



Jefferies 2018 Global Healthcare Conference

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SERES
THERAPEUTICS™

Leading the Microbiome Revolution

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, statements on the timing and results of our clinical trials, the sufficiency of our financial resources, and dysbiosis as an underlying cause of disease or failed response to therapy. 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 8, 2018 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

Opportunity

Phase 3 stage company developing microbiome-based therapeutics, a highly promising new area of medicine

Platform

Leader in microbiome drug development with differentiated capabilities, leading CMC and demonstrated GMP quality, and supportive clinical data

Pipeline

Focused R&D efforts in the areas of infectious diseases and inflammation & immunology, including immuno oncology

Team

Experienced, highly accomplished leadership team

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



Business strategy

Focused R&D on clinical programs

- Prioritize serious diseases where dysbiosis of the gut microbiome has a causal role

**SER-287 for
Ulcerative Colitis**

***SER-109 for recurrent
C. difficile infection***

**Adjunctive microbiome
therapy with
immuno-oncology**

World class, differentiated, microbiome expertise

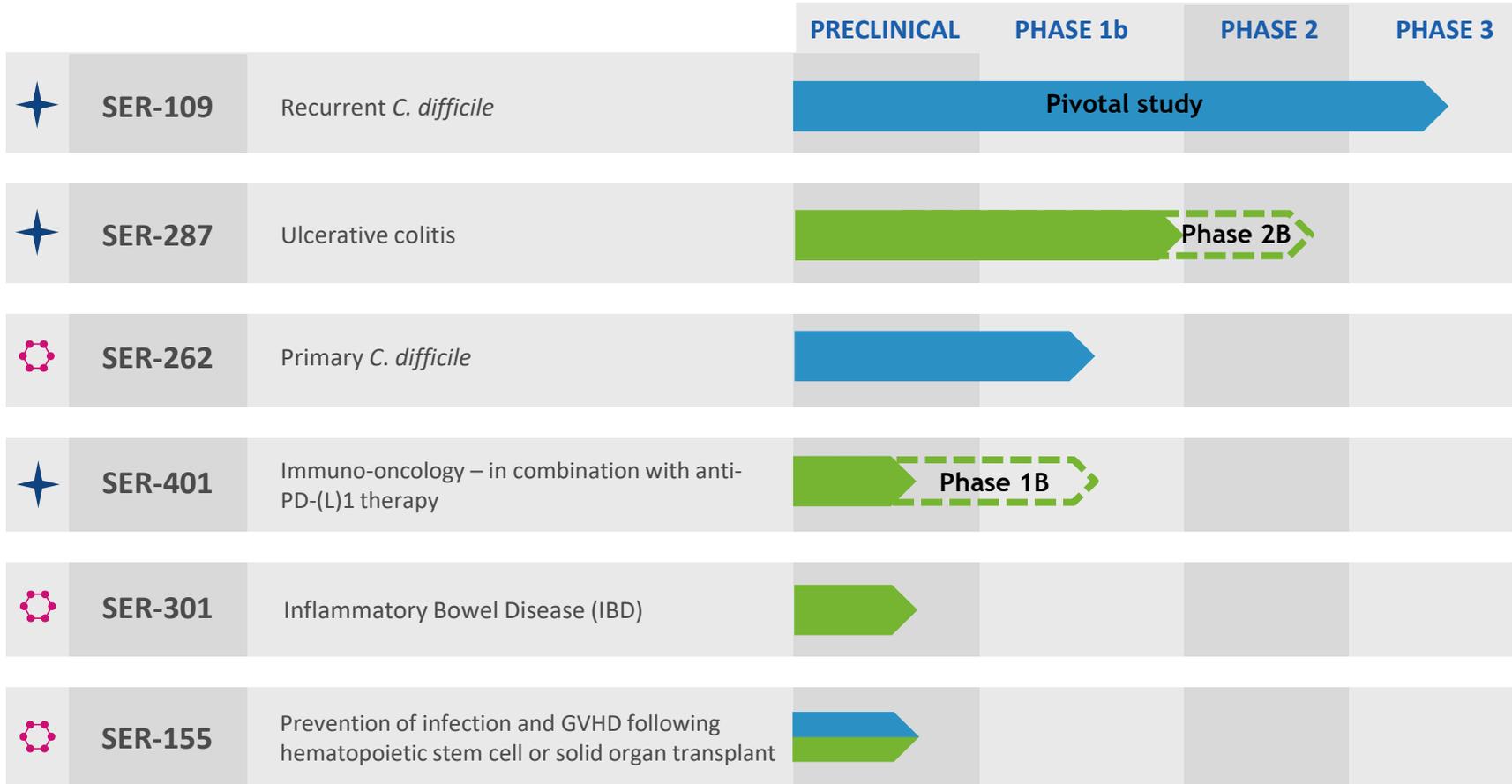
- Computational biology
- Basic microbiome research
- Microbiology
- Translational science
- Clinical development
- Advanced GMP manufacturing

Research in new therapeutic areas

- Collaborations with leading academic centers to efficiently advance research in promising new areas



Robust microbiome therapeutics pipeline



🌸 Synthetically fermented
 ★ Biologically sourced
 ➡ Infectious
 ➡ Inflammatory

Research Collaborations







Clostridium difficile Infection

Overview and R&D Programs



Leading the Microbiome Revolution

C. difficile infection overview

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

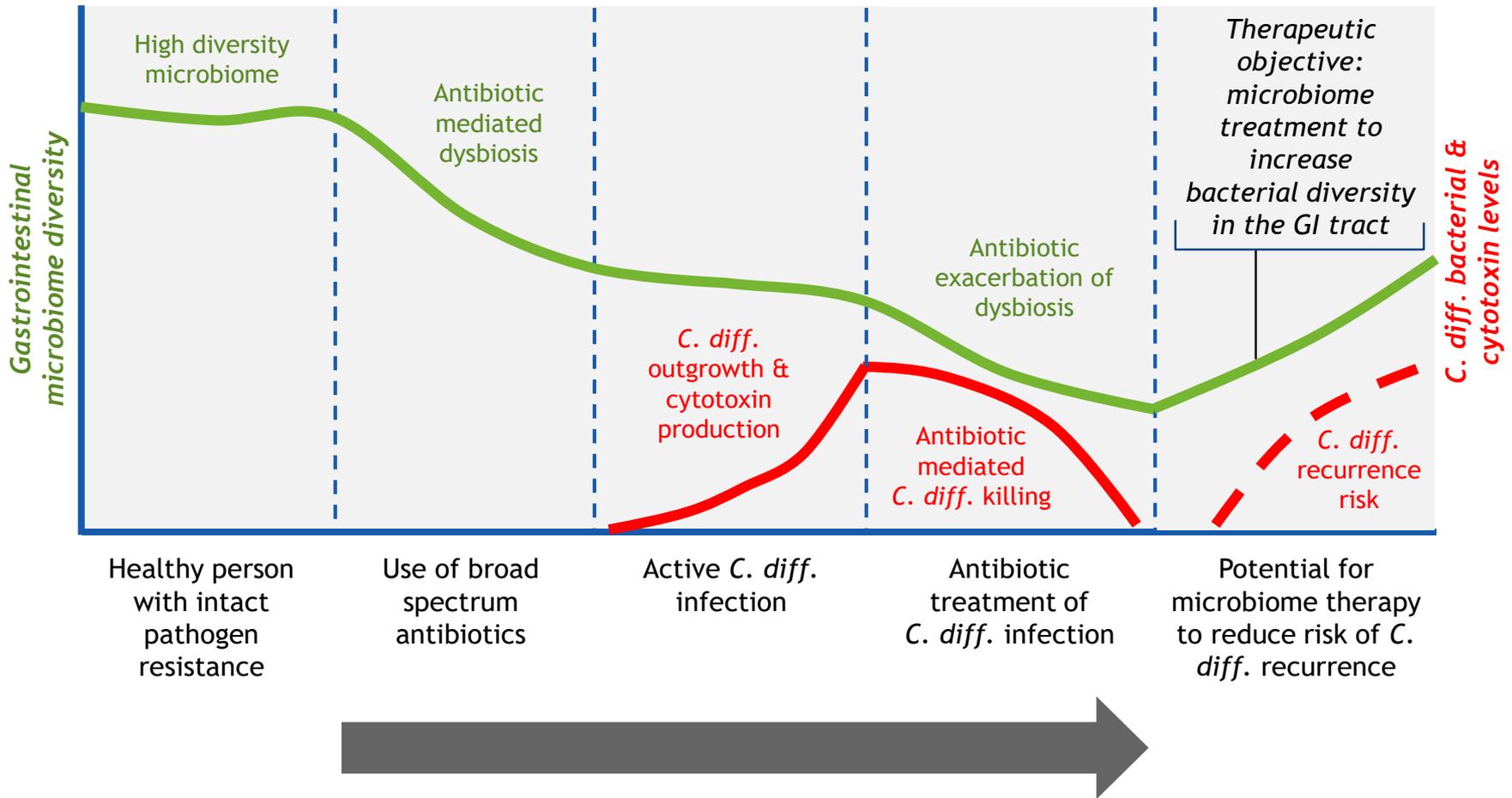
Leading cause of hospital-acquired infection in the US

- 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



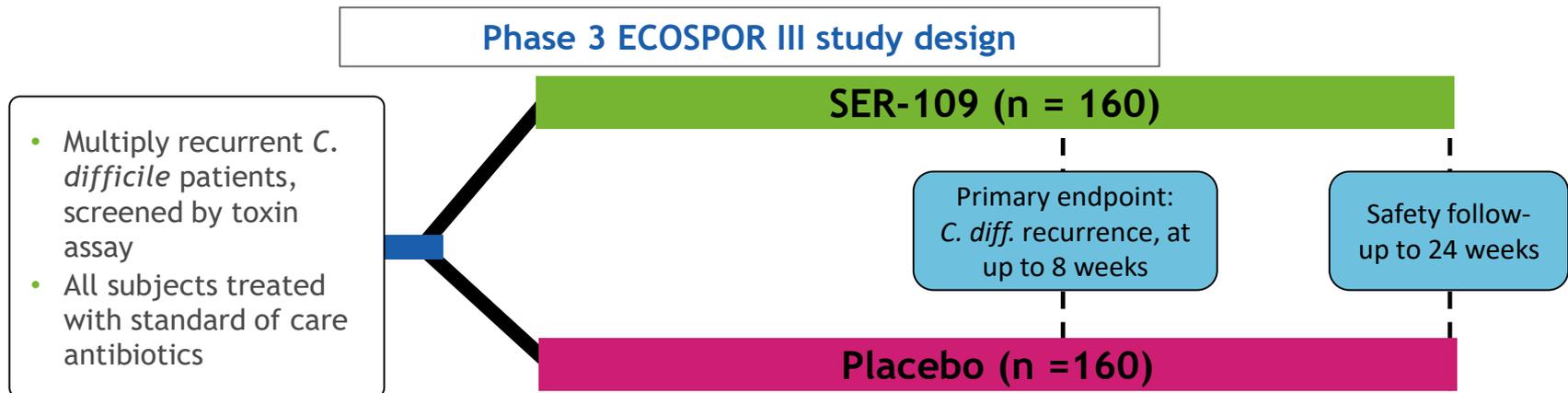
Microbiome therapeutic intervention - Race to Repair

Hypothetical patient course



Phase 3 SER-109 ECOSPOR III study - enrollment progress ongoing

- FDA Breakthrough and Orphan Drug designation
- Based on FDA feedback, ECOSPOR III designated as a Phase 3 study
- Phase 3 study incorporates key learnings from prior clinical studies:
 - SER-109 dose is approximately 10-fold higher than dose used in Phase 2 study
 - *C. difficile* toxin assay to be used at study entry and for primary endpoint



SER-262 Phase 1b dosing study in patients with primary *C. difficile* infection

96 patients with primary *C. difficile* infection

Cohort 1: Tx with 10^4 spores (n=10); placebo (n=2); single dose

Cohort 2: Tx with 10^5 spores (n=10); placebo (n=2); single dose

Cohort 3: Tx with 10^6 spores (n=10); placebo (n=2); single dose

Cohort 4: Tx with 10^7 spores (n=10); placebo (n=2); single dose

Cohort 5: Tx with 10^8 spores (n=10); placebo (n=2); single dose

Cohort 6: Tx with 10^6 spores (n=10); placebo (n=2); over 3 days

Cohort 7: Tx with 10^7 spores (n=10); placebo (n=2); over 3 days

Cohort 8: Tx with 10^8 spores (n=10); placebo (n=2); over 3 days

Primary Objective

Safety and tolerability at 24 weeks

Relative risk of *C. difficile* recurrence compared to placebo at up to 8 weeks

Secondary Objectives

Microbiome engraftment

Time to *C. difficile* recurrence

Relative risk of recurrence at up to 4, 12, and 24 weeks after treatment

Summary of SER-262 Phase 1b preliminary study results

- Preliminary unblinded clinical data available from seven of eight patient cohorts
- No drug related serious adverse events observed
- No relative differences observed in the risk of relative recurrence rates in SER-262 as compared to placebo
 - Study was not powered to detect statistically significant difference in recurrence rates
 - In the small group of placebo treated patients, no recurrences were observed
 - Low *C. diff.* recurrence rate observed in patients treated with vancomycin & SER-262, compared to those treated with metronidazole & SER-262, 4% versus 31%, respectively (p value = 0.0049). Prior randomized Phase 3 studies with vancomycin demonstrate a recurrence rate of ~25%
 - Data suggest that treatment with vancomycin, followed by SER-262, results in more robust and rapid engraftment compared to metronidazole, and thus may lead to corresponding clinical efficacy
- First ever demonstration of engraftment of a rationally-designed microbiome drug candidate
 - Detected a majority of SER-262 strains in patients receiving SER-262; detection of strains was variable across subjects. Of note not all bacterial species engraft with biologically sourced microbiome drug candidates or with FMT.
 - In patients where SER-262 engraftment was observed, global changes to the microbiome were also seen

SER-287 and Ulcerative Colitis



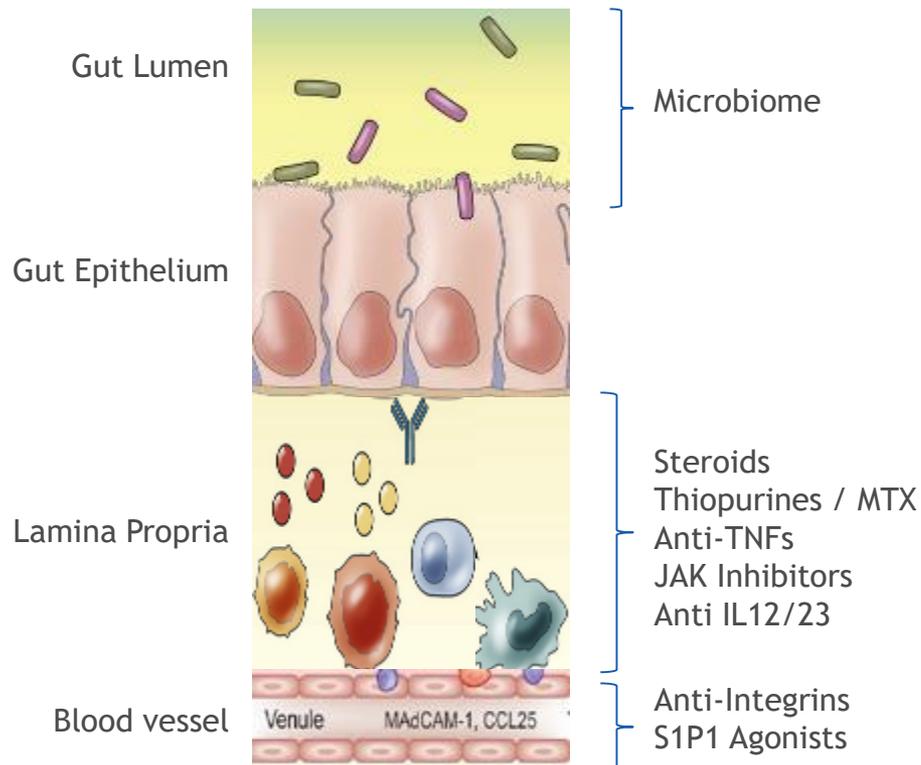
Leading the Microbiome Revolution

Inflammatory Bowel Disease (IBD) opportunity for new mechanistic approaches

Significant need for improved therapies

- Large US population: ~700K ulcerative colitis, ~700K Crohn's
- Fewer than ~1/3 of patients achieve remission with current therapies
- Many therapies are immunosuppressive, limiting widespread use

Modulation of the microbiome is an attractive therapeutic target for Ulcerative Colitis



- 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
- **Potentially synergistic effect with other UC products**

Microbiota transplantation provides clinical proof of concept

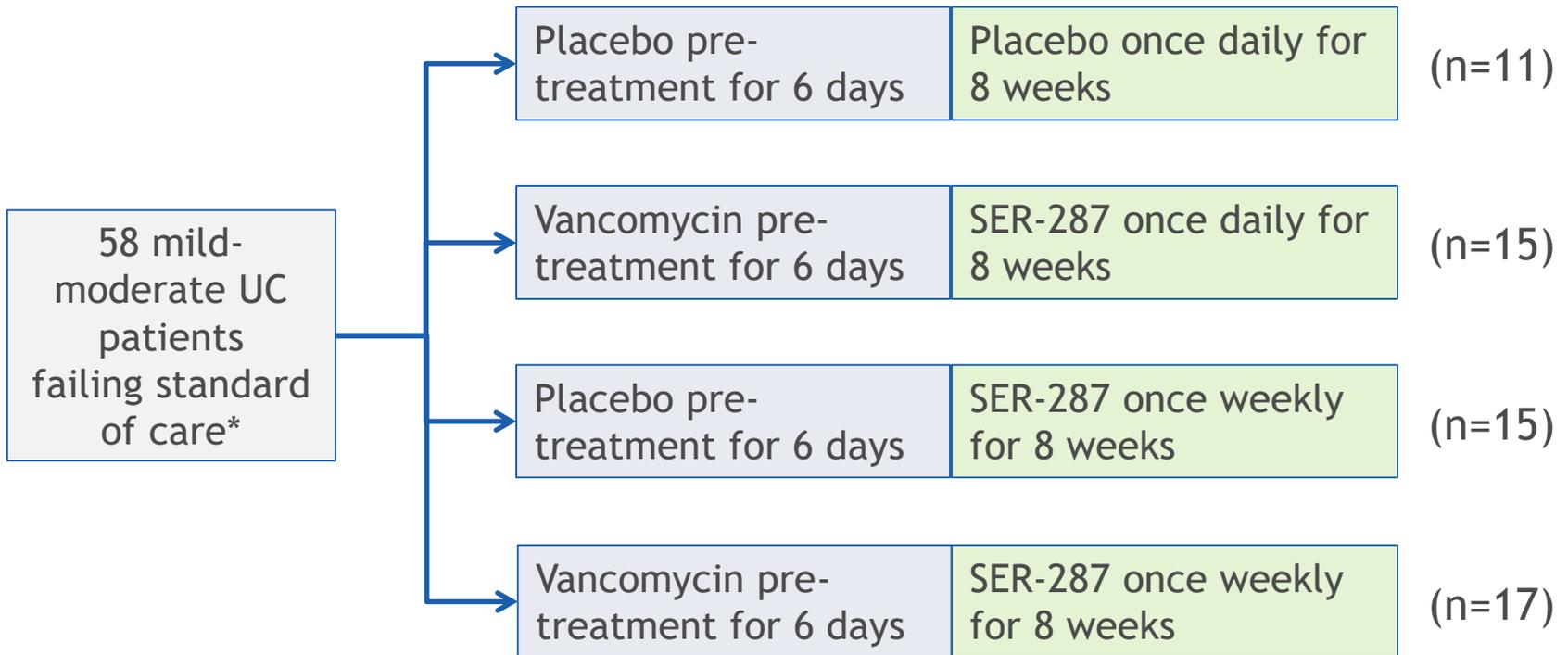
THE LANCET

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

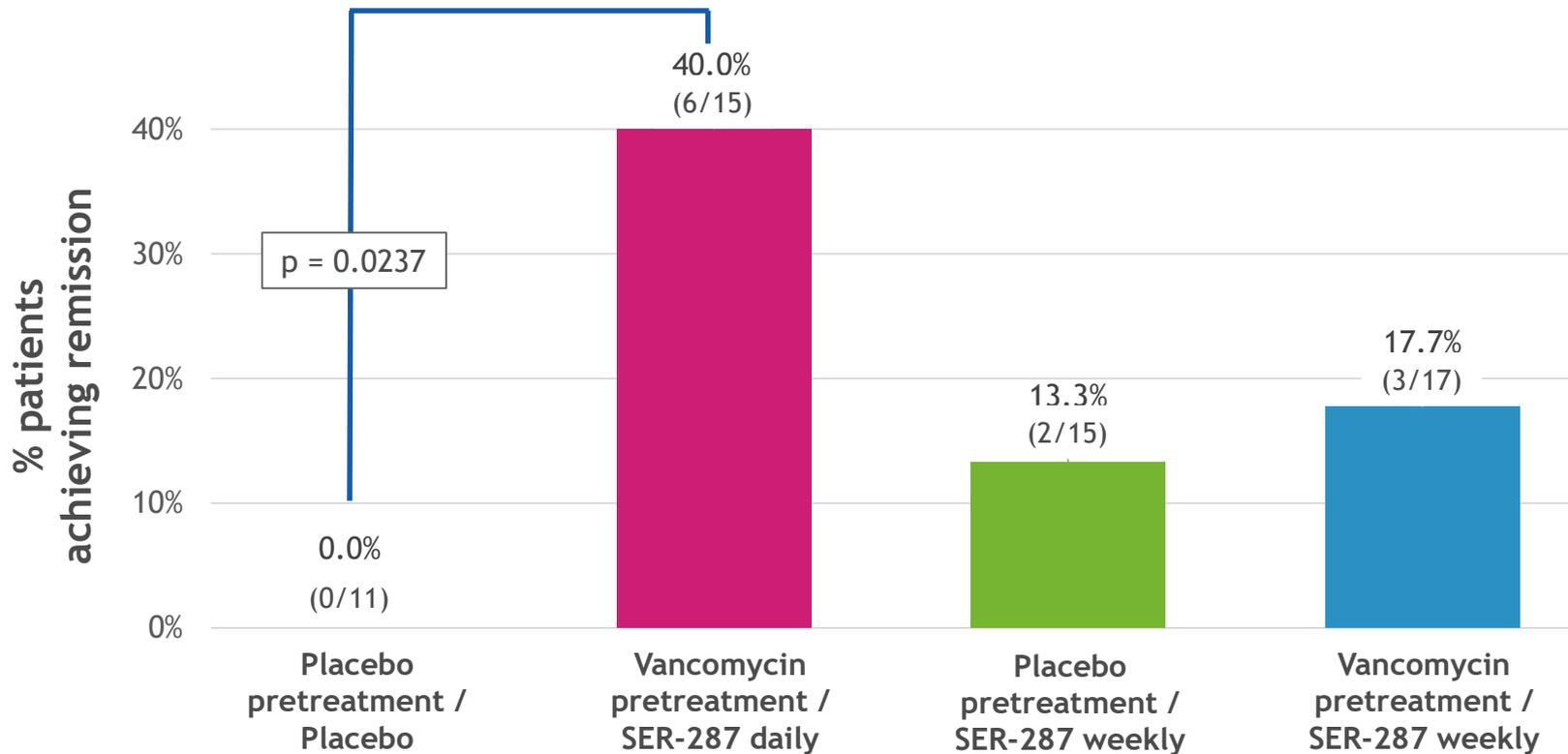
	Faecal microbiota transplantation (n=41)	Placebo (n=40)	Risk ratio (95% CI)	p value
Primary outcome				
Steroid-free clinical remission and endoscopic remission or response*	11 (27%)	3 (8%)	3.6 (1.1-11.9)	0.021

SER-287 Phase 1b Ulcerative Colitis study



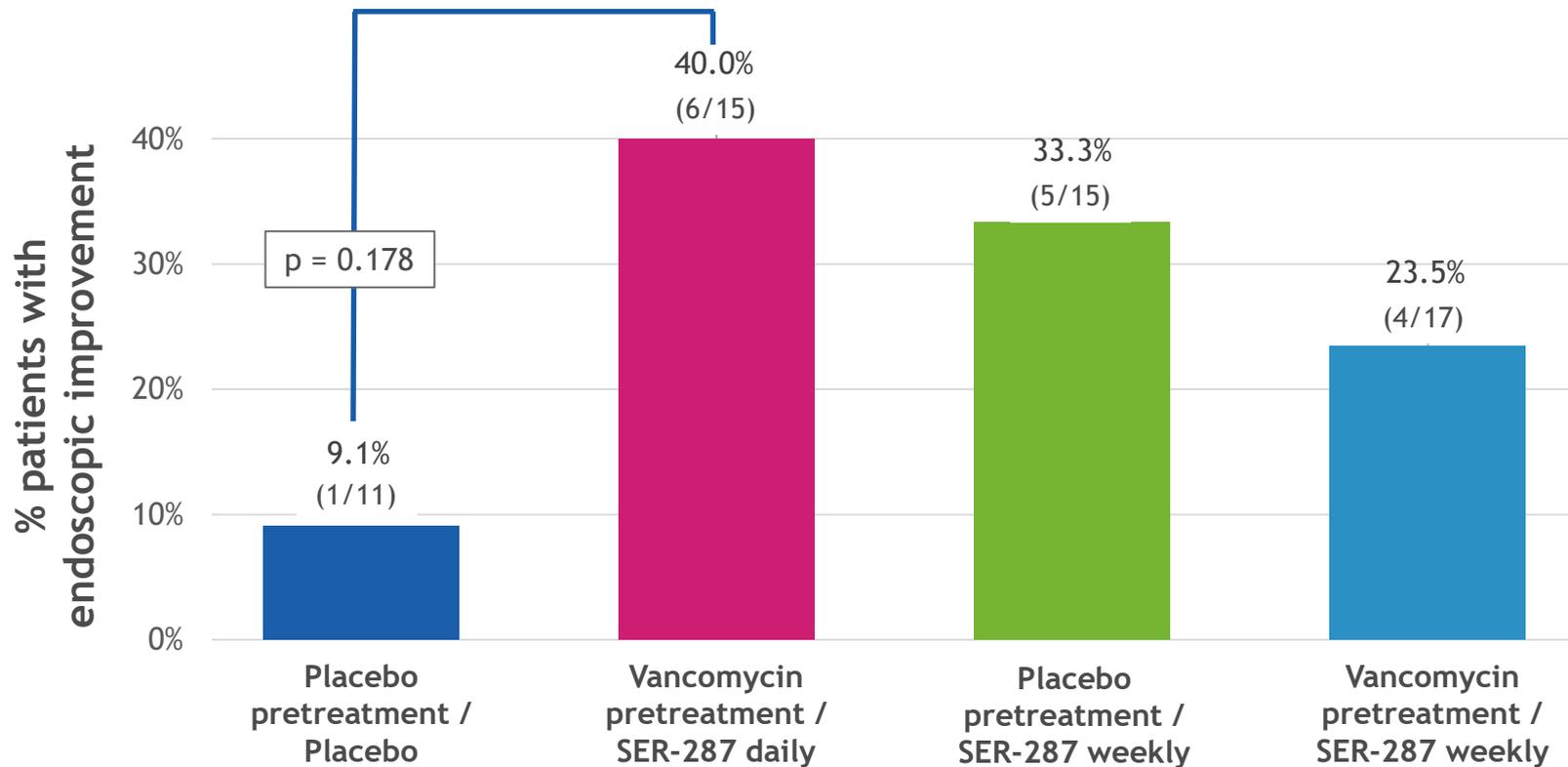
* Study designed to enroll 55 patients, with 15 in SER-287 treatment arms and 10 in the placebo / placebo arm

Significant and dose dependent impact on remission



Remission = Total Modified Mayo score ≤ 2 AND endoscopic subscore ≤ 1
Note: Missing data treated as failure

Dose dependent impact on endoscopic improvement

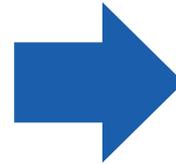


Endoscopic Improvement: Decrease in endoscopic subscore ≥ 1

Note: Endoscopy readings were centrally read by blinded readers, missing data treated as failure

Illustrative endoscopy improvement — SER-287 daily treatment

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



Post-treatment day 64 endoscopy



Favorable SER-287 Phase 1b safety profile

- SER-287 daily arm demonstrated a similar safety profile to placebo
- No serious drug-related adverse events
- No subject discontinuations in the SER-287 daily treatment arm
- Reduced gastrointestinal adverse events provide an independent assessment of efficacy with decreased disease activity
 - SER-287 daily arm GI AEs: 2/15 (13.3%) vs. placebo arm: 5/11 (45.5%)

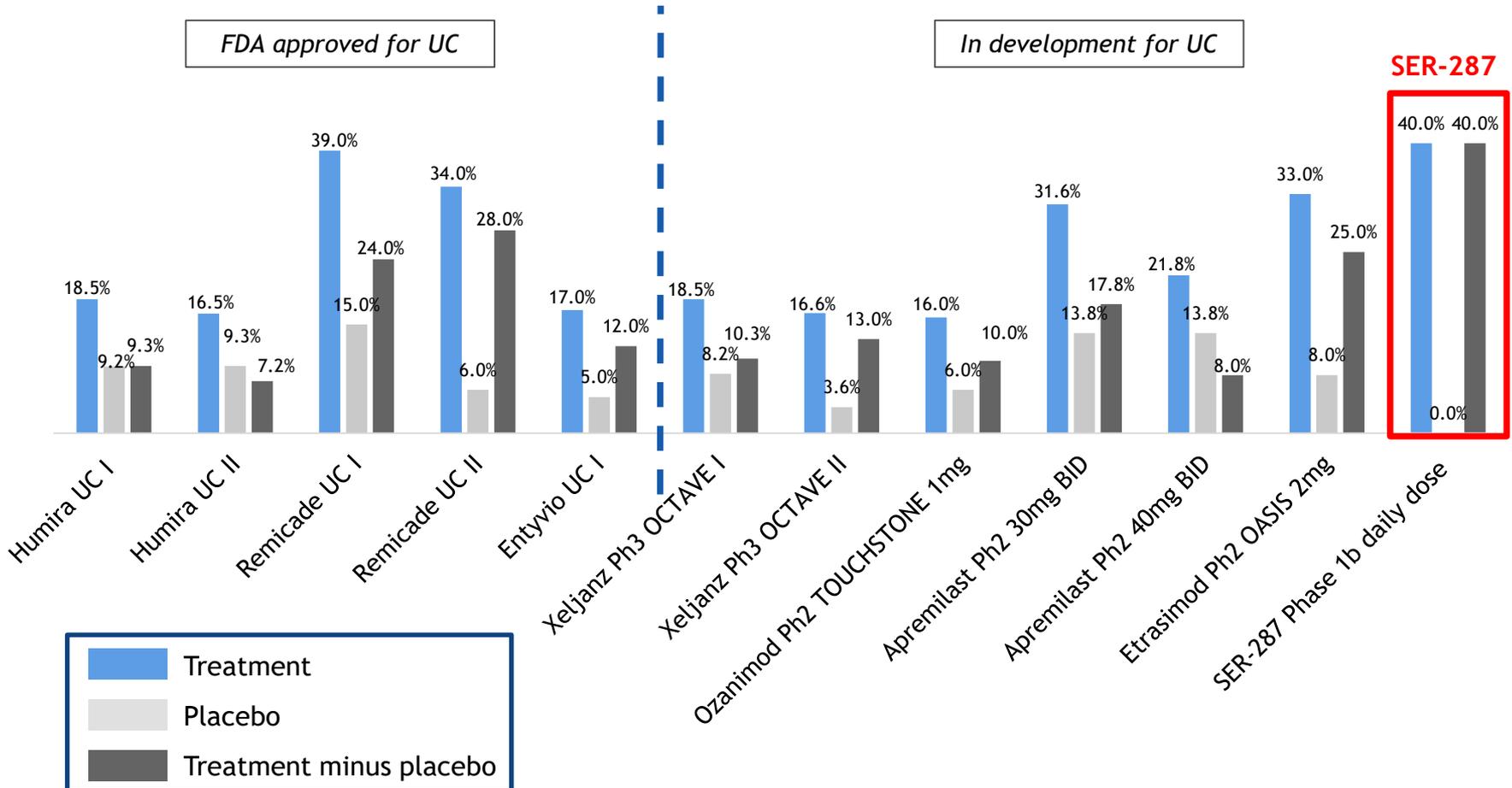
Analyses of post SER-287 treatment impact on disease activity

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, no patients experienced a disease flare in the 26 weeks following the end of treatment (0/11)

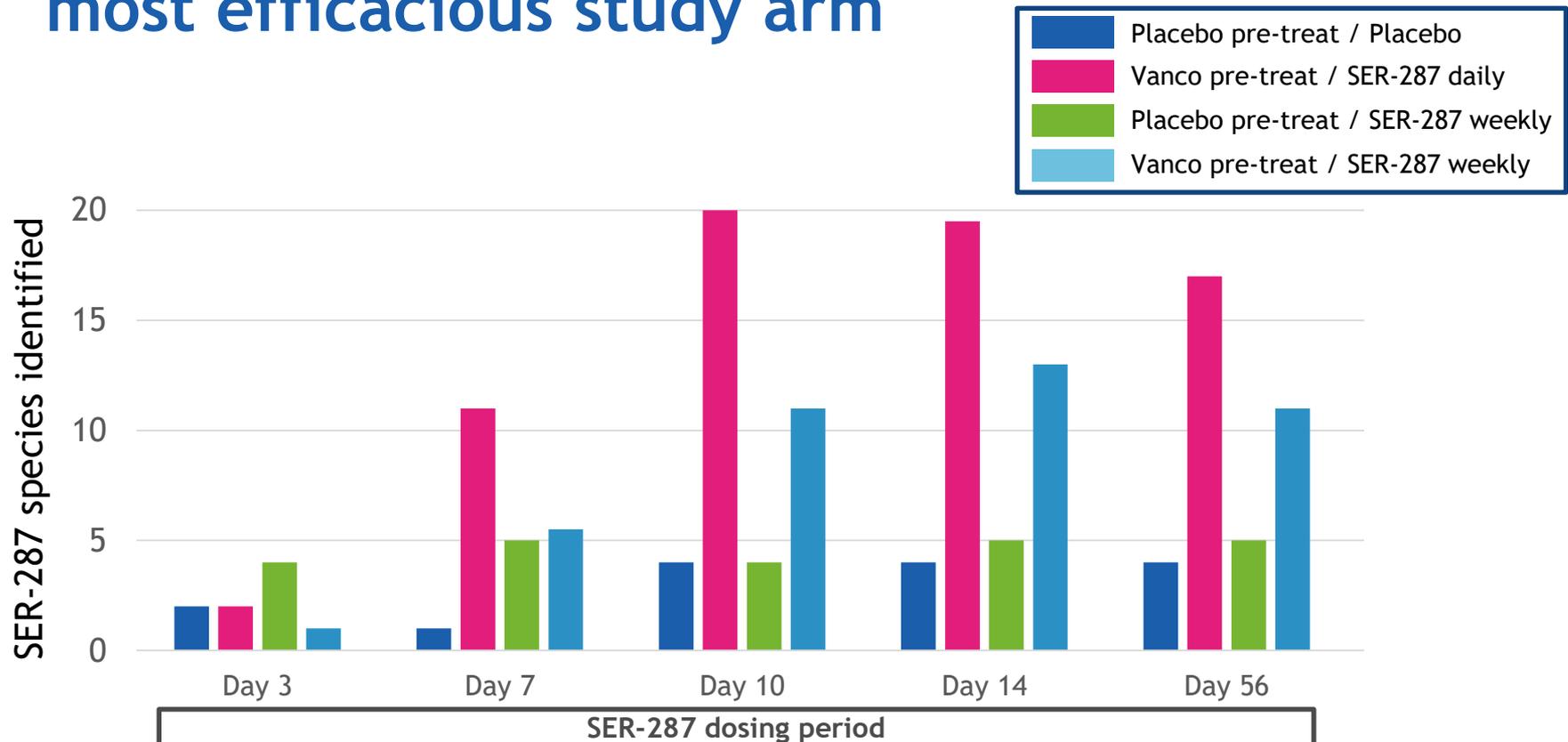
Favorable SER-287 efficacy relative to selected approved and development stage UC drugs

Remission Rates for Induction in Active UC



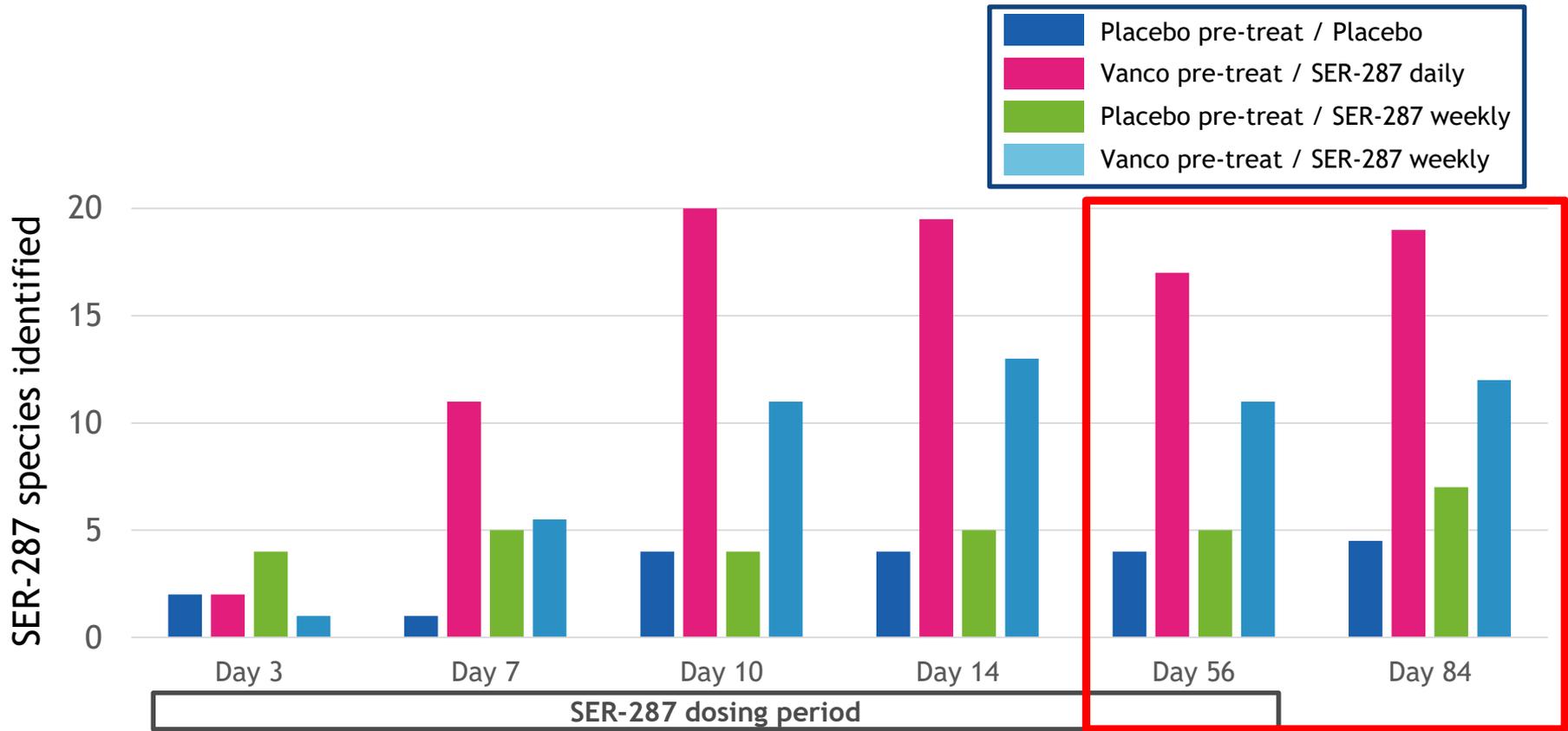
Adapted from Leerink Nov. 27 2017 report: Future of IBD: Category should double by 2023 despite GED-0301 disappointment; Note that study-to-study differences limit the ability to directly compare results.

Robust SER-287 species engraftment; highest in most efficacious study arm



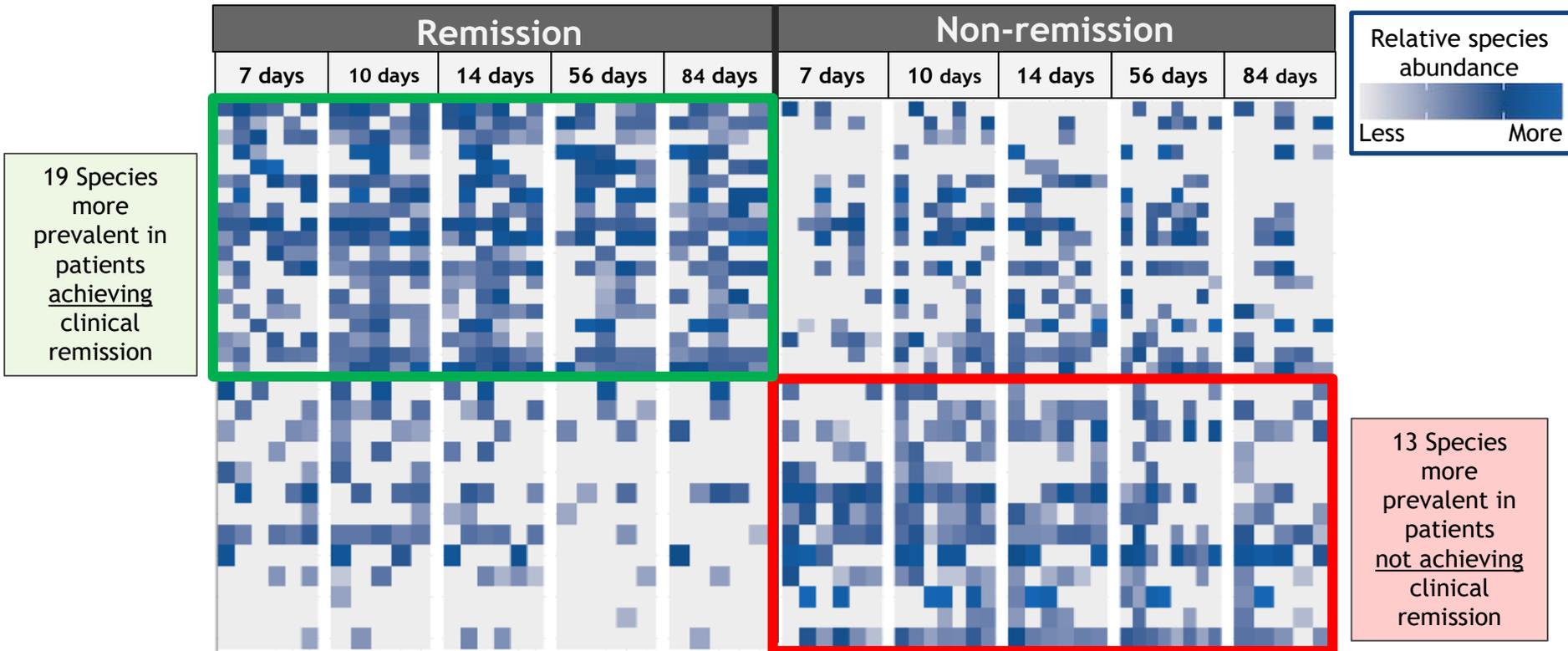
- Statistically significant engraftment in vanco pre-treat / SER-287 daily arm, versus placebo pre-treat / placebo arm, beginning at day 7 and maintained throughout the dosing period
- Statistically significant and dose-dependent engraftment in study arms with vanco pre-treatment / SER-287 versus placebo pre-treat arms
- Data supportive of vancomycin opening ecological niches for SER-287 engraftment

Durable SER-287 engraftment following dosing



- Statistically significant engraftment maintained through at least 4 weeks following SER-287 dosing

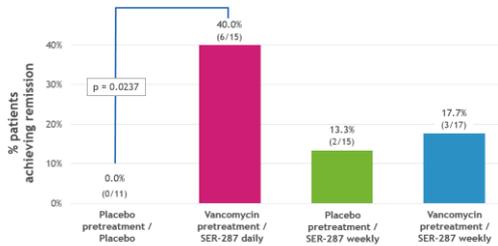
Identified bacterial species signature that associates with clinical remission vs non-remission



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

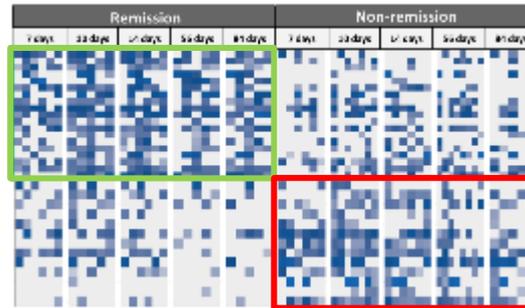
Relative abundance heatmap depiction of bacterial species prevalence from vanco/SER-287 daily study arm patients. Each row represents a single bacterial species and each column represents a single patient at a given timepoint. Shading of each square illustrates the relative abundance of each species.

SER-287 Phase 1b data demonstrate clinical effect and provide supportive molecular mechanistic data



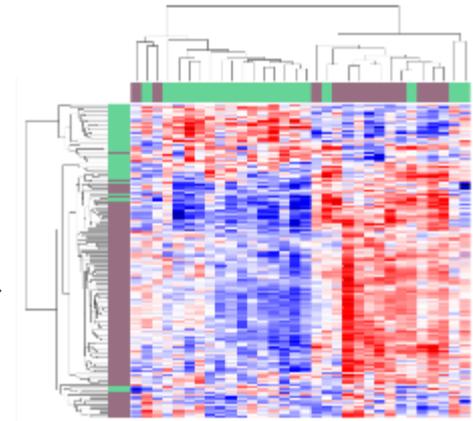
CLINICAL OUTCOME

Dose dependent clinical remission



SPECIES SIGNATURES

Engraftment (PK) associated with clinical remission



METABOLITES & PATHWAYS

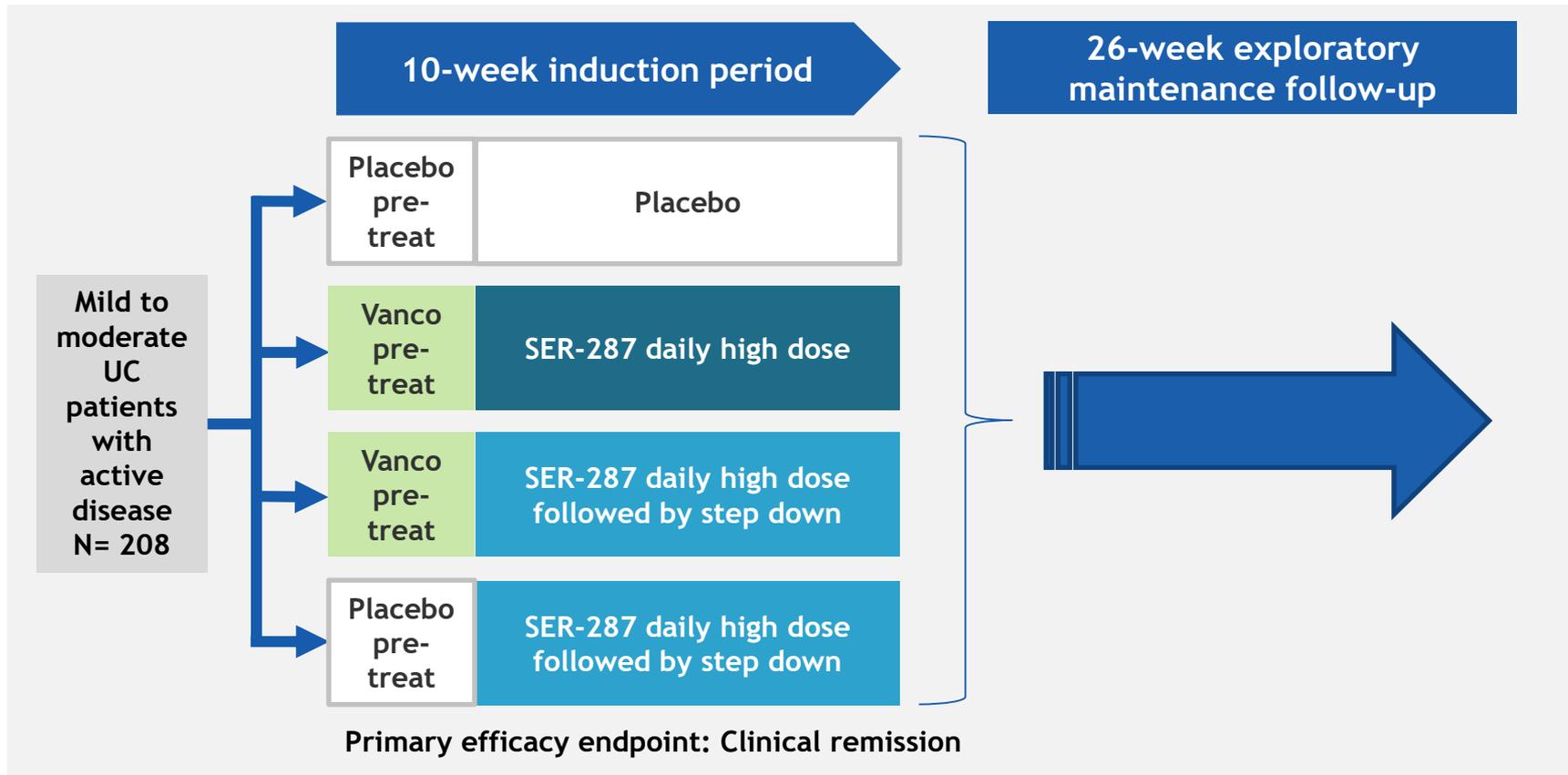
Metabolites and functional pathways (PD) associated with remission and microbiome change



Additional data presented at May 24, 2018
Seres microbiome R&D event

Planned SER-287 Phase 2B study design

- Study to further evaluate induction dosing and longer term maintenance efficacy
- Design expected to support potential FDA registrational data package and with compelling data may be considered a pivotal trial
- Expect to initiate study in the coming months



SER-301: Synthetic fermented Ecobiotic® therapeutic candidate for inflammatory bowel disease

- Oral, mechanistically designed follow-on to SER-287
- Selection of SER-301 bacterial composition based on:
 - SER-287 study data (clinical and microbiome analysis)
 - Preclinical activity of microbiome compositions
- Rationally designed composition has shown activity in mouse model

SER-401 and Immuno-oncology



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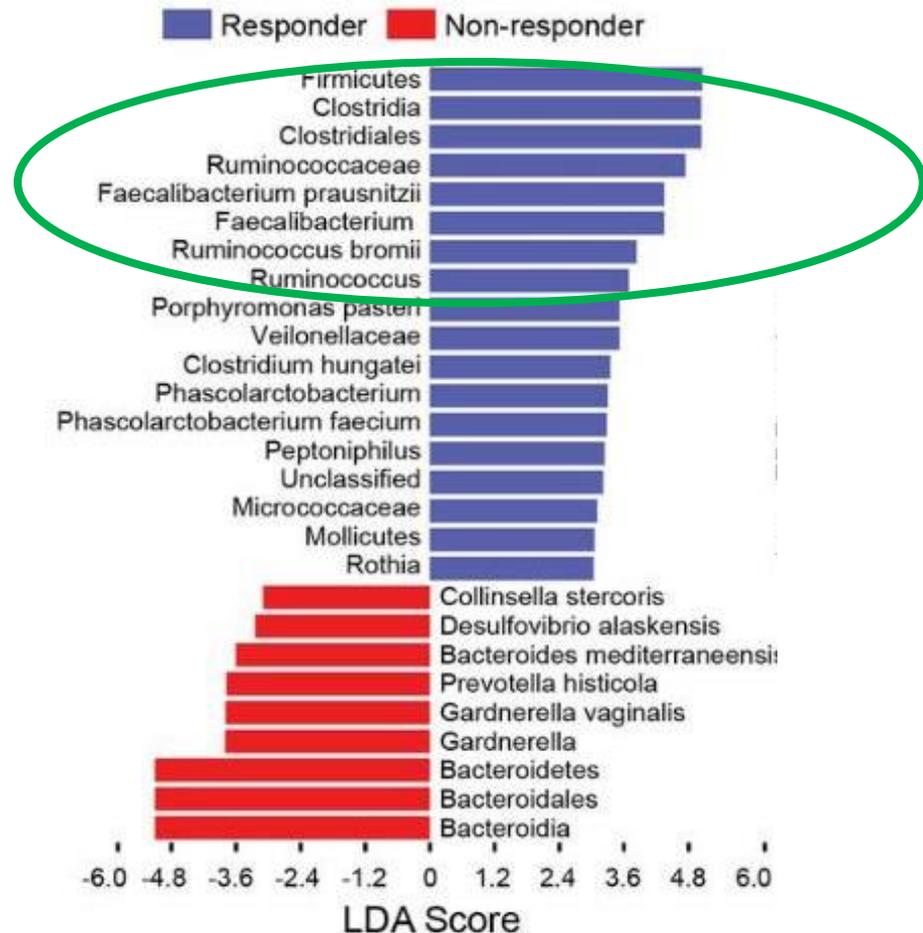
Collaboration to advance microbiome therapeutic into immuno-oncology



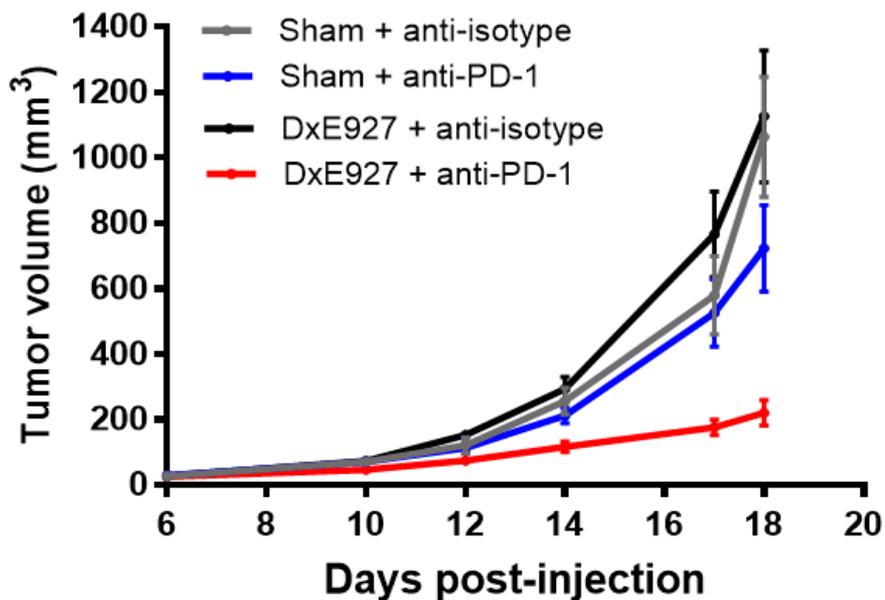
- Objective: Modulate the microbiome to increase the response of check-point inhibitor therapy
- Seres option to license foundational intellectual property from MD Anderson related to the use of bacteria in combination with checkpoint inhibitors
- Planned clinical study start in 2018

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

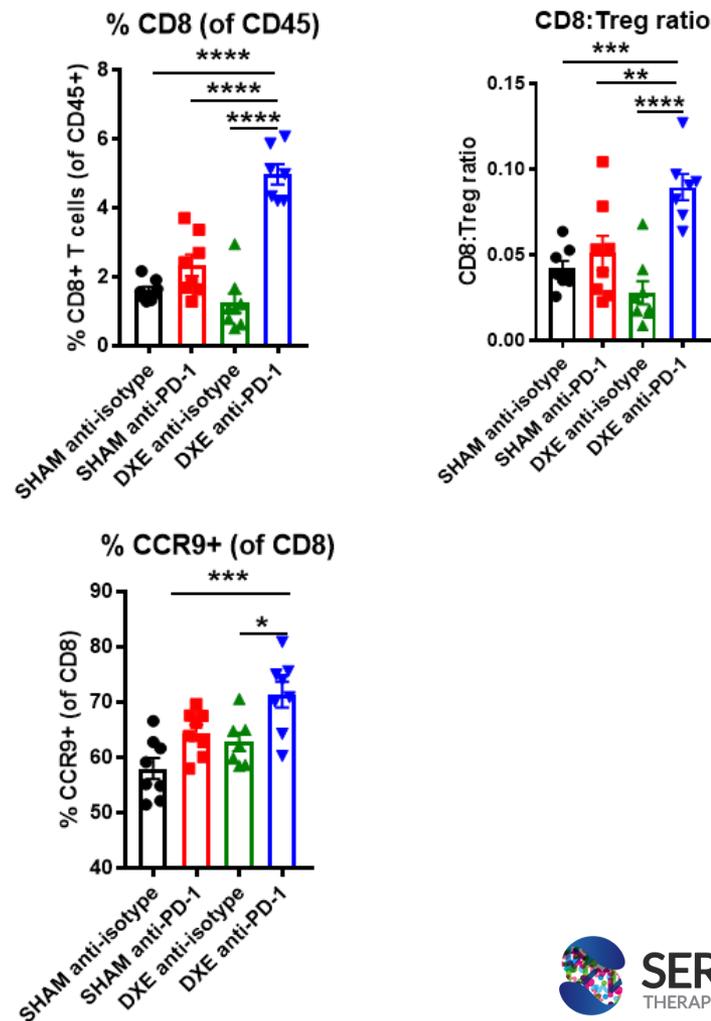
- Signature driven by bacteria in the class Clostridia, family Ruminococcaceae, including Ruminococcus and Faecalibacterium
- All spore formers that leverage deep Seres expertise in the biology and manufacturing of these organisms



Treatment of mice with the microbiome signature composition restores anti-PD-1 efficacy after antibiotics

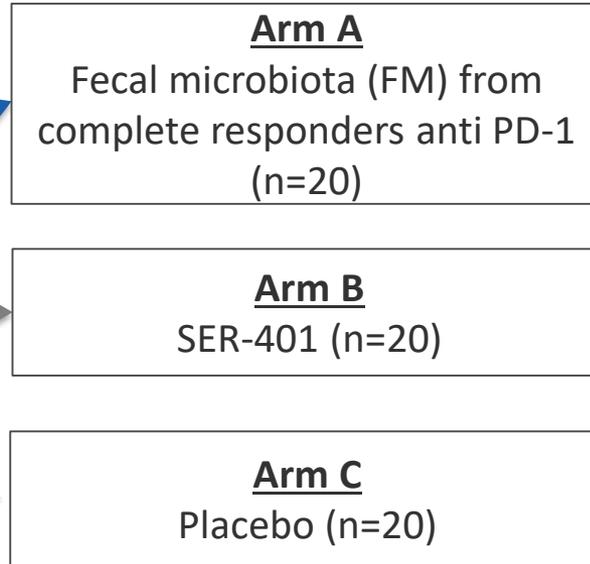


Note: Not all donor-derived bacterial spore compositions result in restoration of anti-PD-1 efficacy



Planned SER-401 Phase 1b study

Patients with metastatic cancer (melanoma) going onto immune checkpoint blockade (anti-PD-1)

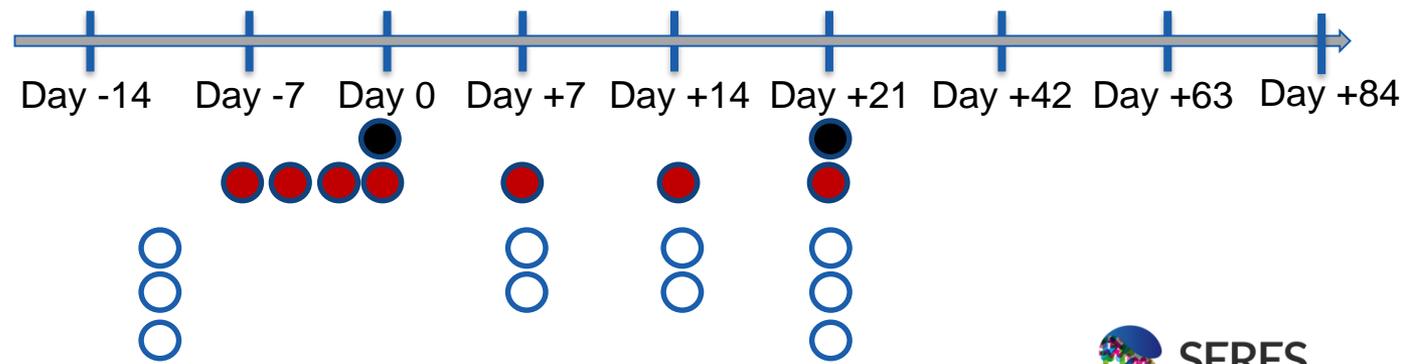


Study objectives

All patients = CT scans with RECIST week 12

Primary endpoint = safety and tolerability

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



Broad IP portfolio and regulatory exclusivity

8 ISSUED US PATENTS + LICENSED IP*

- Demonstrates rationally designed ecologies of spores and microbes are patentable
- 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
- Claims related to SER-109/ *C. difficile* & colitis lead candidates through **2033**

SERES PATENT PORTFOLIO

15 Families of Applications

10 Nationalized

1 Pending PCT

4 Pending Provisionals

REGULATORY EXCLUSIVITY



12 years for new biological composition



10 years for new drug

* Includes additional IP rights including 1) a worldwide exclusive license to Memorial Sloan Kettering Cancer Center patent applications related to the use of bacterial compositions for treating HSCT patients and related areas, 2) exclusive option to license intellectual property rights from MD Anderson related to the use of bacteria in combination with checkpoint inhibitors.

Upcoming Milestones

SER-109: Multiply recurrent *C. difficile* infection - Phase 3 ongoing

SER-287: Ulcerative colitis - Initiate new clinical study in the coming months

Immuno-oncology clinical study start in 2018

Focused R&D efforts to efficiently advance highest priority pipeline programs toward meaningful value inflection points

Resources to operate for at least the next 12 months

Balance Sheet	As of March 31, 2018
Cash, cash equivalents and investments	\$122 M

Cash operating guidance provided May 9, 2018