Seres Therapeutics Overview

April 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 or clinical trial data, the ability of our clinical trials to support approval, the timing of clinical studies, 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 Annual Report on Form 10-K filed on March 2, 2020, the Company’s Current Report on Form 8-K filed on March 18, 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.

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	**Late stage clinical studies ongoing**: • SER-109 Phase 3 top-line data in mid 2020 • SER-287 Phase 2b study* • SER-401 Phase 1b study* • SER-301 initiate clinical development
Team	Experienced, highly accomplished leadership team

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

* Due to COVID-19, SER-287 and SER-401 readout timing is uncertain. As of March 30, 2020, the SER-287 Phase 2b study was ~60% enrolled based on 201 patient target size. Seres is evaluating potential SER-287 study design modifications with the goal of obtaining high quality, clinically interpretable study results.

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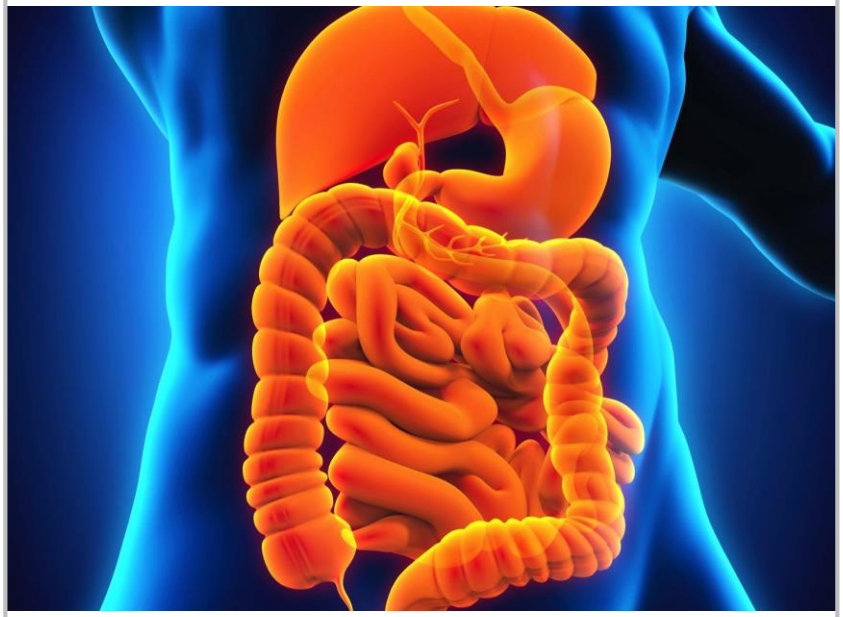
Modulation of the human microbiome is a significant opportunity for novel therapeutics

~30-50 trillion bacterial cells
live in or on the human body



Gut microbiome is an ecosystem powered by microbe-microbe & microbe-host interactions

Alterations of microbiome
result in gain- or loss-of-function that impacts human:

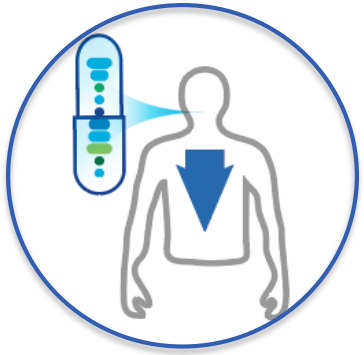
- Resistance to pathogens
- Gut & systemic inflammation
- Innate & adaptive immunity
- Regulation of metabolism

Microbiome is associated with human disease:

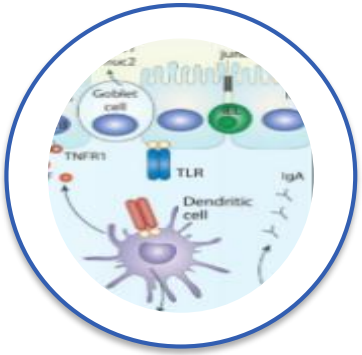
- Infectious (e.g. *C. difficile*)
- Inflammatory (e.g. Ulcerative colitis)
- Cancer (e.g. tumor progression)
- Metabolic & Cardiovascular (e.g. NASH)
- Neurological (e.g. depression)

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

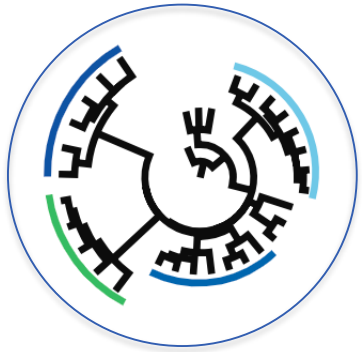
Ecobiotic® Live Microbiome Biotherapeutics are encapsulated consortia of commensal bacteria with specific pharmacologic properties



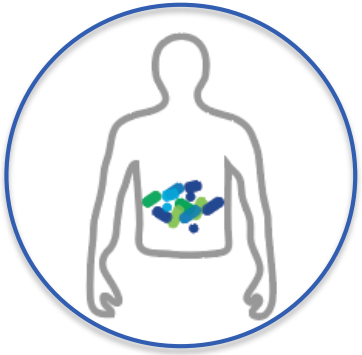
Formulated for **oral delivery** using current Good Manufacturing Practices (cGMP)



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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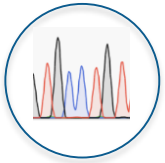
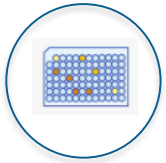
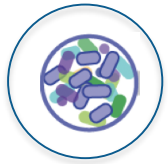
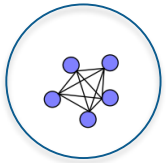
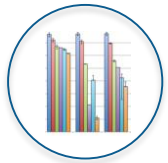
Industry-leading, in-house drug discovery, development & manufacturing platforms

Disease Target Identification	Hit-to-Lead Identification	Lead Optimization & Bioprocess	End-to-End GMP Manufacturing
Microbiome Biomarker Discovery	Consortia Design	Pharmacological Properties Validation	Orally-delivered formulation
 Clinical sample biorepository	 Broad strain library & culturing know-how	 Ex vivo & in vivo disease modeling	 Donor-derived & multi-strain fermentation
 Proprietary genomic & metabolomic analytics	 Genomic & host function screening	 Culturing know-how & advanced drug formulations	 Anaerobic, spore & lyophilized technologies
 World-class collaborations	 In-silico drug design for functional targets		 Late clinical stage drug release assays

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Two-pronged strategy

Advanced clinical programs to meaningful data readouts	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 *C. difficile* infection	
SER-401 Ph 1b for immuno-oncology	

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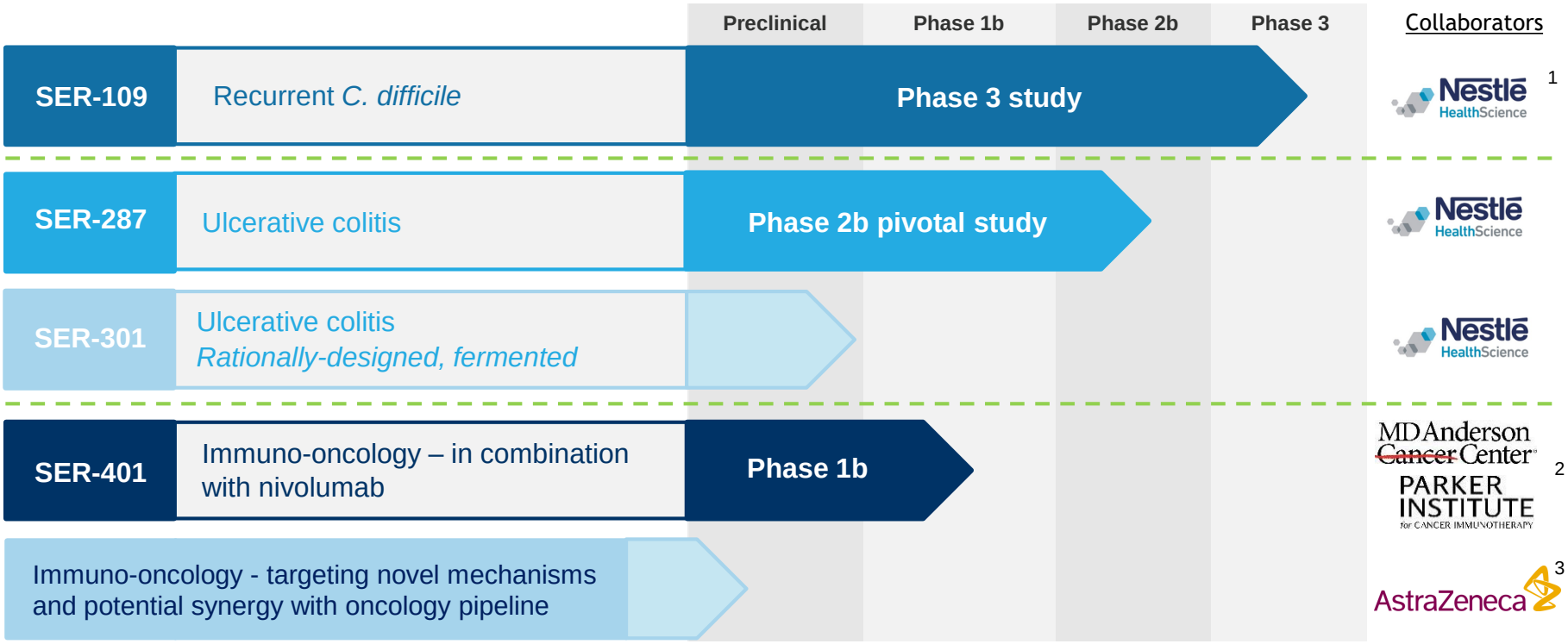
Prioritized pipeline



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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Clostridium difficile Infection

Overview and SER-109 Phase 3 study

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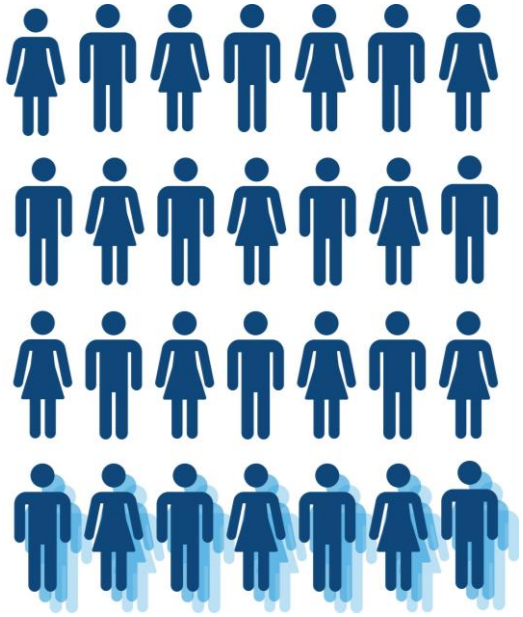
C. difficile infection overview and market opportunity

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 ~ $5B 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

Source: L.E.K. analysis of interviews, survey, and secondary research; * 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

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NEW

Increasing FMT safety concerns highlight the urgent 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

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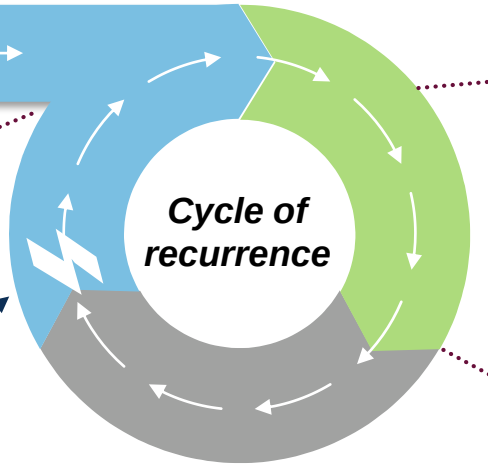
Breaking the CDI cycle requires both *antibiotics* and a *microbiome therapeutic*

CDI onset:

Microbiome disruption followed by *C. difficile* exposure and spore germination

More antibiotics for CDI



Spores unaffected, dysbiosis exacerbated

CDI recurs

A 2-pronged treatment approach

1 ***CDI-targeted antibiotics to kill the vegetative bacteria***

2 ***Potential for a microbiome drug to break the cycle of recurrent CDI by restoring microbiome health***

SER-109

(investigational drug candidate)

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SER-109 is an investigational, donor derived, spore-based therapeutic designed to break the cycle of recurrent in CDI by restoring the microbiome

Strong Scientific Rationale

Breaks cycle of rCDI by preventing spore germination through microbiome restructuring

Evidence Towards Understanding MOA

SER-109 engraftment associated with reduced recurrence

Addresses Significant Unmet Need

Substantial need for a new, FDA-approved treatment for multiply recurrent CDI patients

Reliable Composition

Purified bacterial spores biologically sourced from healthy screened donors

Convenient Dosing & Administration

Oral dose of 4 capsules once daily for 3 days

Safety

Prior clinical studies demonstrated favorable tolerability and safety

Granted FDA Status

Obtained FDA breakthrough and orphan drug designations

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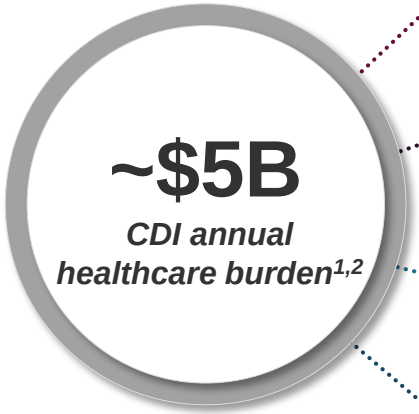
Substantial burden on the U.S. healthcare system



- **Significant portion of CDI economic burden is attributed to CDI recurrence[1]**
- **Estimated ~170K recurrent CDI cases occur every year[1]**
- **Cumulative hospitalized days attributable to a recurrent CDI episode is ~2 days[2]**
- **Total annual cost of a recurrent CDI patient is >$34K[3]**

1. Desai, et al. *BMC Infectious Diseases* (2016) 16:303; 2. Zhang, et al. *Clinical Infectious Diseases* (2018) 66:9; 3. Rodrigues, et al. *Infect Control Hosp Epidemiol* (2016),1–7;

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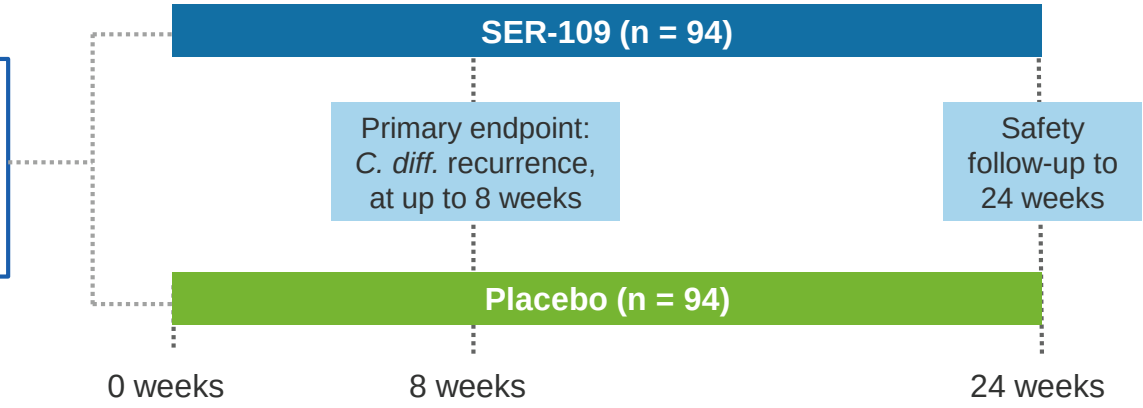
ECOSPOR III may serve as basis for BLA submission; enrollment complete, top-line results expected in mid-2020*

- Multiply recurrent *C. difficile* patients
- All subjects treated with standard of care antibiotics



Key study features:

Toxin testing to ensure inclusion of subjects with active rCDI, and for accuracy of endpoint	~10X 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

- 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

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* Due to COVID-19 ECOSPOR III enrollment has been halted; Company expects at least 181 patients enrolled.

Commercial readiness activities initiated

- ✓ *C. difficile* market opportunity assessment
- ✓ Key stakeholder primary research (physician, patient, and payer)
- ✓ Recurrent CDI patient segmentation and site-of-care analysis
- ✓ Publication and congress plan developed
- ✓ Deepening advocacy relationships

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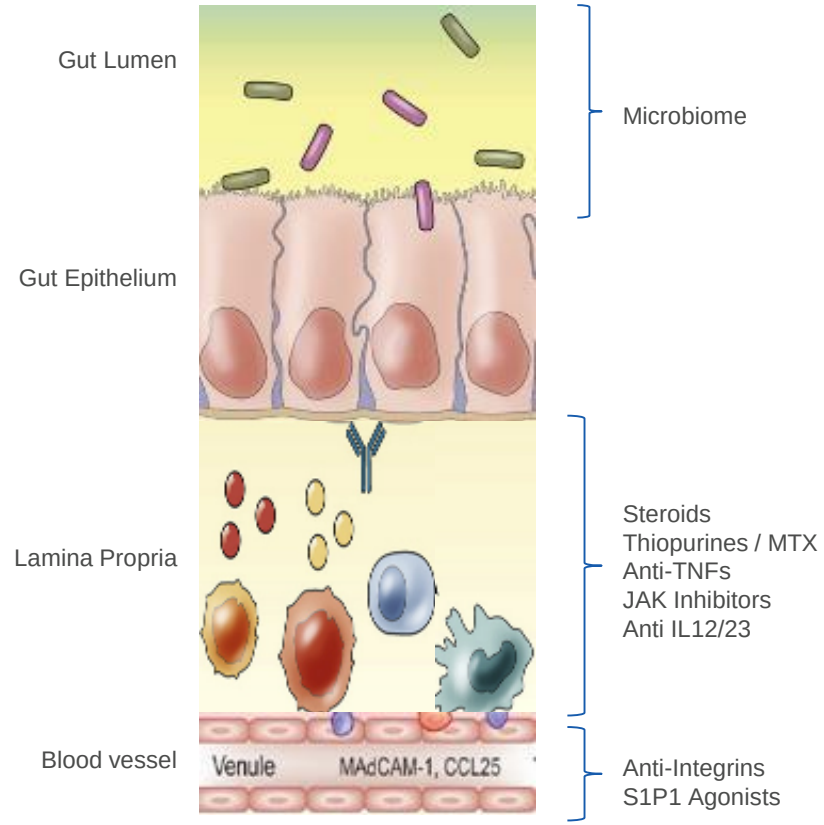
The dysbiotic microbiome may be a trigger of inflammation in ulcerative colitis



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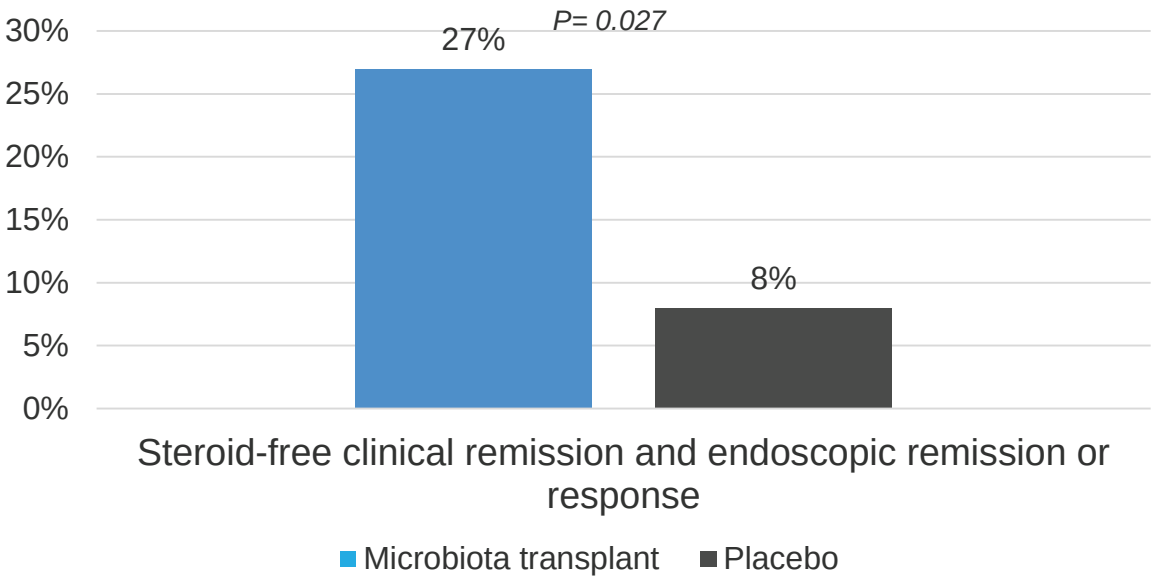
Published study regarding microbiota transplantation provided clinical proof-of-concept in ulcerative colitis

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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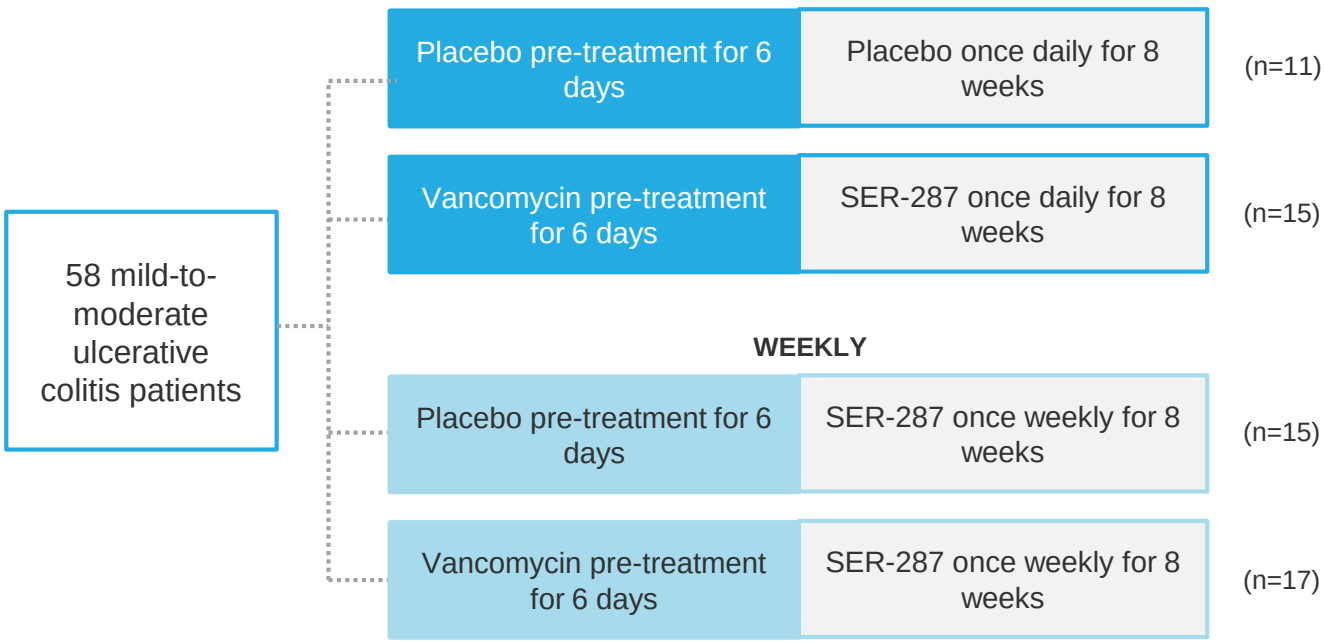
SER-287 Phase 1b ulcerative colitis study



Primary Objectives

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

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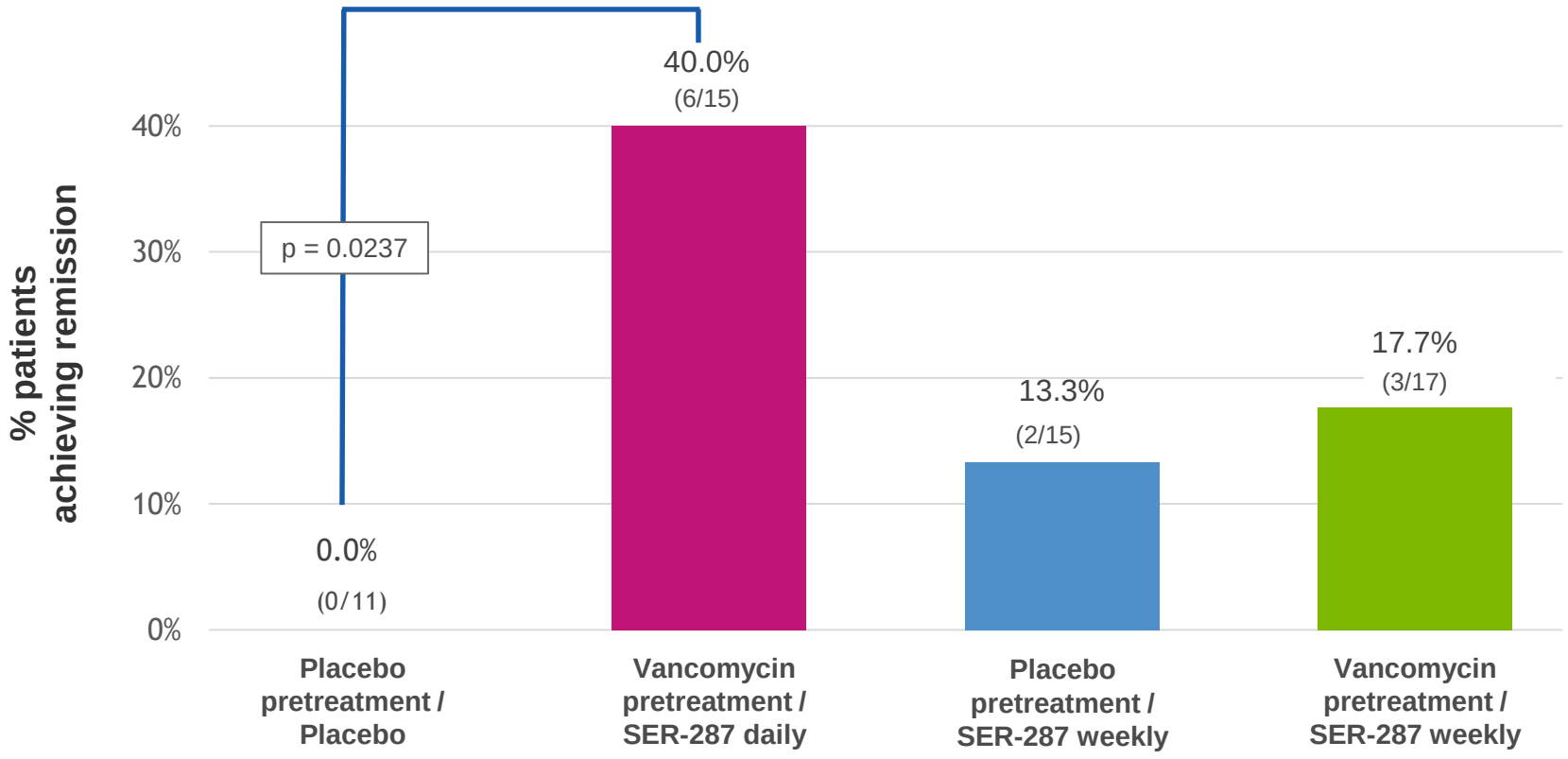
Phase 1b study results – Statistically significant clinical remission improvement observed in Vanco/SER-287 daily treatment arm



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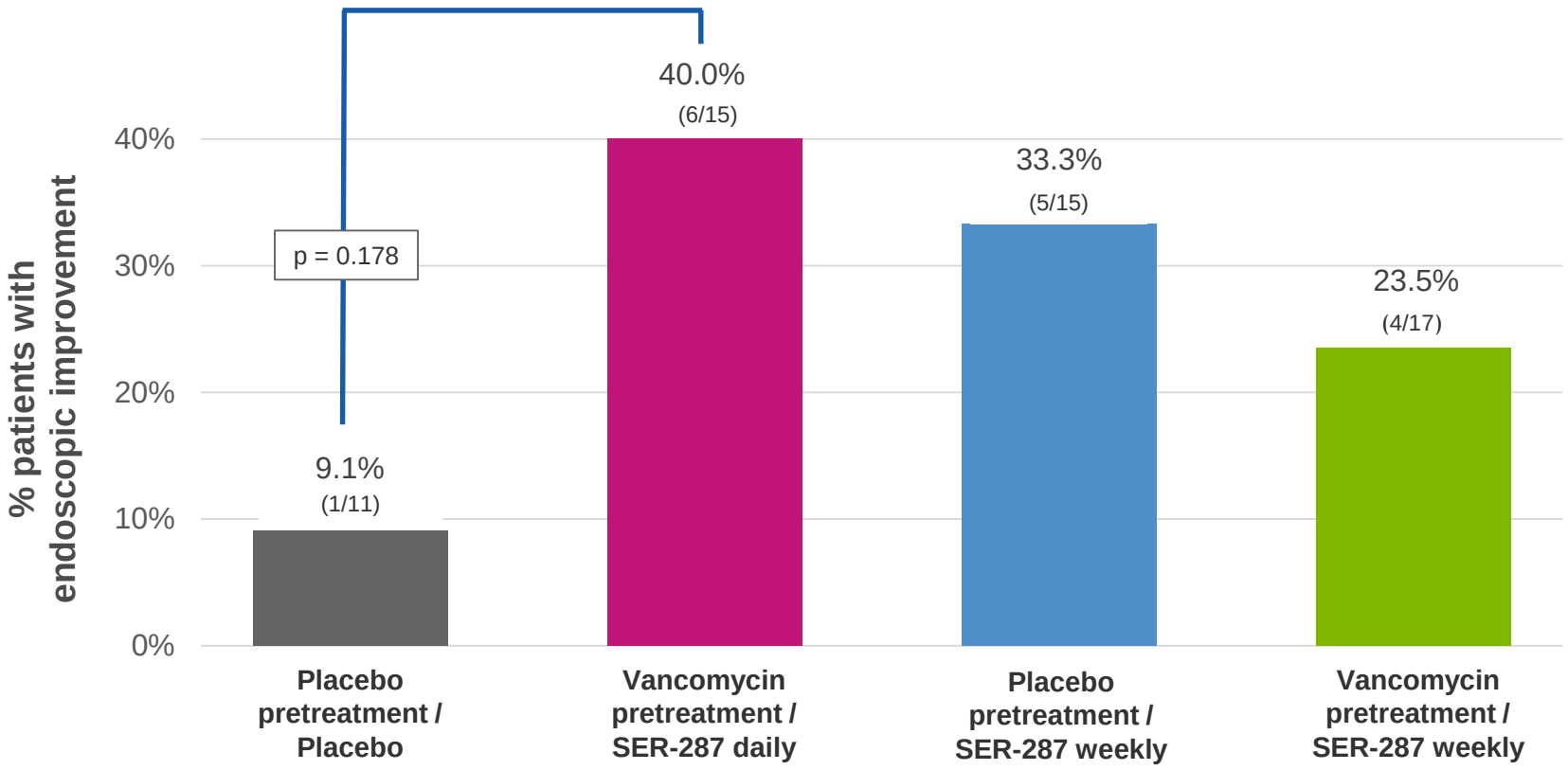
Phase 1b study results - Dose dependent impact on endoscopic improvement in Vanco/SER-287 daily treatment arm



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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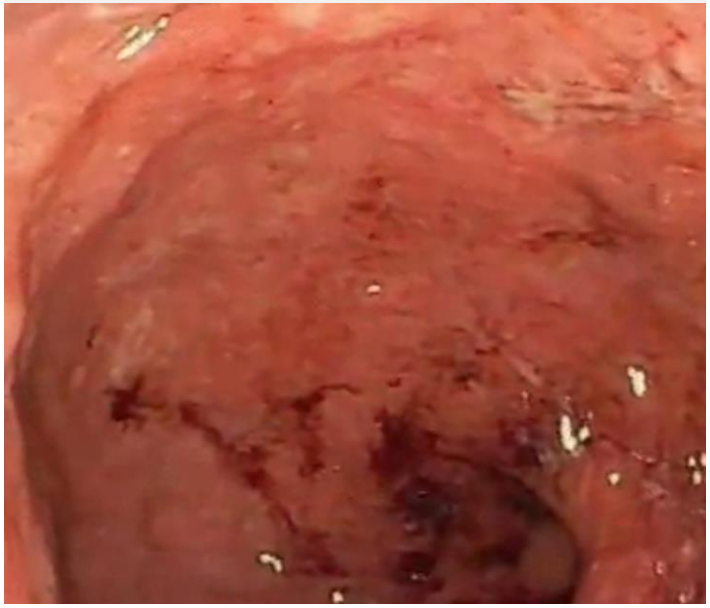
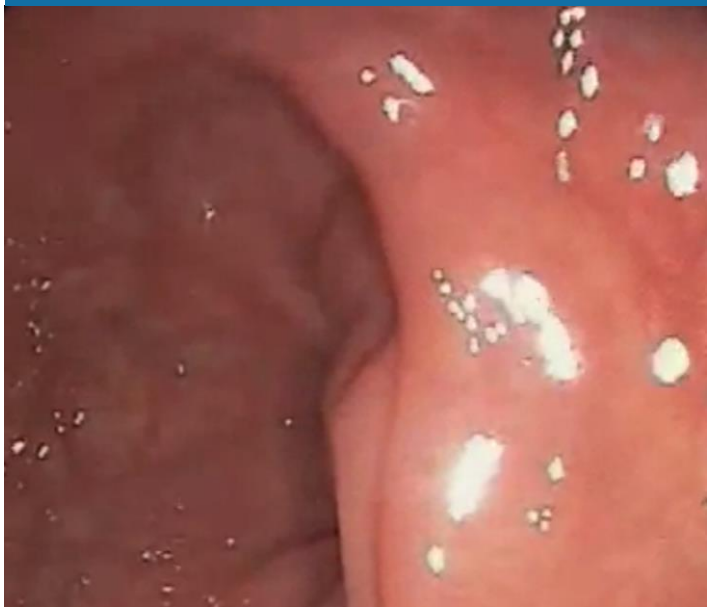
Illustrative endoscopy improvement — Vanco/SER-287 daily treatment

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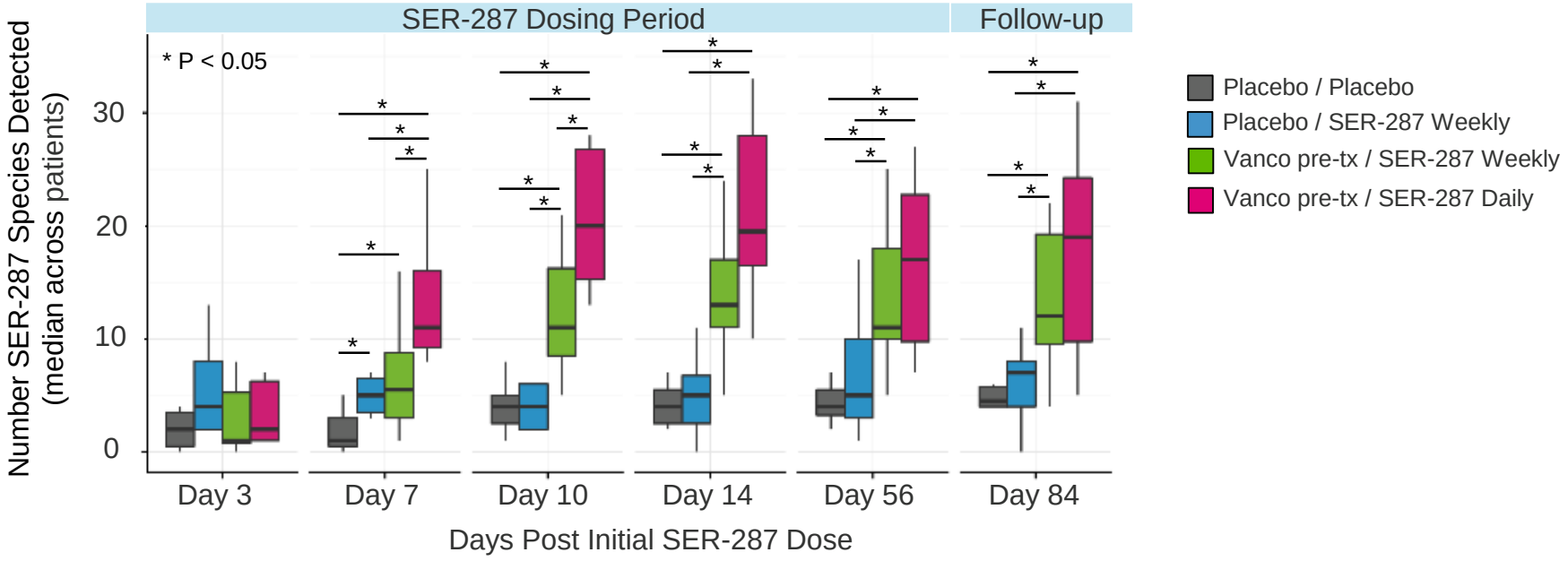
Phase 1b study results – SER-287 bacteria engrafted in subjects and was durable to four weeks after dosing



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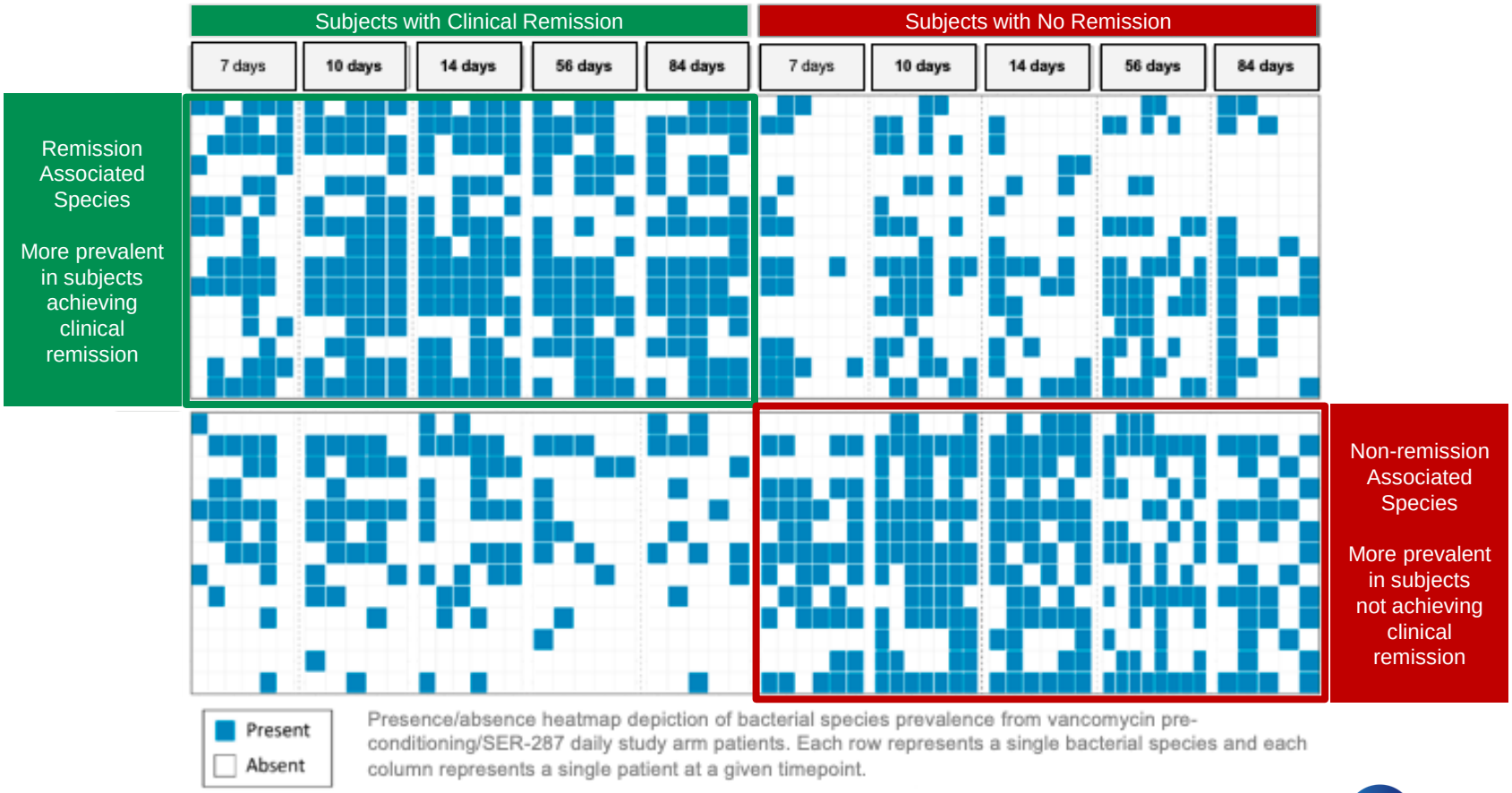
Phase 1b study results — Identified bacterial species signature that associates with clinical remission vs non-remission

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



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.

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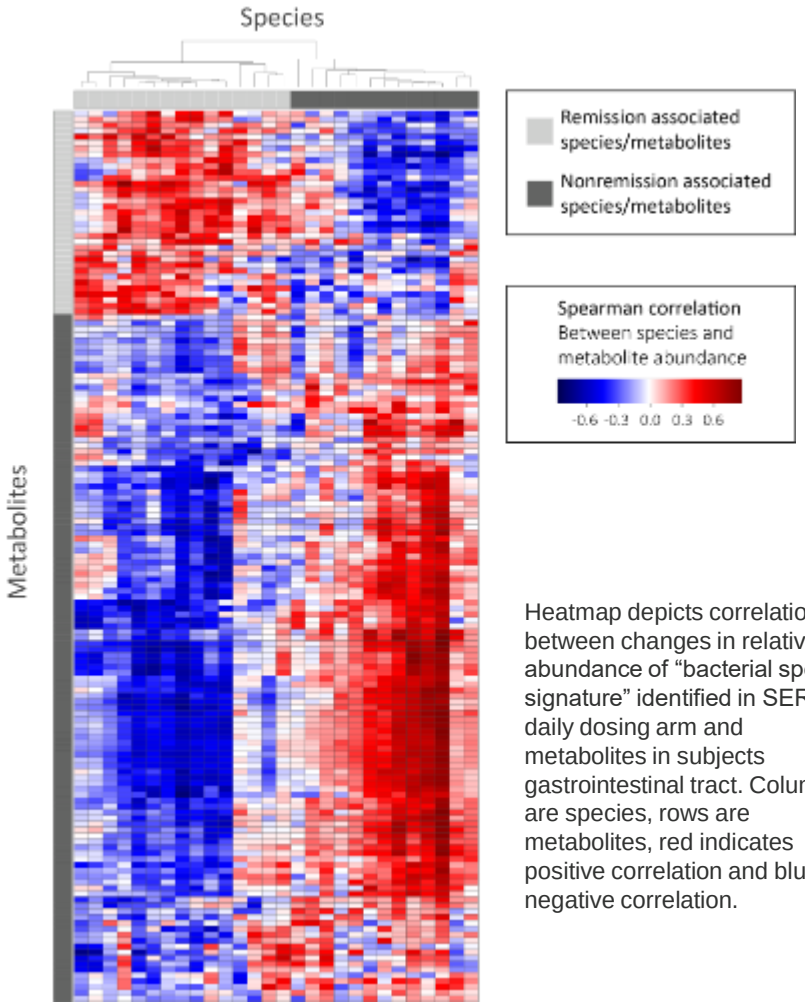
Microbiome signature of remission strongly correlated with metabolite shifts in patients administered SER-287



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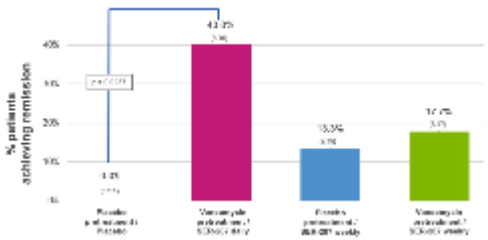
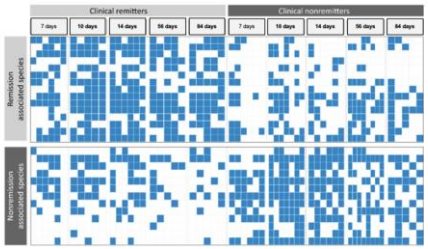
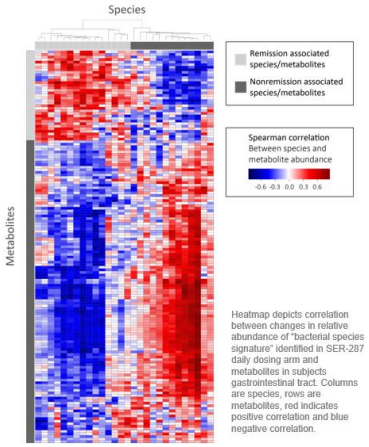
SER-287 Phase 1b data provide evidence of clinical activity and provide supportive mechanistic data







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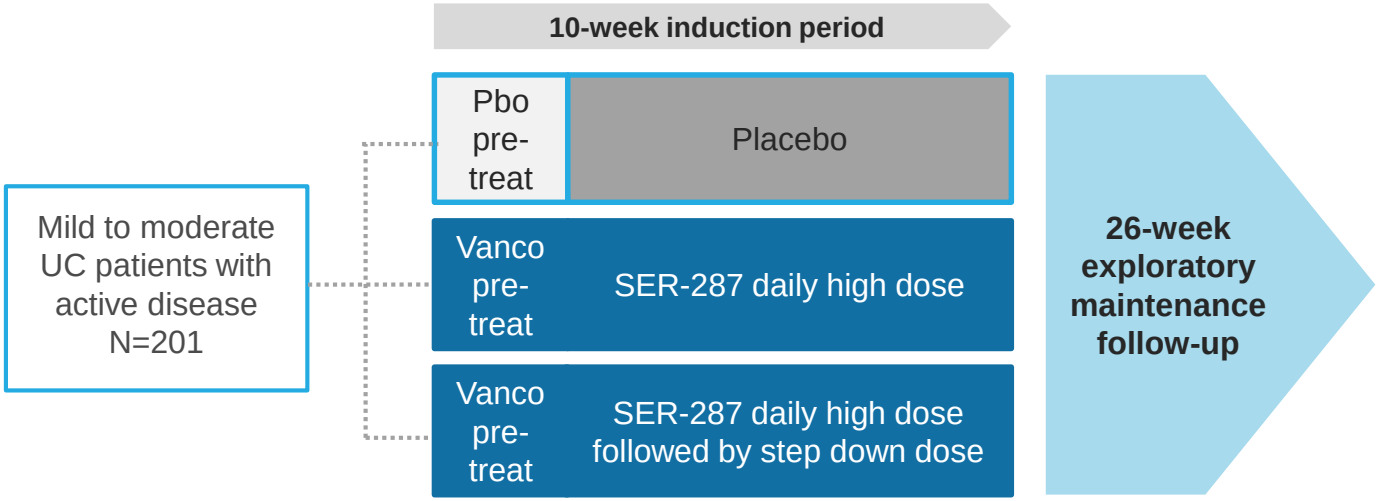
Ongoing SER-287 ECO-RESET Phase 2b study in patients with mild-to-moderate active ulcerative colitis



- 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
- Due to COVID-19, SER-287 readout timing is uncertain. As of March 30, 2020, the SER-287 Phase 2b study was ~60% enrolled based on 201 patient target size. Seres is evaluating potential SER-287 study design modifications with the goal of obtaining high quality, clinically interpretable study results

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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

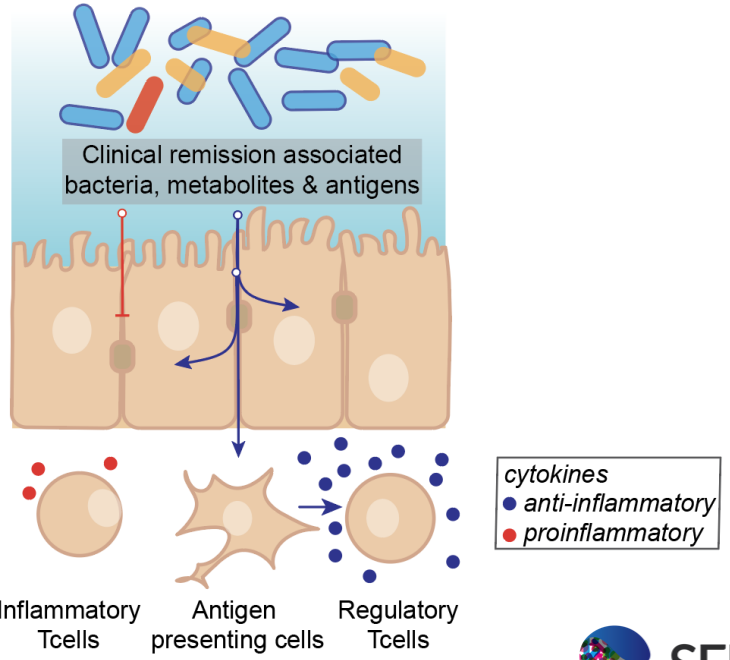
Incorporates key insights from SER-287 Phase 1b clinical study data

- 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



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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

- **Lead candidate designated — SER-301 for ulcerative colitis**
- **Activities to initiate clinical development ongoing**

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SER-401 and Immuno-oncology

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Collaborations to advance microbiome therapeutic into immuno-oncology

MD Anderson Cancer Center

PARKER INSTITUTE for CANCER IMMUNOTHERAPY

- 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

AstraZeneca

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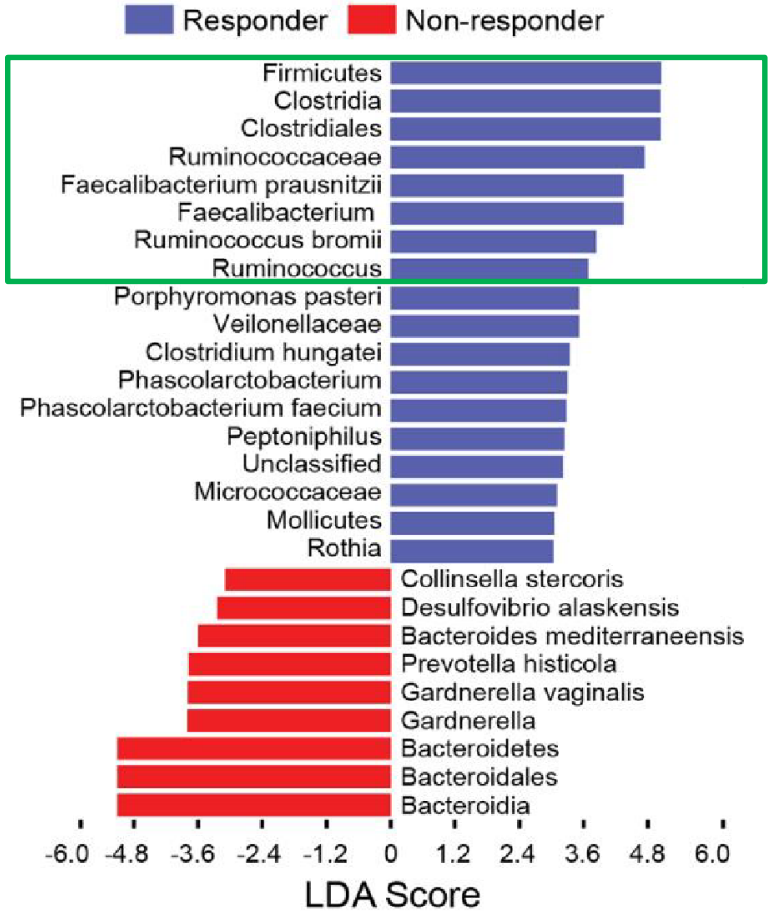
MD Anderson collaborators have identified a microbiome signature in melanoma patients who respond to anti-PD-1

- SER-401 composition driven by bacteria consistent with responder profile
  - Class Clostridia, family *Ruminococcaceae*
  - E.g., *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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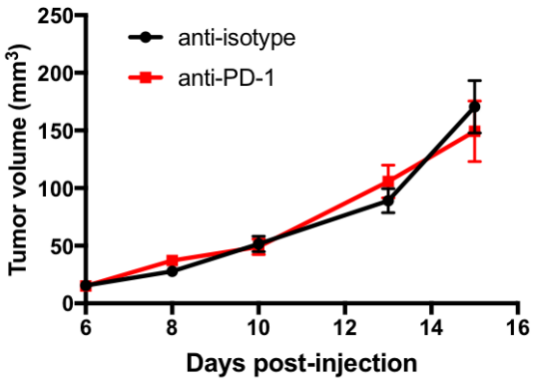
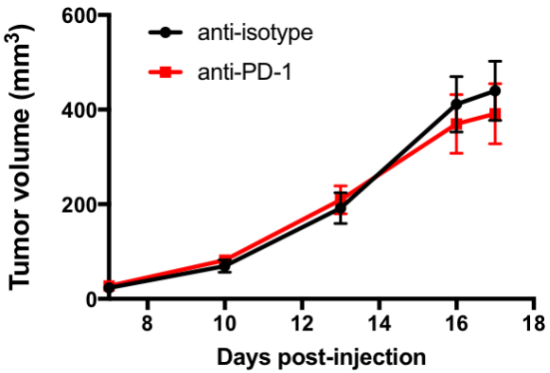
Based on preclinical studies, gut microbiome is essential for anti-PD1 efficacy

No anti-PD-1 response when microbiome is absent

Antibiotic treated mice

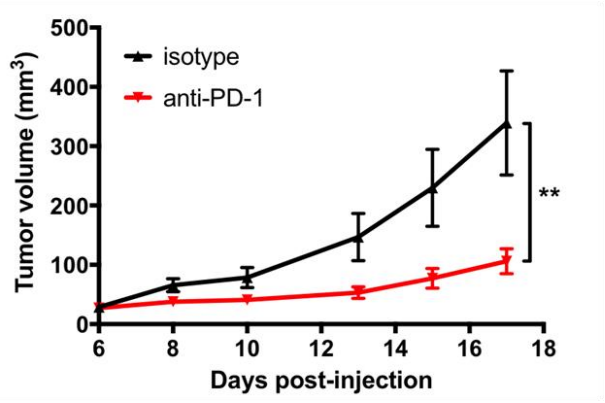


Germ free mice

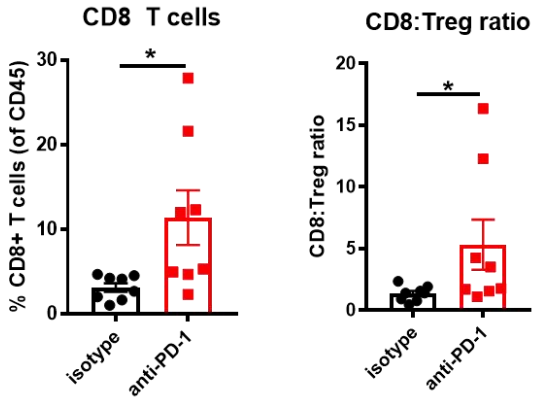


Robust anti-PD-1 response with SER-401

SER-401 administered mice



Tumor infiltrate at end of study



Data presented at AACR meeting March 2019

Germ Free tumor model: MC38

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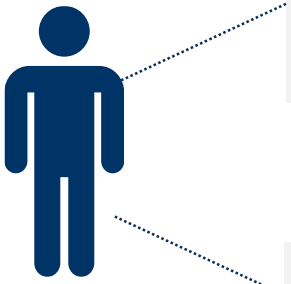
Ongoing SER-401 Phase 1b study



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)

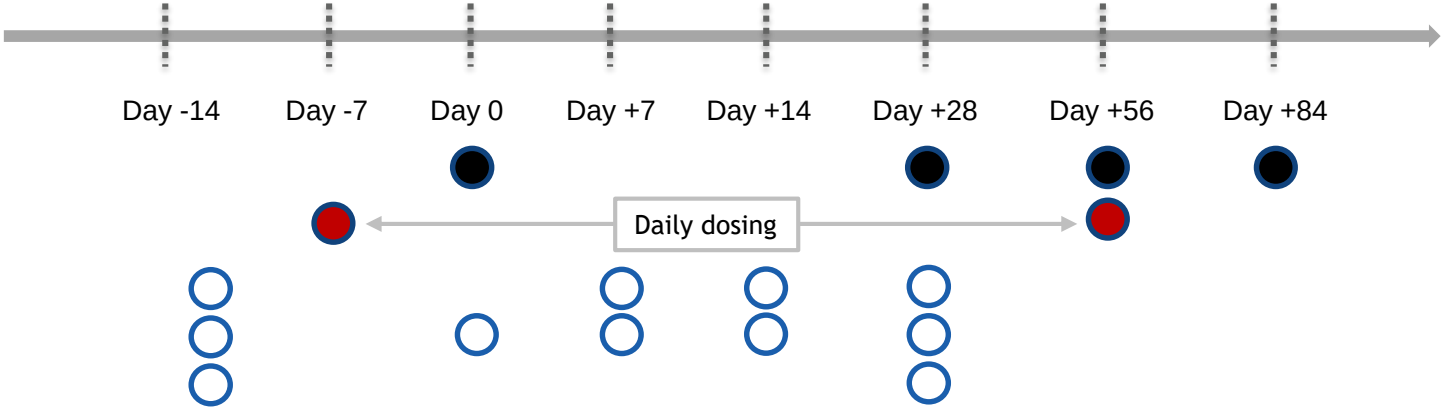
Placebo (n=10)

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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Broad IP portfolio and regulatory exclusivity

PATENT PORTFOLIO OF OWNED & LICENSED PATENTS AND APPLICATIONS*

- 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**
13	**Nationalized**
1	**Pending Provisionals**

PROJECTED BIOSIMILAR REGULATORY EXCLUSIVITY

12 years for new biological composition

10 years for new drug

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Significant value drivers anticipated in 2020

SER-109	Recurrent *C. difficile* infection – Phase 3 enrollment complete; top-line data in mid 2020
SER-287	Ulcerative colitis – Phase 2b study ongoing; ~60% enrolled as of March 30, 2020; study design modifications are under evaluation
SER-401	Metastatic melanoma – Phase 1b study ongoing
SER-301	Next generation platform, rationally designed fermented compositions; Activities to initiate clinical development ongoing*
Discovery efforts	AstraZeneca collaboration targeting novel I-O mechanisms and potential synergy with AstraZeneca oncology pipeline

Balance Sheet	As of end of Q4 2019
Cash, cash equivalents and investments	$94.8 M

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

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