

Seres Therapeutics Overview

Stifel 2019 Healthcare Conference

November 19, 2019



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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 or clinical trial data, the ability of our clinical trials to support approval, the timing of clinical studies, 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 Report on Form 10-Q filed on Nov. 5, 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 top-line data in H2 2020
- SER-109 Phase 3 top-line data in mid 2020
- SER-401 Phase 1b preliminary results in H2 2020
- SER-301 initiate clinic development in early 2020

Team

Experienced, highly accomplished leadership team

Significant corporate progress 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
- ✓ Strengthened balance sheet through \$61 million public offering and \$25M debt capital, with potential for additional \$25M

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



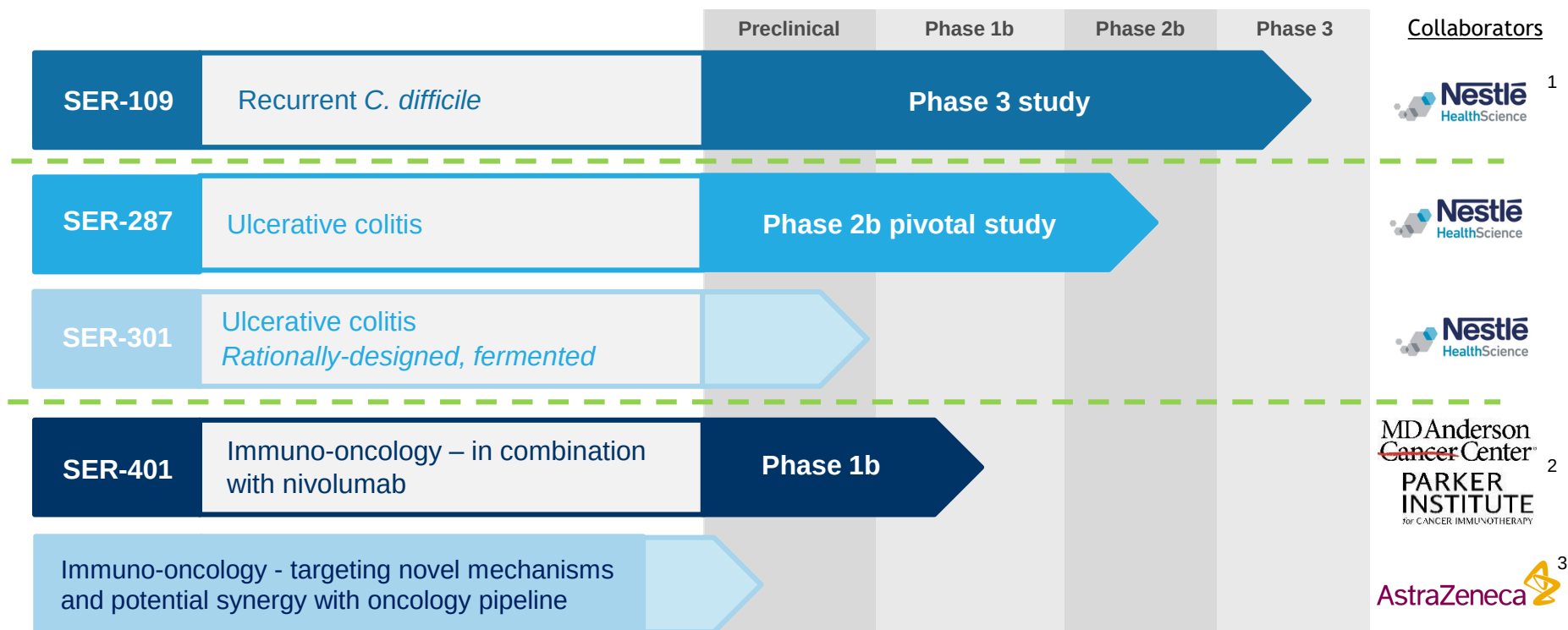
**Significant
opportunity for
microbiome
therapeutics to
impact disease
outcomes**



Two pronged strategy

Expedientiously 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 candidate designated - SER-301 for ulcerative colitis
SER-109 Ph 3 for <i>C. difficile</i> 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.

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

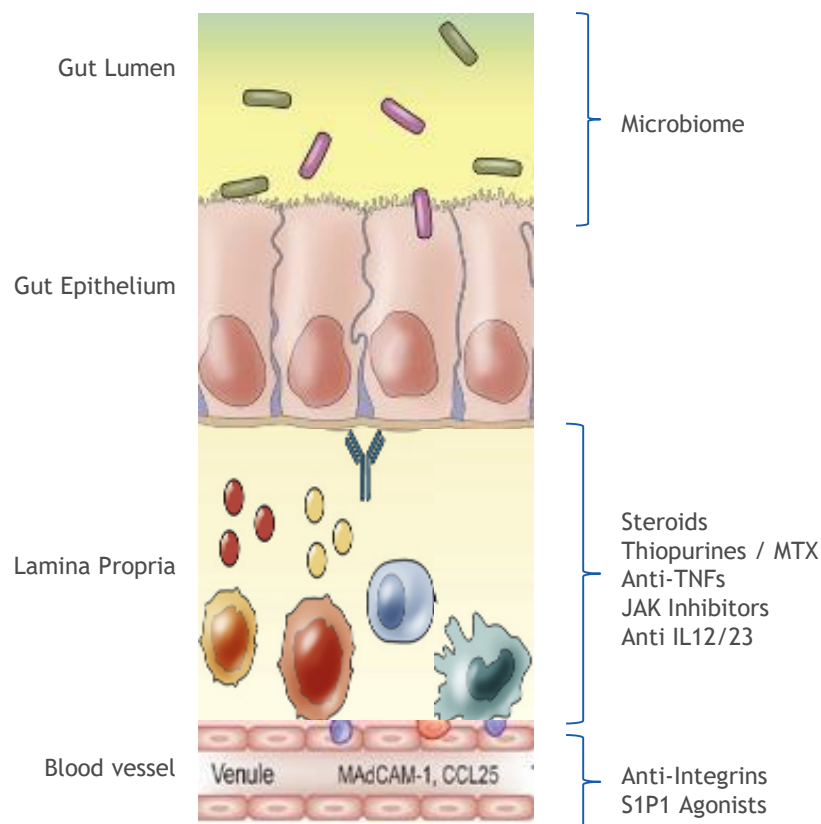
- Large US population: ~700K ulcerative colitis
- Fewer than ~1/3 of patients achieve remission with current therapies
- Many therapies are immunosuppressive



~700K in the United States

<1/3 achieve remission

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

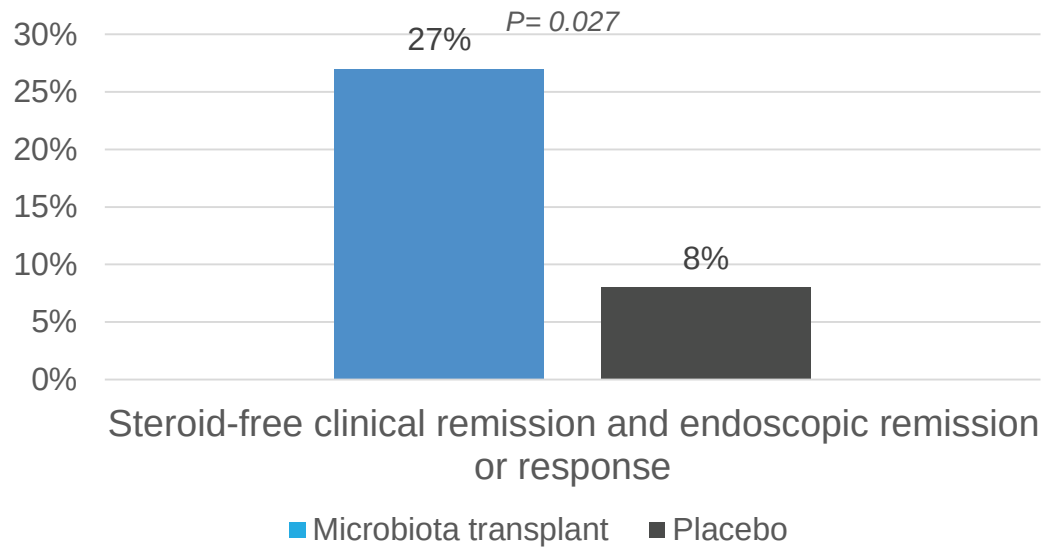
Published study regarding microbiota transplantation provided clinical proof-of-concept in ulcerative colitis



THE LANCET

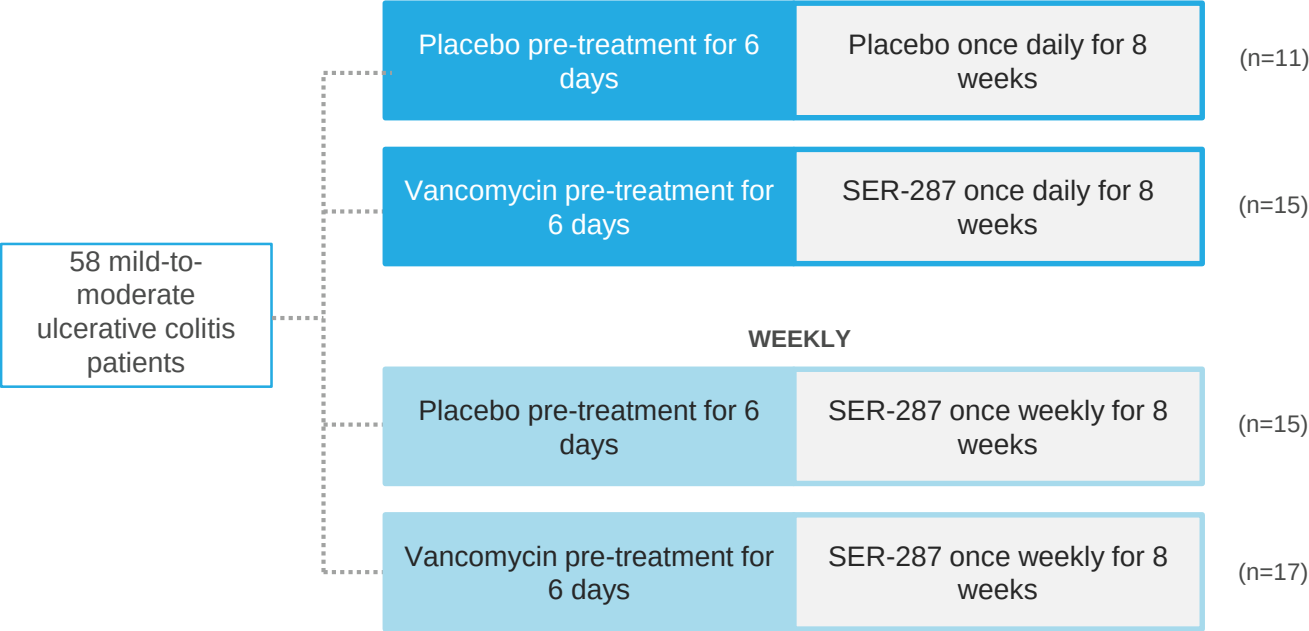
Multidonor intensive faecal microbiota transplantation for active ulcerative colitis: a randomised placebo-controlled trial

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





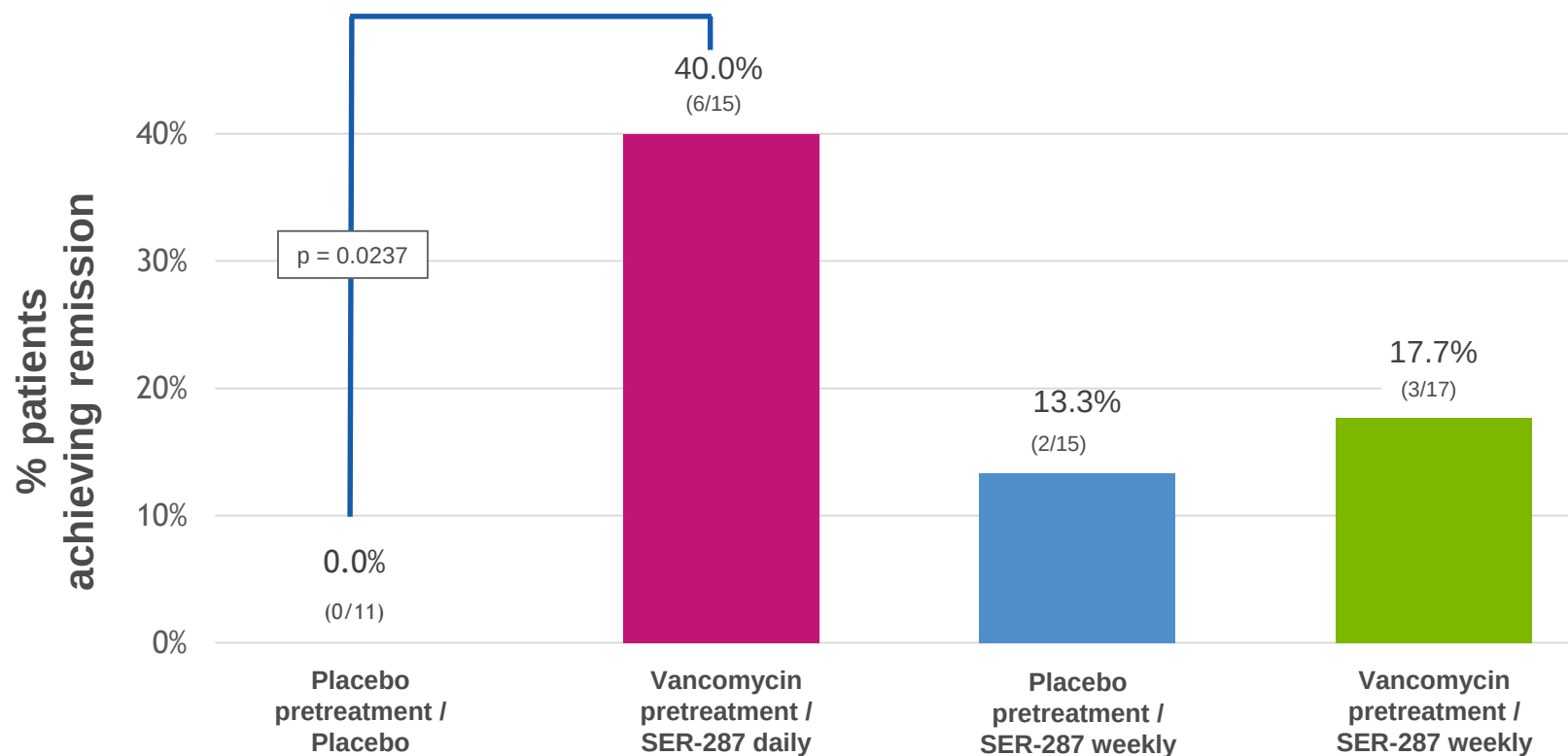
SER-287 Phase 1b ulcerative colitis study



Primary Objectives

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

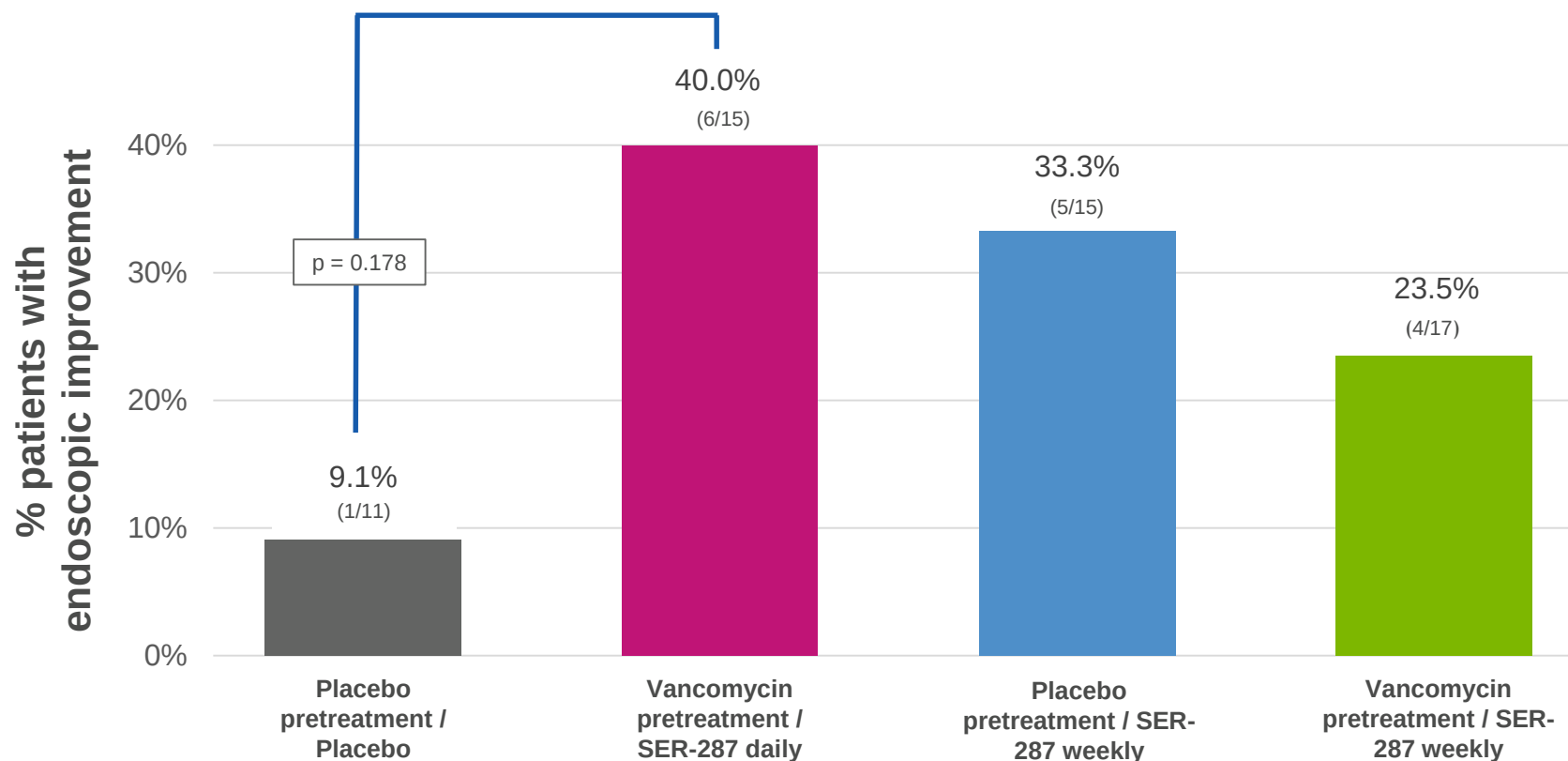
Phase 1b study results – Statistically significant clinical remission improvement observed in Vanco/SER-287 daily treatment arm



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

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

Illustrative endoscopy improvement — Vanco/SER-287 daily treatment



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



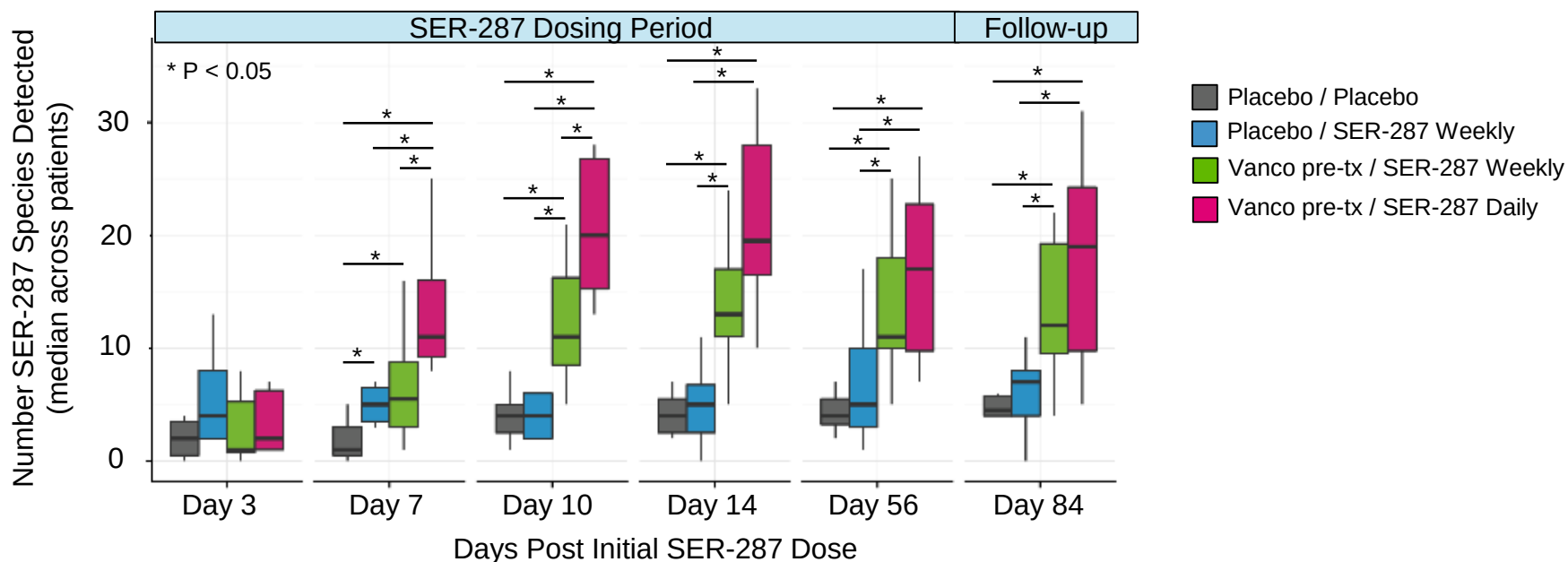
Post-treatment day 64 endoscopy



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%)

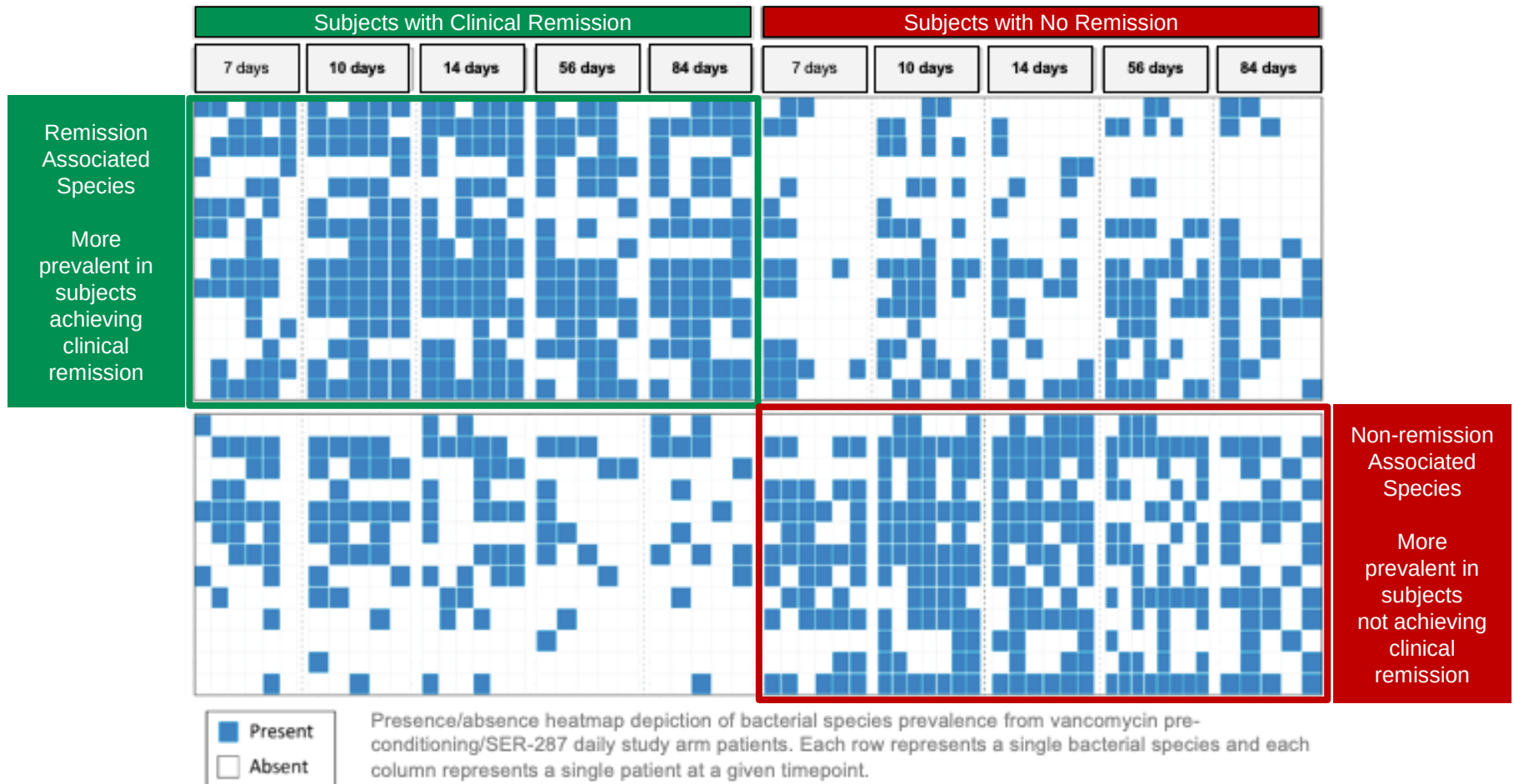
Phase 1b study results – SER-287 bacteria engrafted in subjects and was durable to four weeks after dosing



- 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

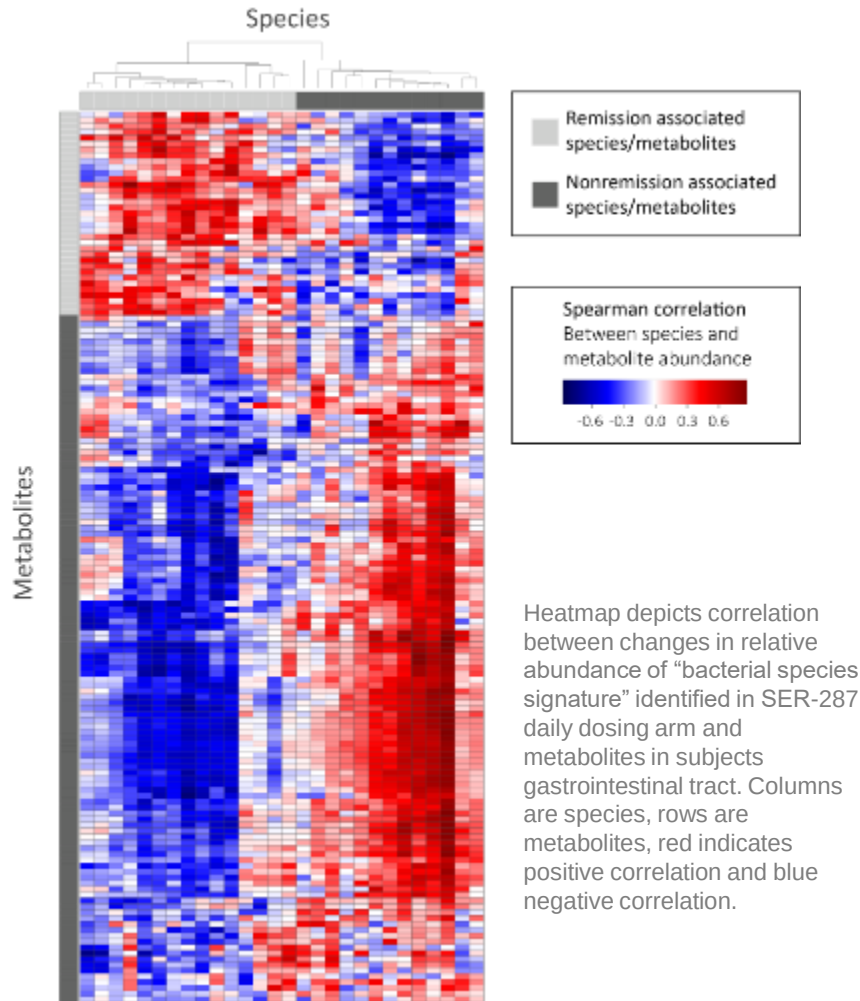


Phase 1b study results - Identified bacterial species signature that associates with clinical remission vs non-remission



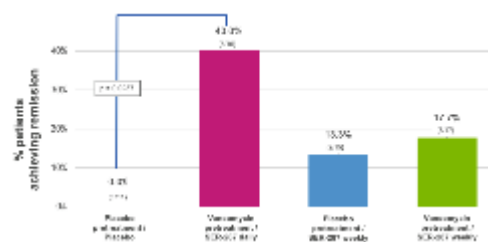
- Predictive species include both SER-287 bacteria and others augmented by treatment
- Functional characterization of signature species is informing drug mechanism of action

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



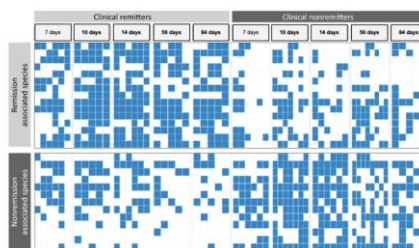
- Strong correlation between signature species and stool metabolites that predict clinical remission
- Metabolomic signature of clinical remission represents diverse functional pathways
- Many pathways identified are implicated in IBD and immune dysregulation

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



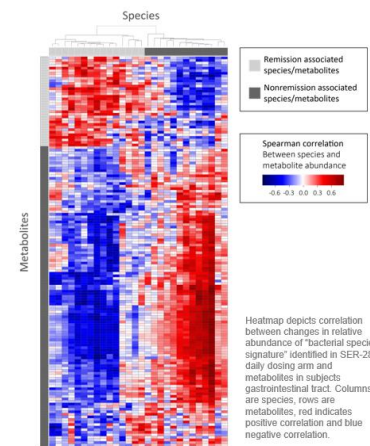
CLINICAL RESULTS

Dose dependent clinical remission



SPECIES SIGNATURES

Engraftment (PK) associated with clinical remission



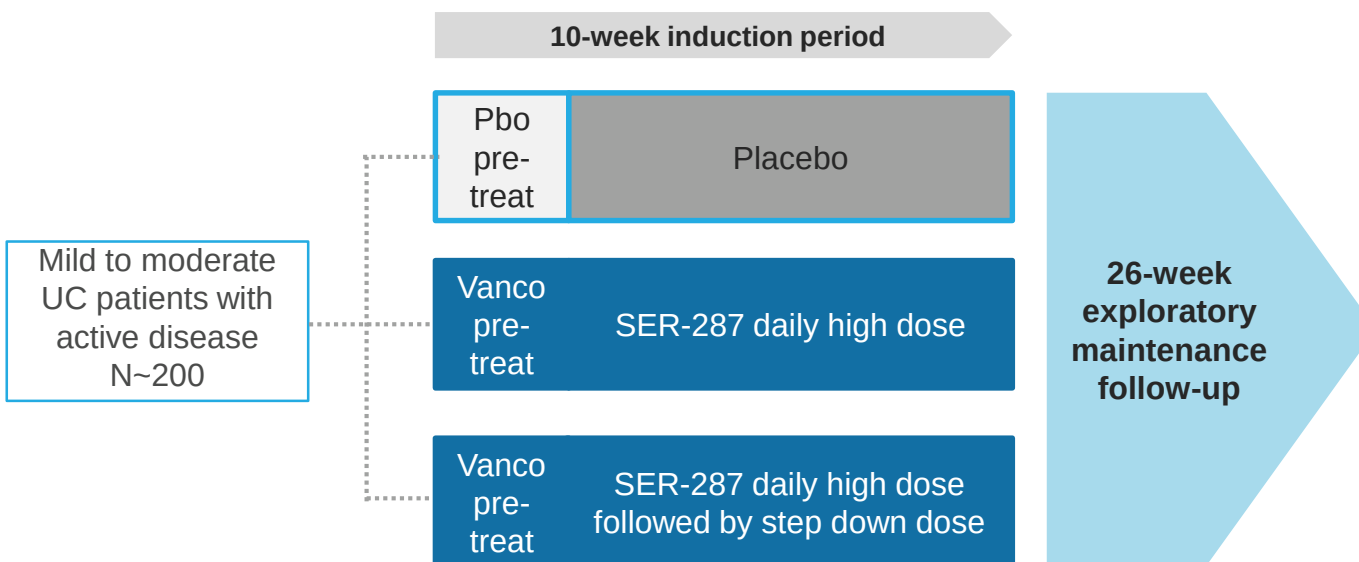
METABOLITES & PATHWAYS

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

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 top-line data in H2 2020**

SER-301: A next-generation, rationally designed live microbiome therapeutic candidate for the treatment of ulcerative colitis

Designed via in-human reverse translation discovery platform to modify the microbiome & microbe-associated metabolites

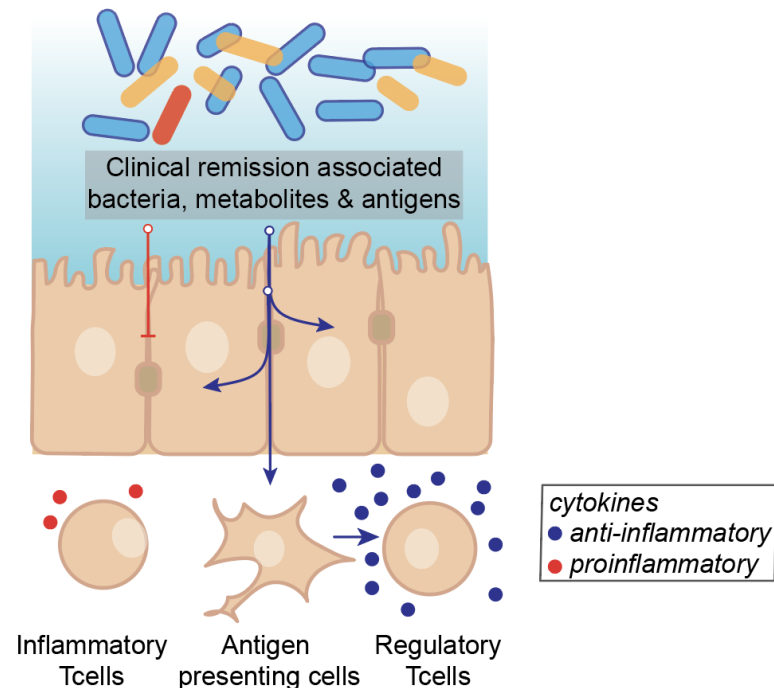
Incorporates key insights from SER-287 Phase 1b clinical study data

- Species & microbial-derived metabolites associated with clinical remission
- Species confirmed to engraft & colonize gut in human subjects with UC

- 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

Results and mechanistic hypotheses based on preclinical data

SER-301 catalyzes changes in microbiome & microbial-derived metabolites to reduce inflammation



Rationally designed fermented products may provide important advantages to microbiome therapeutics

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

Anticipate initiation of SER-301 clinical development in early 2020

Clostridium difficile Infection

Overview and SER-109 Phase 3 study



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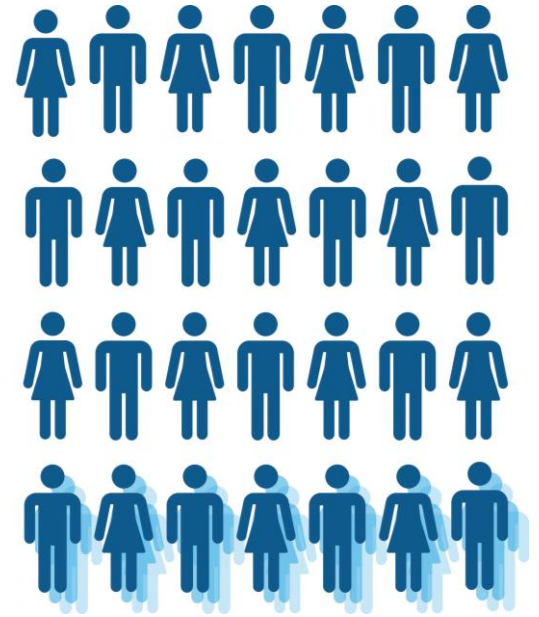


C. difficile infection overview and market opportunity

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

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

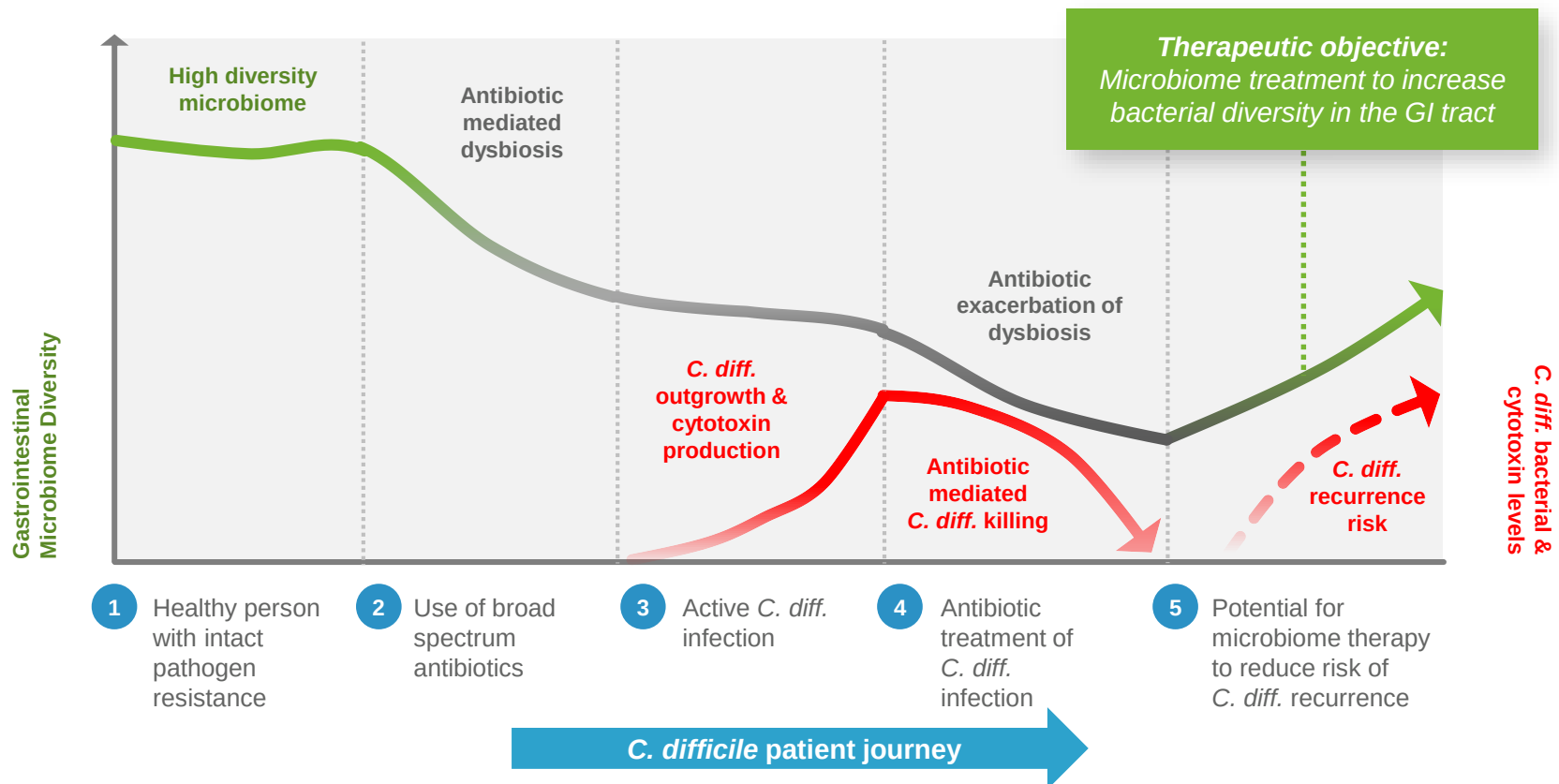
- ~ 453K cases of primary CDI within the U.S. each year
- ~ 170K episodes per year (100K episodes of first recurrence; ~ 73K episodes of 2+ recurrences)
- Estimated ~ \$4.8B in healthcare burden each year
- Unregulated FMT is viewed as effective, but inconvenient treatment given its invasive route of administration, high unmet medical need for FDA approved treatment options



25% of primary *C. difficile* recur

~29K deaths/year

Microbiome therapeutic intervention – Hypothetical patient course



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

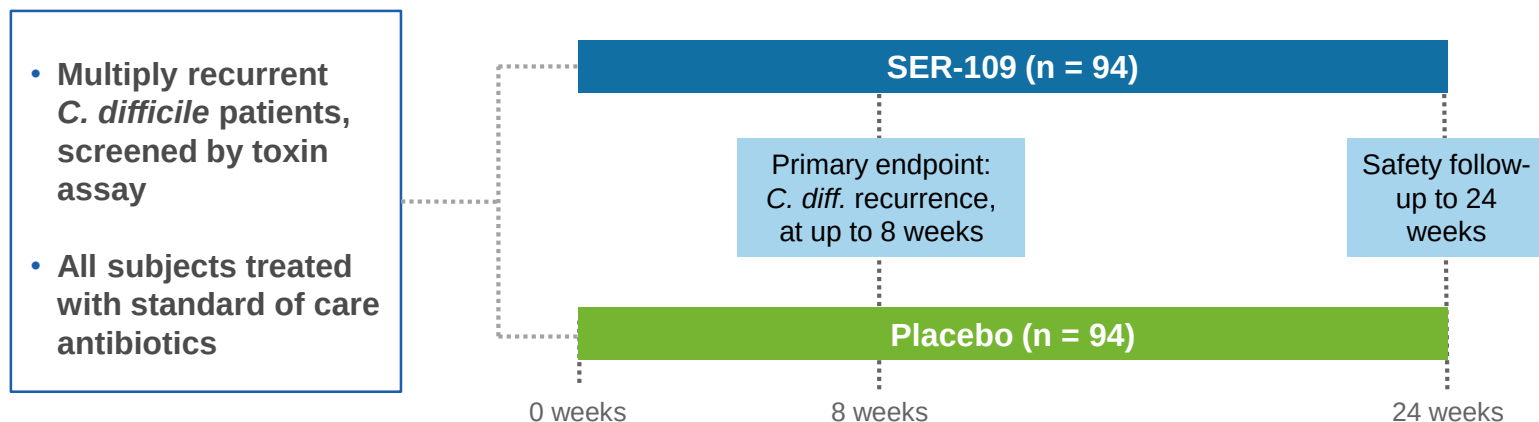


- Oral, donor derived, spore based therapeutic candidate designed to reestablish gastrointestinal microbiome diversity and resistance to *C. difficile* recurrence
- Multiple studies, and the widespread use of Fecal Microbiota Transfer (FMT), provide proof-of-concept
- Completed Phase 2 study in patients 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



ECOSPOR III may serve as basis for BLA submission



Anticipate SER-109 top-line results mid-2020

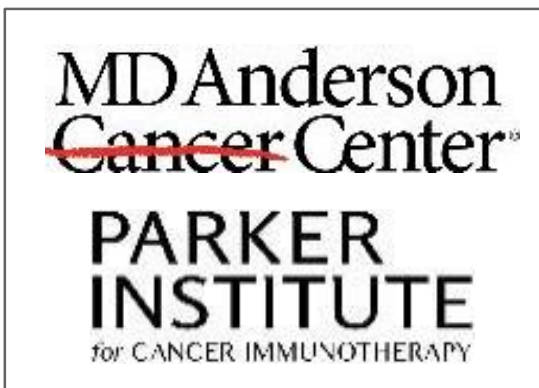
- *Based on FDA communications, Company believes ECOSPOR III has potential to be a single pivotal study that may support SER-109 product registration.*
- *Potential FDA approval based on successful ECOSPOR III study results would depend on the strength of the data, and additional safety data may be required.*

SER-401 and Immuno-oncology



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Collaborations to advance microbiome therapeutic into immuno-oncology



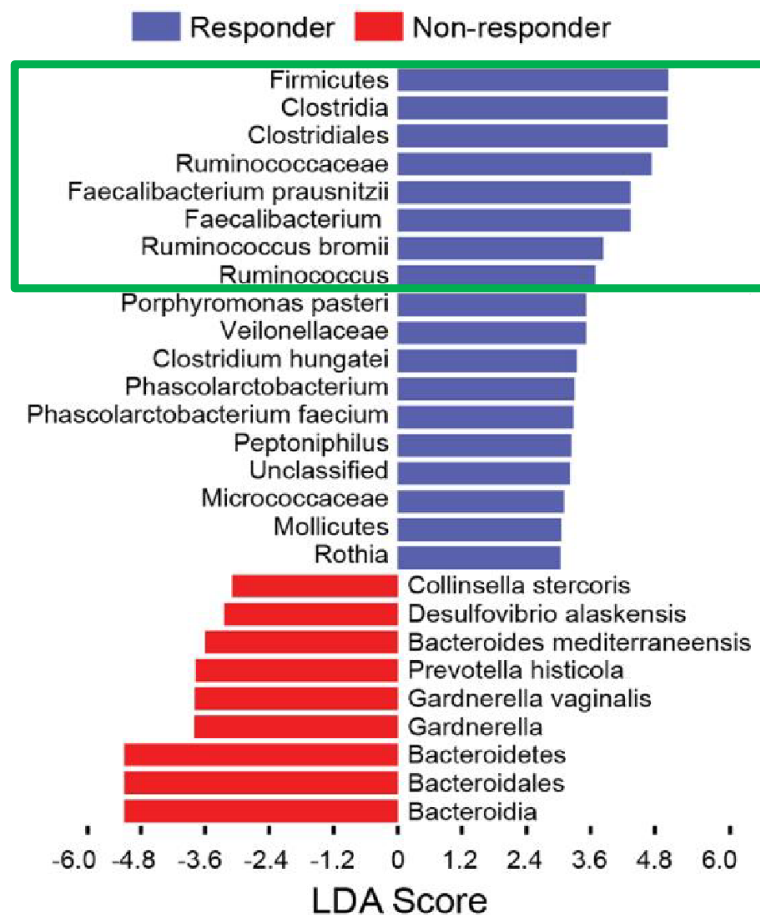
- SER-401 Phase 1b study with anti-PD-1 (nivolumab) in patients with metastatic melanoma
- **Initiated March 2019**
- Seres option to license foundational intellectual property from MD Anderson related to the use of bacteria in combination with checkpoint inhibitors



- 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

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

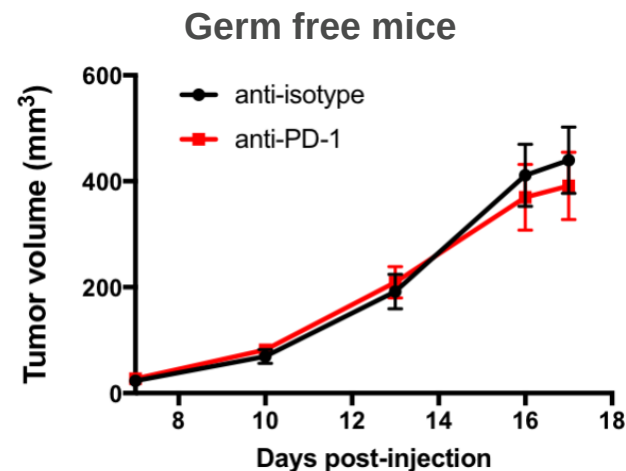
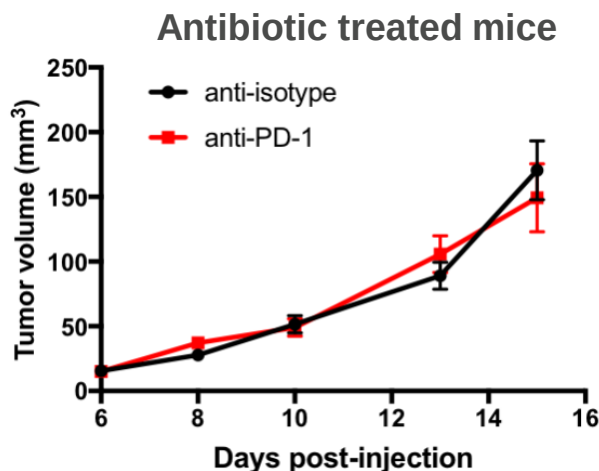
- SER-401 composition driven by bacteria consistent with responder profile
- Class Clostridia, family *Ruminococcaceae*
- E.g., *Ruminococcus* and *Faecalibacterium*
- All spore formers that leverage deep Seres expertise in the biology and manufacturing of these organisms



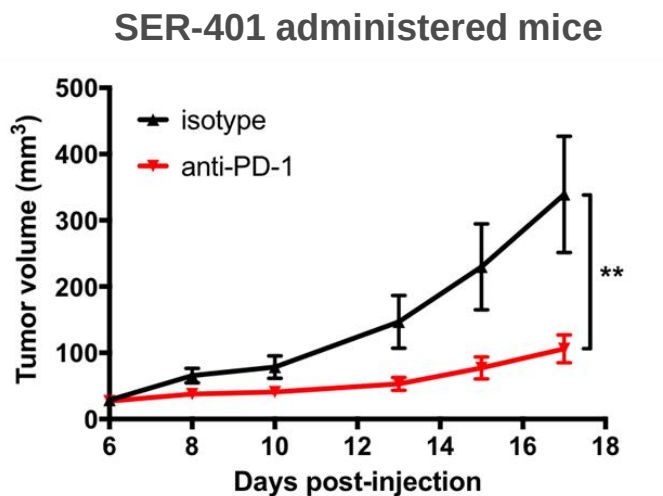
Based on preclinical studies, gut microbiome is essential for anti-PD1 efficacy



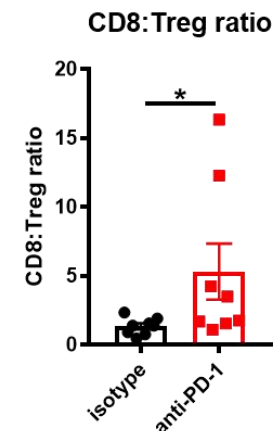
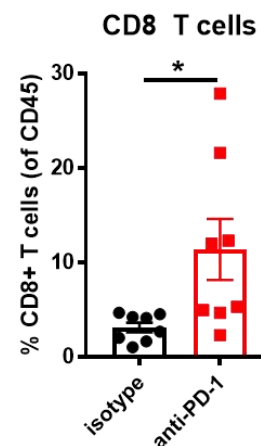
No anti-PD-1 response when microbiome is absent



Robust anti-PD-1 response with SER-401



Tumor infiltrate at end of study



Germ Free tumor model: MC38

Ongoing SER-401 Phase 1b study

First patient dosed in
March 2019

Study Objectives

Primary endpoint = safety and tolerability

All patients = CT scans with RECIST week 12

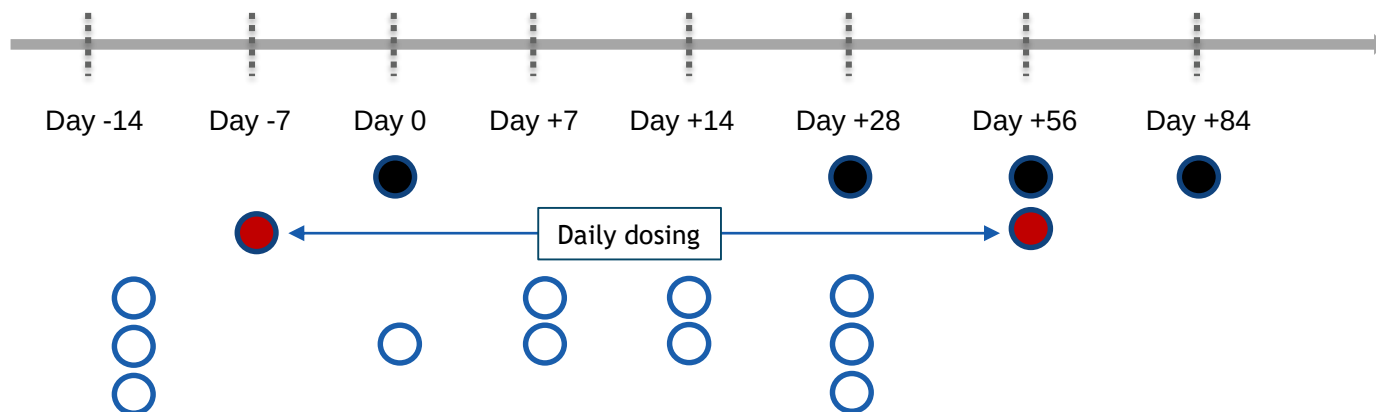
Secondary endpoints = engraftment,
response and correlative studies
(immune correlates in blood and tumor,
metabolites)



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

Placebo (n=10)

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



Anticipate SER-401 Phase 1b study results in H2 2020



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**
- 13 Issued US Patents obtained

15

Families of Applications

8

Nationalized

1

Pending Provisionals

PROJECTED BIOSIMILAR REGULATORY EXCLUSIVITY



12

years for new biological composition



10

years for new drug



Significant value drivers anticipated in 2020

SER-287	Ulcerative colitis – Phase 2b study ongoing; Top-line data in H2 2020
SER-109	Recurrent <i>C. difficile</i> infection – Phase 3 ongoing; top-line data in mid 2020
SER-401	Metastatic melanoma – Phase 1b study ongoing; Preliminary results expected in H2 2020
SER-301	Next generation platform, rationally designed fermented compositions; Initiate SER-301 clinical development for UC in early 2020
Discovery efforts	AstraZeneca collaboration targeting novel I-O mechanisms and potential synergy with AstraZeneca oncology pipeline

Balance Sheet	As of end of Q3 2019
Cash, cash equivalents and investments	\$83.8 M

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



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