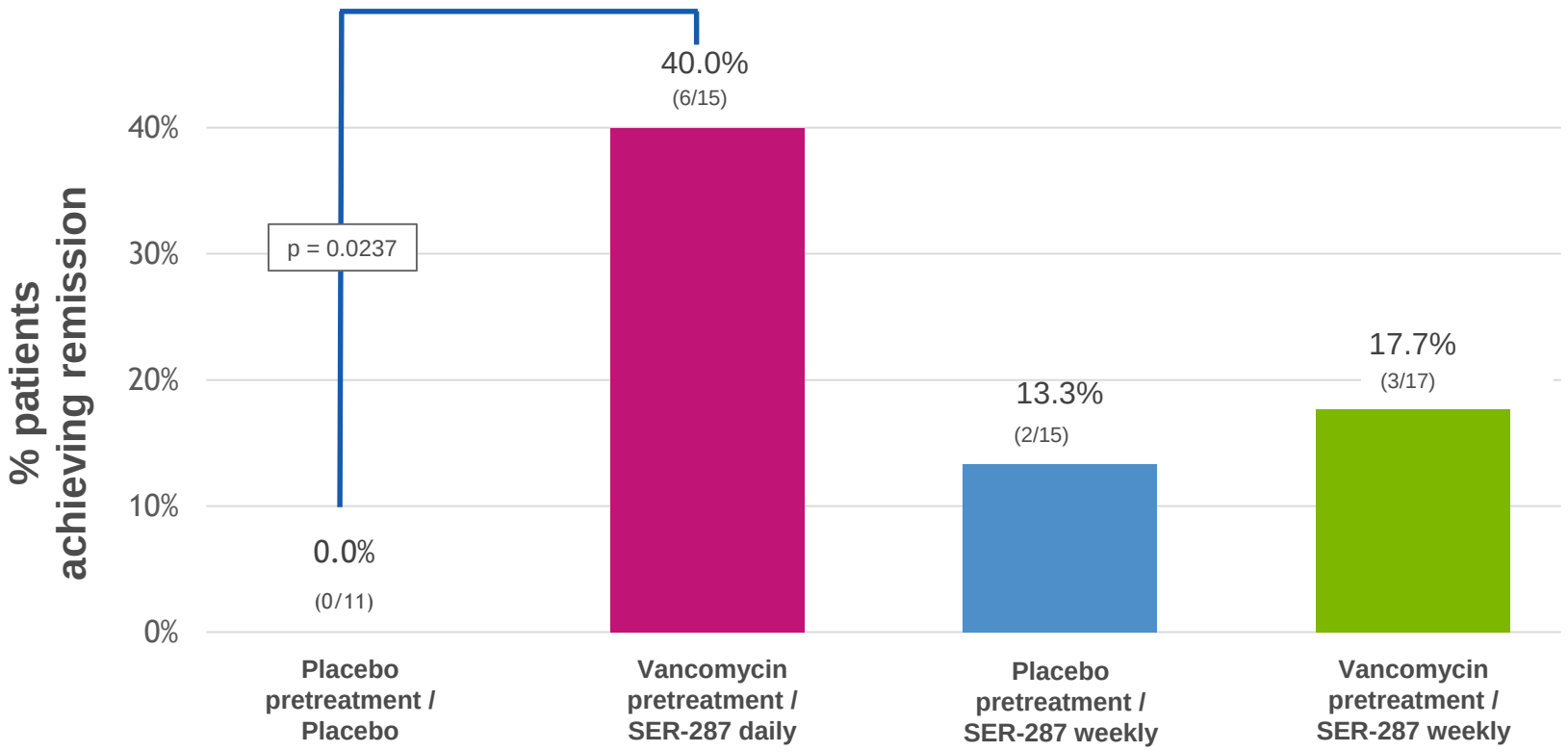
Phase 1b study results – Statistically significant clinical remission improvement observed in Vanco/SER-287 daily treatment arm



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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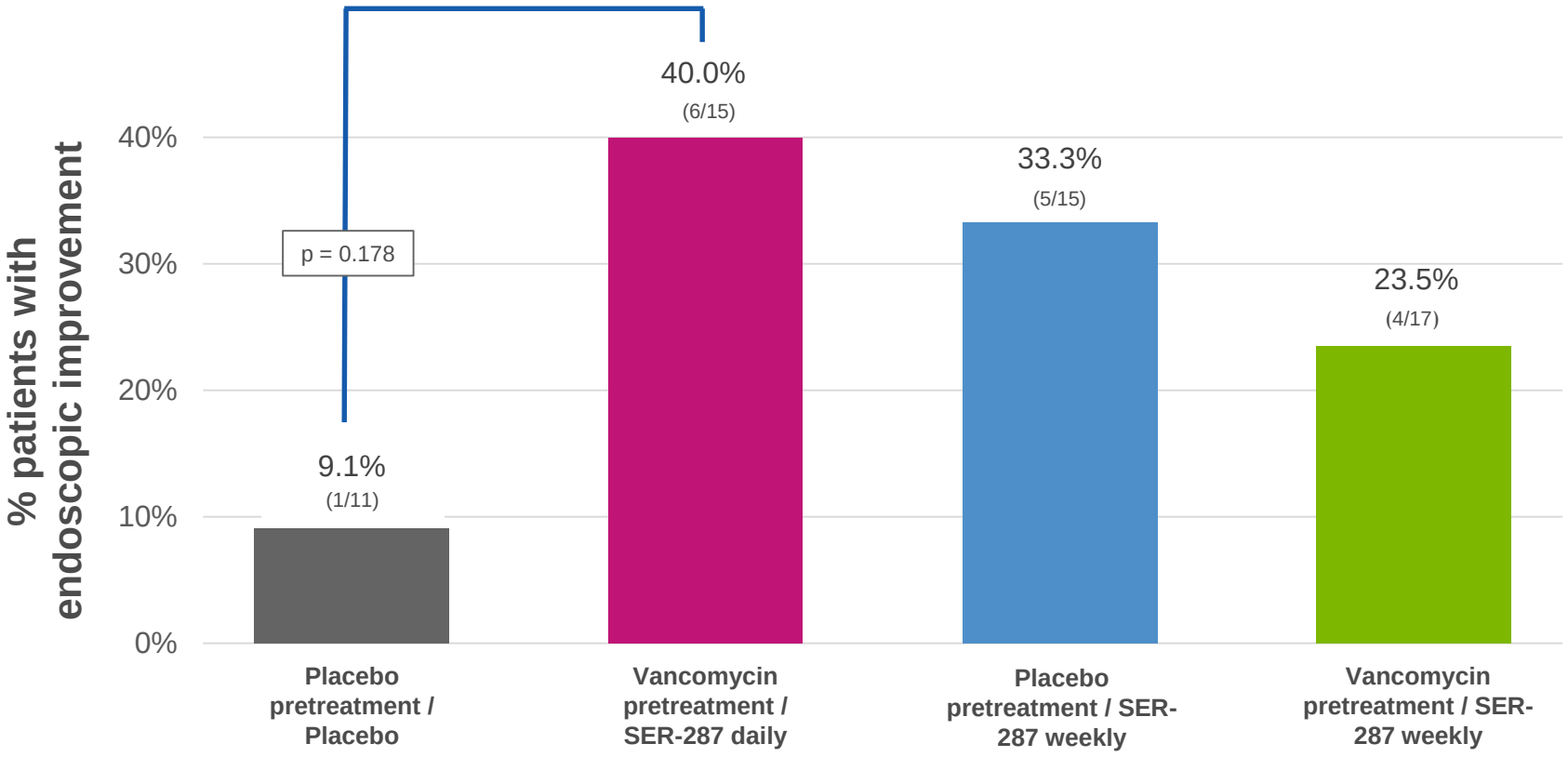
Phase 1b study results - Dose dependent impact on endoscopic improvement in Vanco/SER-287 daily treatment arm



Endoscopic Improvement: Decrease in endoscopic subscore ≥ 1
Note: Endoscopy readings were centrally read by blinded readers, missing data treated as failure; statistical significance not found in SER-287 weekly arms

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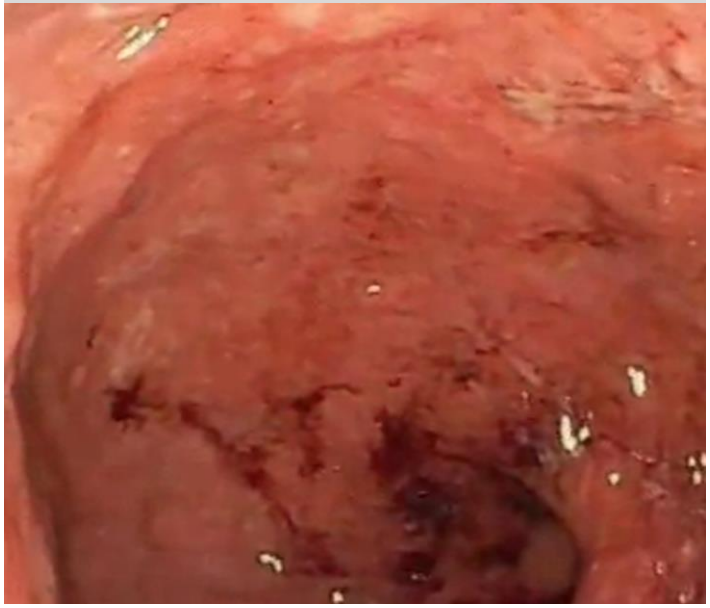
Illustrative endoscopy improvement — Vanco/SER-287 daily treatment

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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SER-287 Phase 1b – long term disease activity

SER-287 Phase 1b patients were followed for up to 26 weeks post treatment:

- Of the 11 patients treated with SER-287 who achieved clinical remission, preliminary data showed that no patients experienced a disease flare in the 26 weeks following the end of treatment (0/11)

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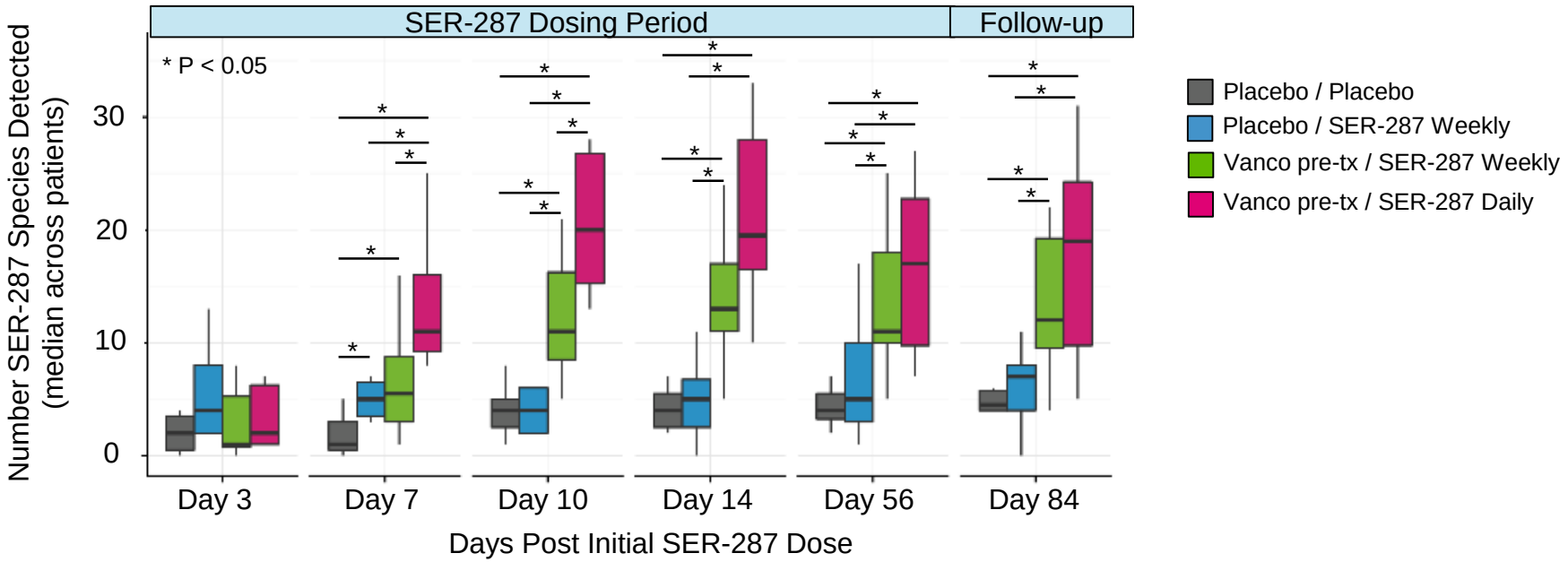
Phase 1b study results – SER-287 bacteria engrafted in subjects and was durable to four weeks after dosing



- Statistically significant engraftment, as compared to placebo, in vanco pre-treat / SER-287 daily arm, beginning at day 7 and durable throughout the dosing period
- Data supportive of vancomycin opening ecological niches for SER-287 engraftment
- Statistically significant engraftment was durable at 4 weeks following SER-287 dosing

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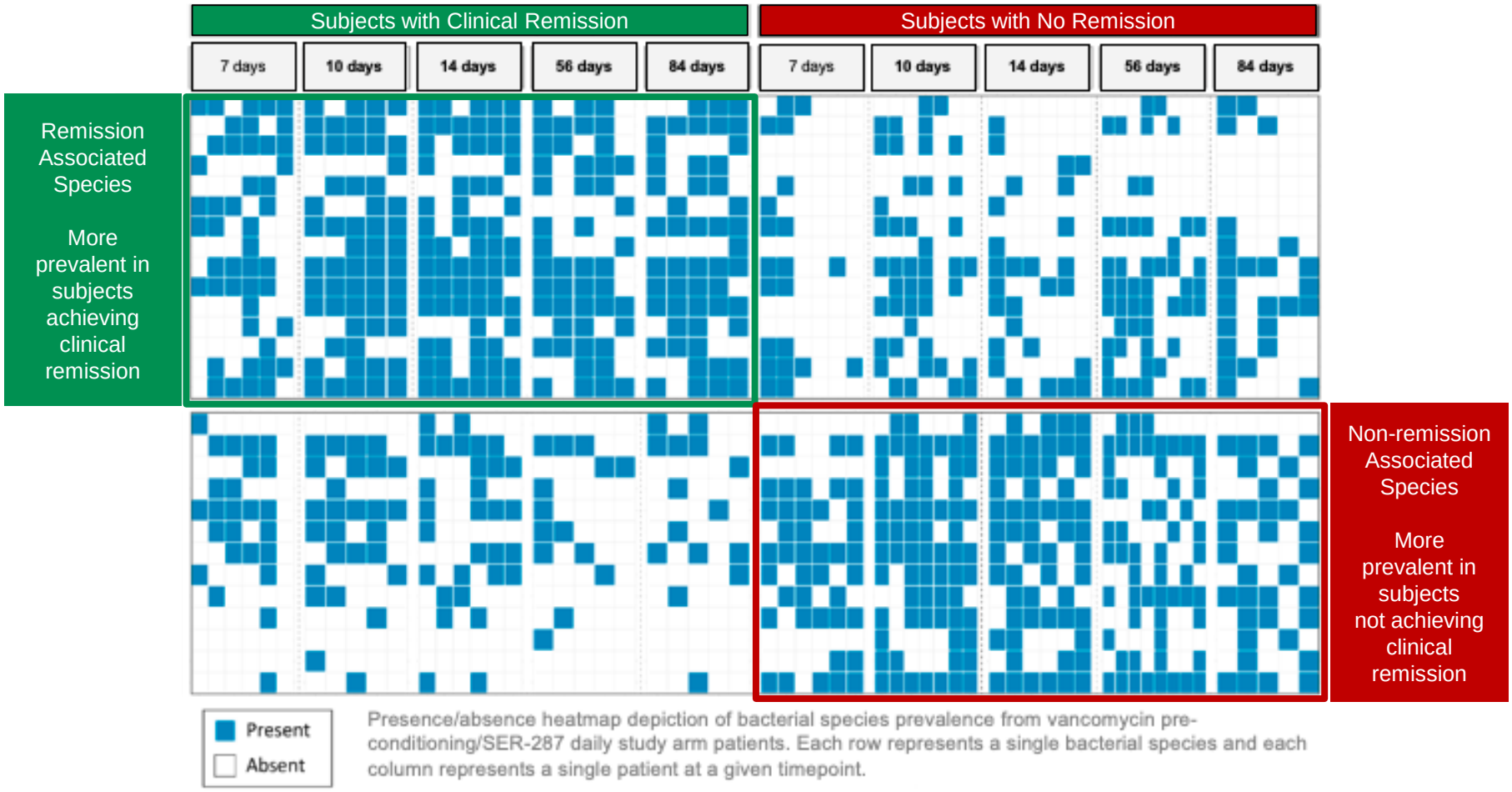
Phase 1b study results - Identified bacterial species signature that associates with clinical remission vs non-remission



Presence/absence heatmap depiction of bacterial species prevalence from vancomycin pre-conditioning/SER-287 daily study arm patients. Each row represents a single bacterial species and each column represents a single patient at a given timepoint.

- Predictive species include both SER-287 bacteria and others augmented by treatment
- Functional characterization of signature species is informing drug mechanism of action

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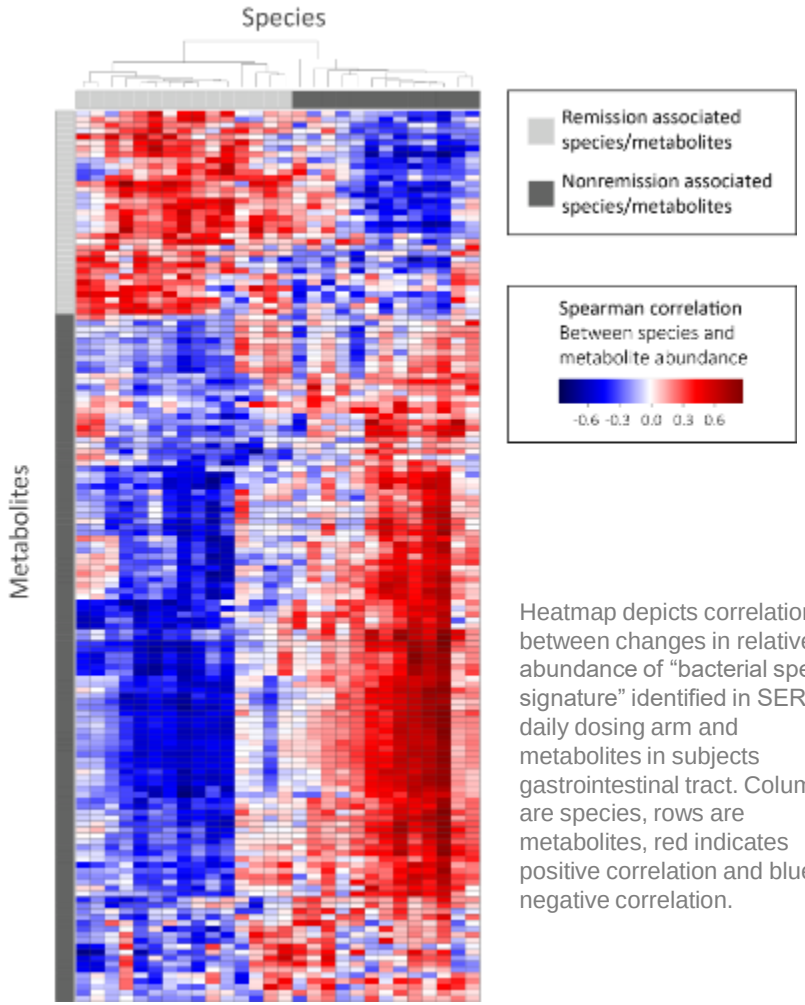
Microbiome signature of remission strongly correlated with metabolite shifts in patients administered SER-287



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

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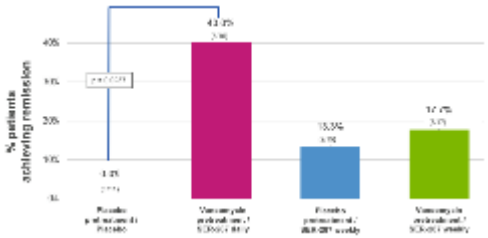
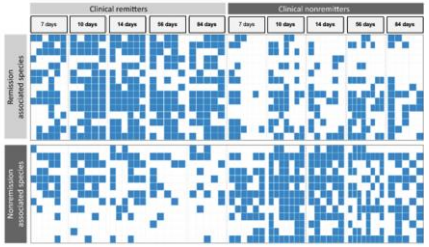
SER-287 Phase 1b data provide evidence of clinical activity and provide supportive mechanistic data



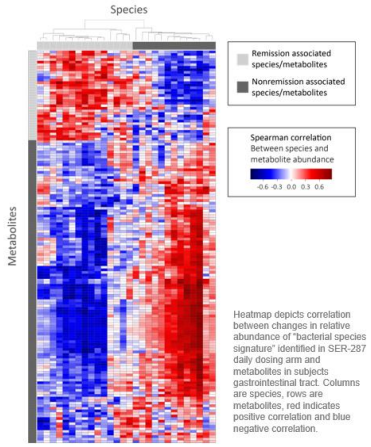
CLINCAL RESULTS

Dose dependent clinical remission



SPECIES SIGNATURES

Engraftment (PK) associated with clinical remission



METABOLITES & PATHWAYS

Metabolites and functional pathways (PD) associated with remission and microbiome change

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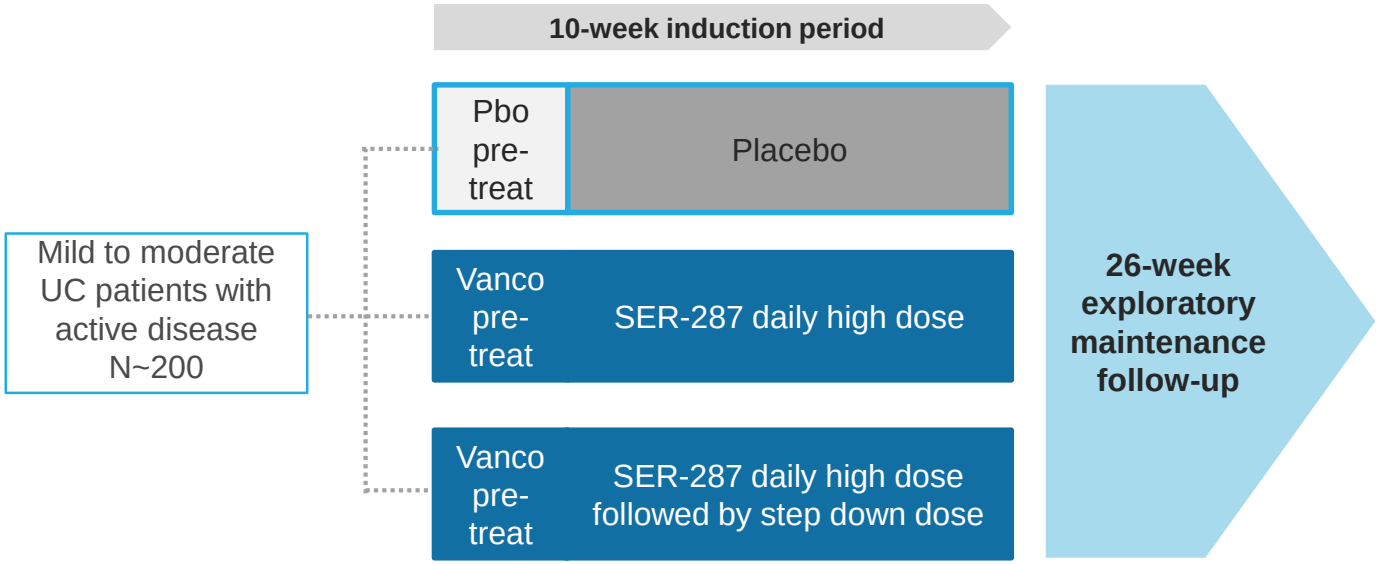
Ongoing SER-287 ECO-RESET Phase 2b study in patients with mild-to-moderate active ulcerative colitis

Study initiated December 2018



- FDA Fast Track designation obtained in April 2019
- FDA feedback has indicated that results from this Phase 2b study, in conjunction with data from a second pivotal study, could support BLA submission
- Seres received $40 million in milestone payments (Q4 2018) from Nestlé Health Science associated with Phase 2b study start
- **Anticipate ECO-RESET completion of enrollment by mid-2020; Top-line data in Q3 2020**

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SER-301: Rationally designed fermented therapeutic candidate for inflammatory bowel disease

Oral, mechanistically designed follow-on to SER-287

Selection of SER-301 bacterial composition to be based on:

- SER-287 study data (clinical and microbiome analysis)
- Preclinical activity of microbiome compositions

Rationally designed compositions have shown activity in mouse model

Anticipate initiation of SER-301 clinical development by early 2020

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Clostridium difficile Infection

Overview and SER-109 Phase 3 study

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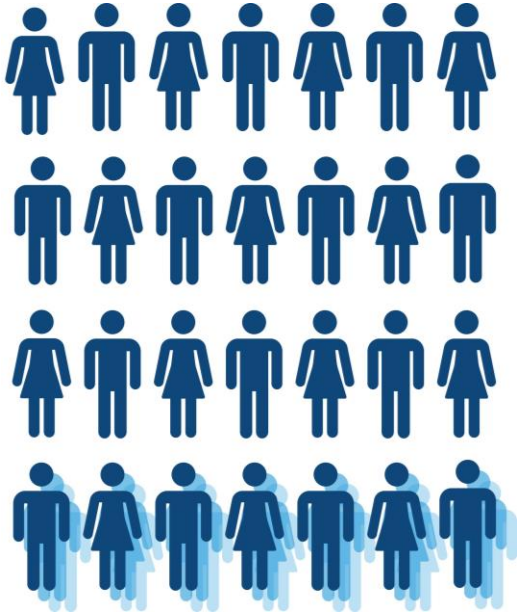
C. difficile infection overview

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

Leading cause of hospital-acquired infection in the US

- Approximately 29,000 deaths/year
- ~25% of patients with primary *C. difficile* recur
- Risk of relapse increases with each recurrence
- Multiply recurrent *C. difficile* infection incidence increased 188% between 2001-2010



25% of primary *C. difficile* recur

~29K deaths/year

Sources: Leffler and Lamont, New England Journal of Medicine, 2015; Ma et al. Annals of Internal Medicine, 2017.

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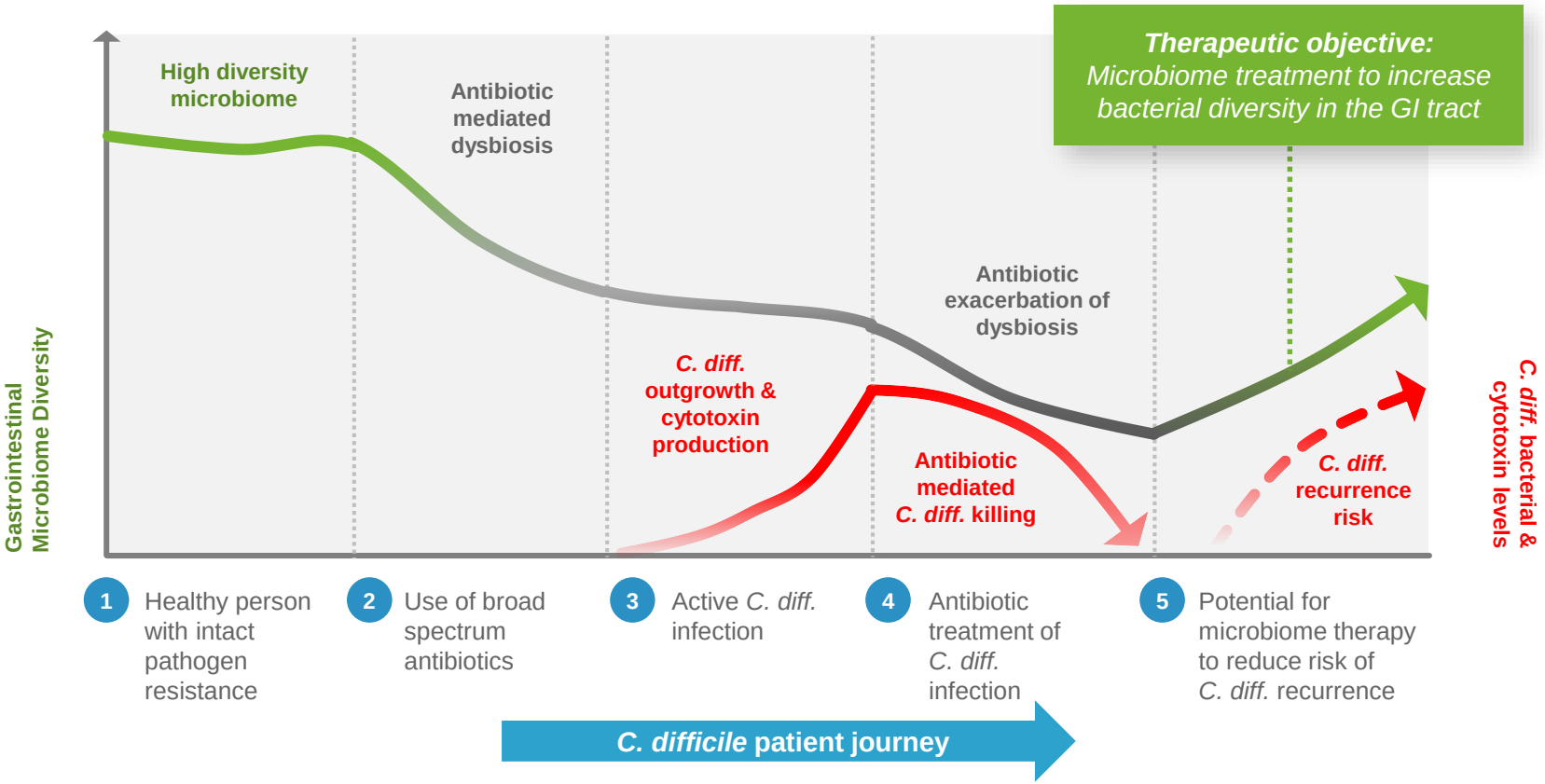
Microbiome therapeutic intervention – Hypothetical patient course



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SER-109 development in recurrent *C. difficile* infection supported by strong clinical and mechanistic evidence

- Oral, donor derived, spore based therapeutic candidate designed to reestablish gastrointestinal microbiome diversity and resistance to *C. difficile* recurrence
- Multiple studies, and the widespread use of Fecal Microbiota Transfer (FMT), provide proof-of-concept
- Completed Phase 2 study in patients with recurrent *C. difficile* infection
  - Well tolerated with no drug related SAEs
  - Demonstrated to result in a statistically significant increase in microbiome diversity
  - Increase secondary bile acid levels linked to inhibition of *C. difficile* growth
- Obtained FDA Breakthrough and Orphan Drug designations

SER-109 capsules

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Original SER-109 ECOSPOR III Phase 3 study designed to support BLA submission with a single trial

- SER-109 ECOSPOR III study design incorporates learnings from prior clinical studies:
  - SER-109 dose is approximately 10-fold higher than Phase 2 study
  - *C. difficile* toxin assay used to ensure inclusion of patients with active *C. difficile* infection, and for primary endpoint analysis
- Original 320 patient study designed to provide a definitive assessment of SER-109 efficacy, and a comprehensive evaluation of safety
- Based on previous FDA feedback, original ECOSPOR III designated as a Phase 3 study that, with favorable study results, could support BLA submission as a single pivotal trial

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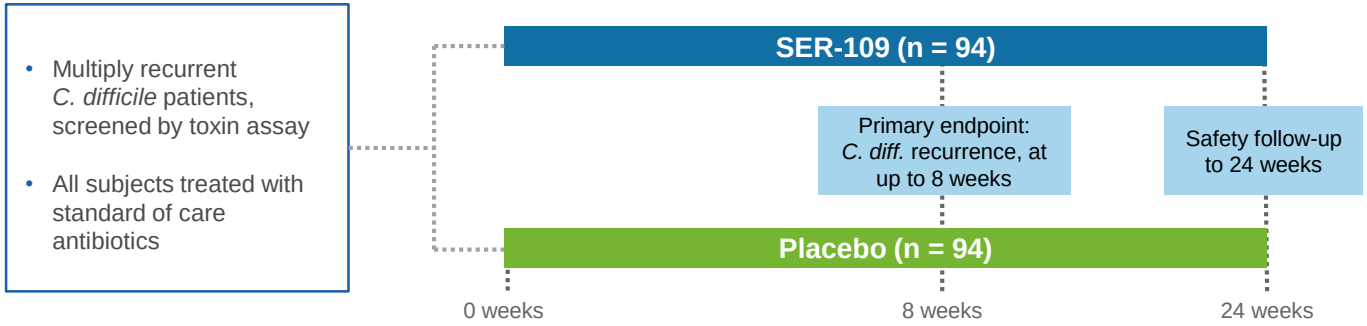
ECOSPOR III design modified with the goal of rapidly achieving a well powered efficacy readout

- ECOSPOR III size reduced from 320 to 188 patients with the goal of expediting clinical results
- Size and powering calculations informed by prior SER-109 study results, published *C. difficile* infection trial data, and available preliminary blinded and open label study data
- Company believes modified study design will maintain statistical power to demonstrate efficacy
- Seres has informed FDA regarding ECOSPOR III study modification and plans to further discuss options to expediate the SER-109 development path toward potential BLA submission
- In prior communications with the FDA regarding a potential reduction in ECOSPOR III study size, the agency indicated that the status of the study as a potential registrational study would depend on the specific statistical outcome of the trial. A smaller study design could require additional confirmatory evidence of efficacy, such as a second Phase 3 study, and additional safety data.



Anticipate SER-109 enrollment completion by the end of 2019; Top-line results in early 2020

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SER-401 and Immuno-oncology

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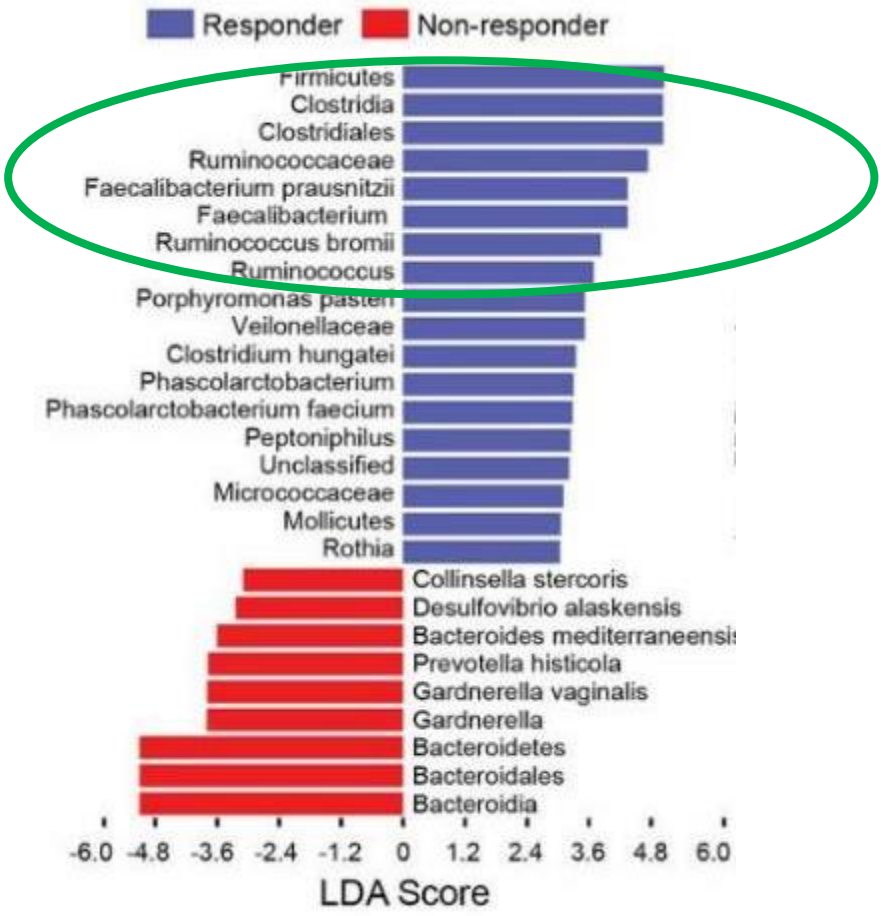
MD Anderson collaborators have identified a microbiome signature in melanoma patients who respond to anti-PD-1

- SER-401 composition driven by bacteria consistent with responder profile
  - Class Clostridia, family *Ruminococcaceae*
  - Ex. *Ruminoccocus* and *Faecalibacterium*
- 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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Collaborations to advance microbiome therapeutic into immuno-oncology

- SER-401 Phase 1b study with anti-PD-1 (nivolumab) in patients with metastatic melanoma
  - ***Initiated March 2019***
- Seres option to license foundational intellectual property from MD Anderson related to the use of bacteria in combination with checkpoint inhibitors

- Three-year collaboration focused on advancing mechanistic understanding of the microbiome in augmenting the efficacy of cancer immunotherapy
  – ***Announced March 2019***
- Extend science beyond PD-(L)1 therapies
- Generate additional data with SER-401 including, potential synergy with AstraZeneca compounds
- $20M of committed capital paid over two years; In addition, AstraZeneca reimburses Seres for collaboration activity

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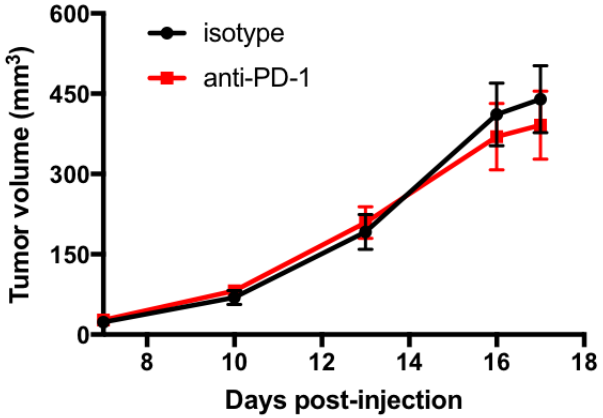
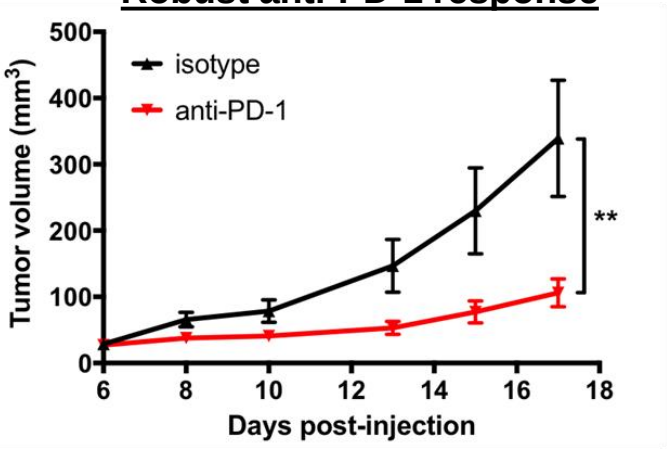
Colonization of germ free (GF) mice with SER-401 drug substance restores response to anti-PD-1

Data presented at AACR meeting March 2019

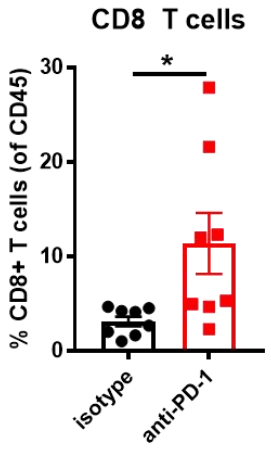
Germ free mice – No anti-PD-1 response

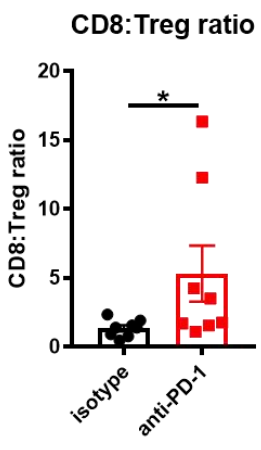


SER-401 administered mice – Robust anti-PD-1 response



Tumor infiltrate at end of study





Germ Free tumor model: MC38

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Ongoing SER-401 Phase 1b study

First patient dosed in March 2019

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)

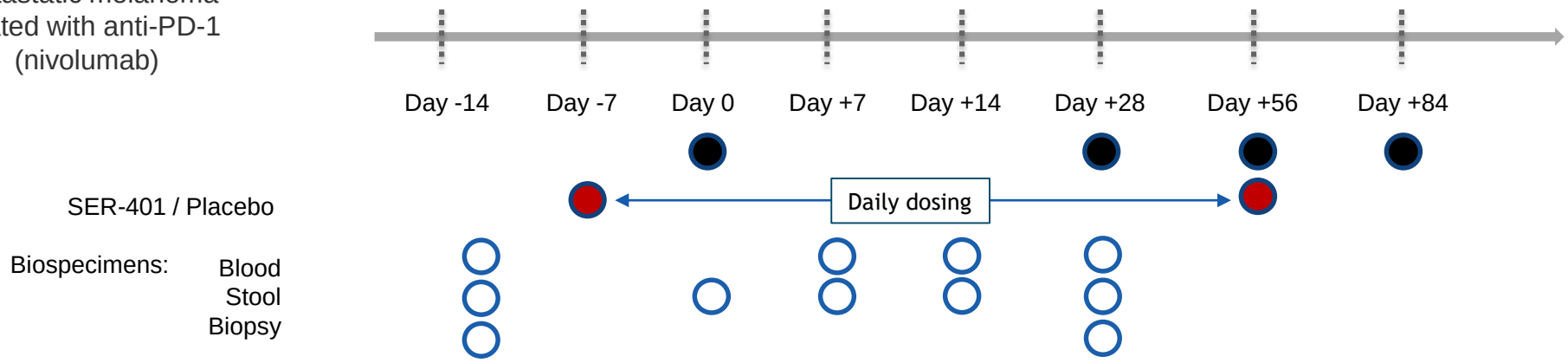
Placebo (n=10)

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)



Anticipate SER-401 Phase 1b study results in 2020

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

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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
- Issued claims related to SER-109/ *C. difficile* & *SER-287 / ulcerative colitis* lead candidates extend through **2033**
- 12 Issued US Patents obtained

18 Families of Applications

10 Nationalized

3 Pending Provisionals

PROJECTED BIOSIMILAR REGULATORY EXCLUSIVITY

12 years for new biological composition

10 years for new drug

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Four significant value drivers anticipated in 2020

SER-287	Ulcerative colitis – Phase 2b study ongoing; Completion of enrollment by mid-2020 and top-line data in Q3 2020
SER-109	Recurrent *C. difficile* infection – Phase 3 ongoing; Completion of enrollment by end-2019 and top-line data in early 2020
SER-401	Metastatic melanoma – Phase 1b study ongoing; Preliminary results expected in 2020
SER-301	Next generation platform, rationally designed fermented compositions; Initiate SER-301 clinical development for UC by early 2020
Discovery efforts	AstraZeneca collaboration targeting novel I-O mechanisms and potential synergy with AstraZeneca oncology pipeline

Balance Sheet	As of end of Q1 2019
Cash, cash equivalents and investments	$53.6 M

* The ending Q1 2019 cash balance did not include the first of three non-cancellable annual installment payment due under the terms of the collaboration with AstraZeneca of $6.7 million received in April 2019.
Upcoming potential milestones though 2020 includes $10M for SER-301 start of clinical development and the second of three $6.7M milestones, expected in 2020, associated with ongoing collaboration with AstraZeneca.

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