

Cowen and Company 38th Annual Health Care Conference

Roger J. Pomerantz, M.D.

President, Chief Executive
Officer and Chairman

March 14, 2018



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 Annual Report on Form 10-K filed on March 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

Infectious Disease

- A diverse microbiome resists colonization by exogenous pathogens
- Exposure to broad spectrum antibiotics, and resulting gut microbiome dysbiosis, increase risk for *C. difficile* infection and colonization / infection by multi-drug resistant organisms

Inflammation and Immunology

- Microbiome known to alter regulatory T cells and Th17 T cell activation
- Role in inflammatory bowel disease (Ulcerative Colitis and Crohn's disease) as well as allergy, rheumatoid arthritis and multiple sclerosis
- The composition of the microbiome has been demonstrated to impact the efficacy and safety of immuno-oncology checkpoint inhibitors

Metabolic Disease

- Effects on glucose utilization, digestion and bile acid metabolism
- Role of microbiome implicated in several metabolic diseases (e.g. diabetes, obesity, liver diseases)



Selected references: Infectious disease / *C. difficile*: Leffler and Lamont, NEJM, 2015; Ulcerative colitis: Paramsothy et al. Lancet, 2017; Moayyedi et al. Gastroenterology, 2015; Immuno-oncology: Vetizou M et al., Science 2015.; Sivan A. et al., Science 2015.; Dubin et al., Nature, 2016. NASH: Le Roy et al., Hepatology, 2012. Metabolic disease: Perry et al. Nature, 2016, Ridaura VK et al., Science 2013; Primary sclerosing cholangitis: Tabibian JH et al., Hepatology, 2016.

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

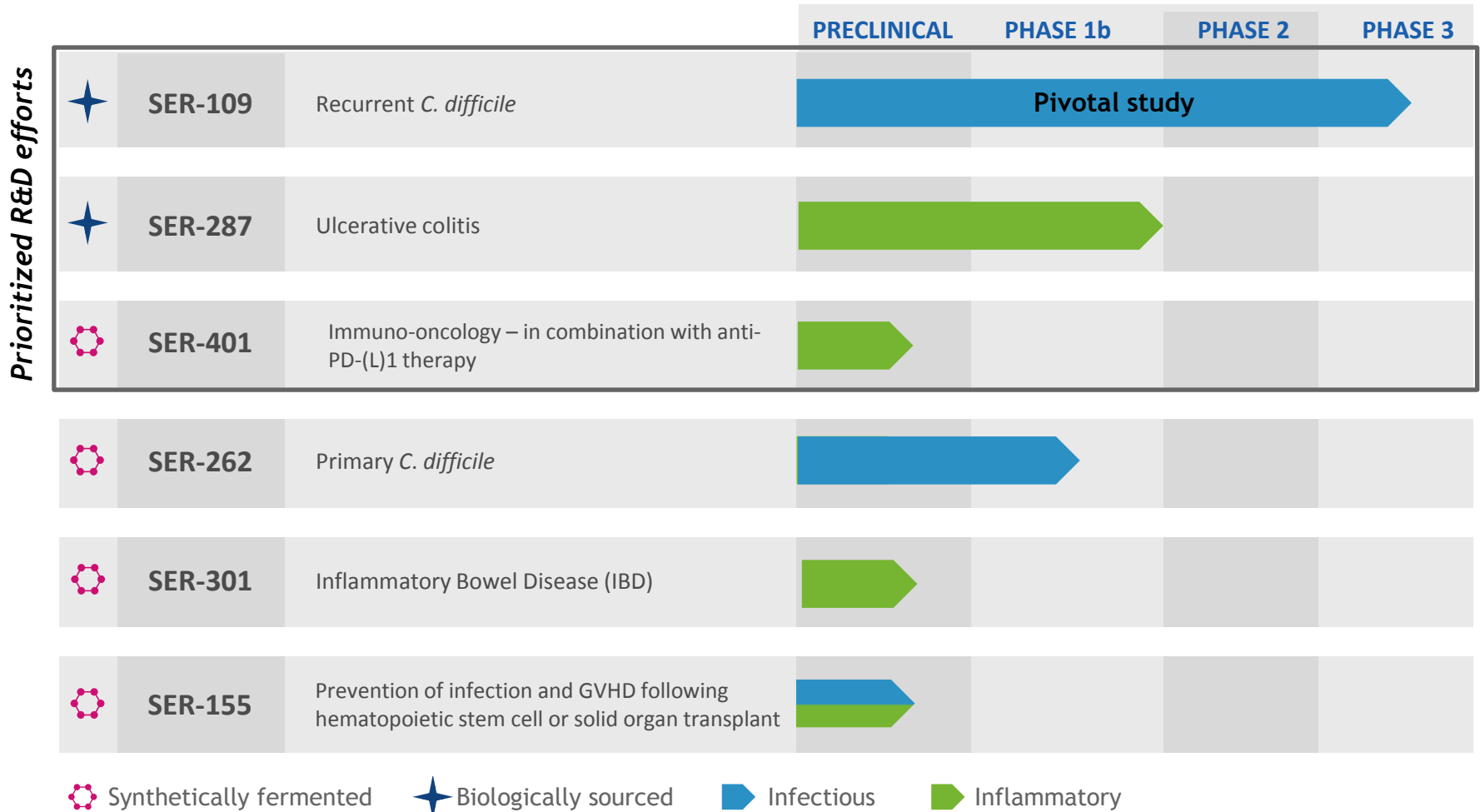
- Computational biology
- Basic microbiome research
- Microbiology
- Translational science
- Clinical development
- Advanced GMP manufacturing

Research in new therapeutic areas

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



Robust microbiome therapeutics pipeline



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

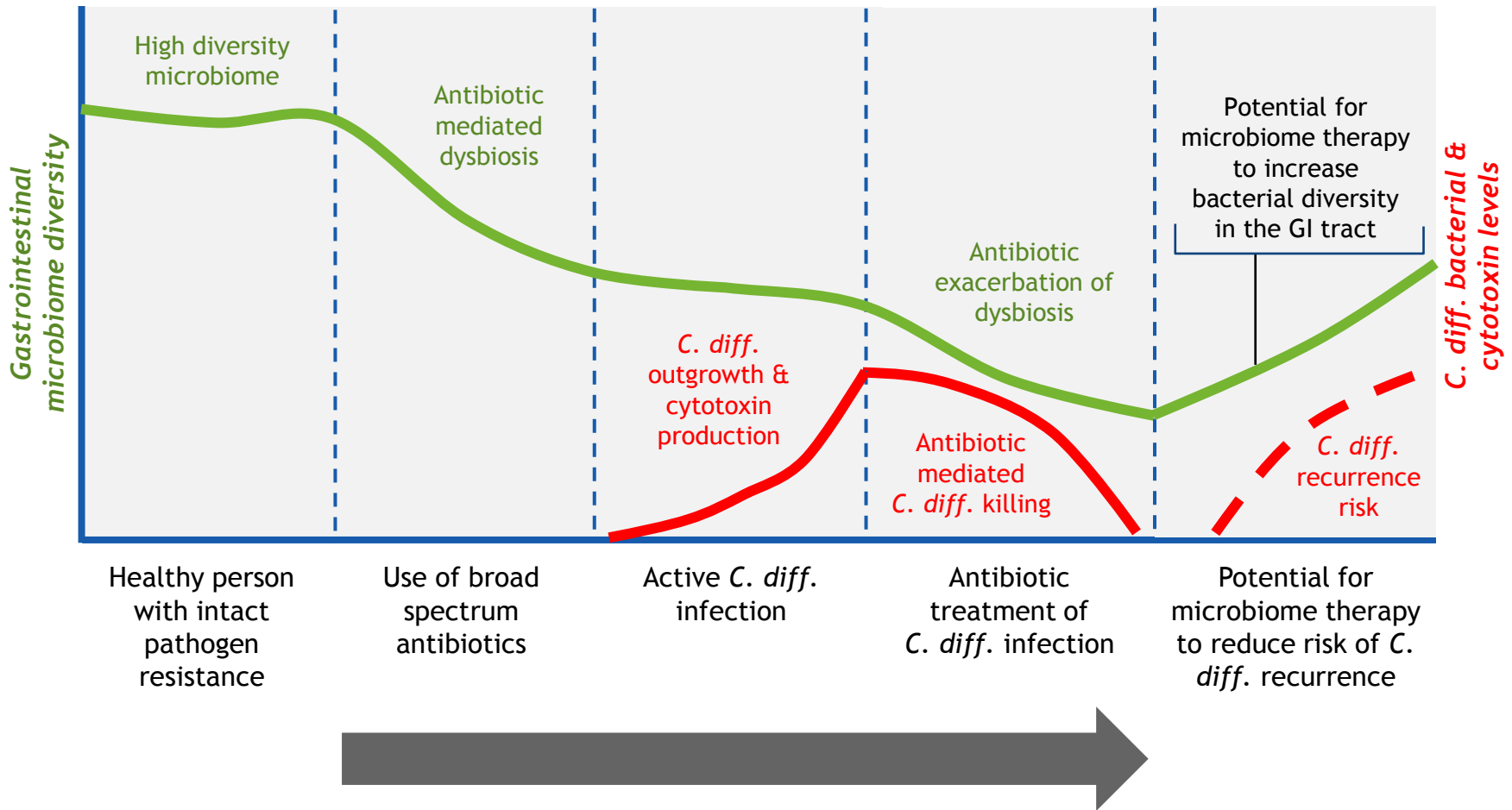
Leading cause of hospital-acquired infection in the US

- 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



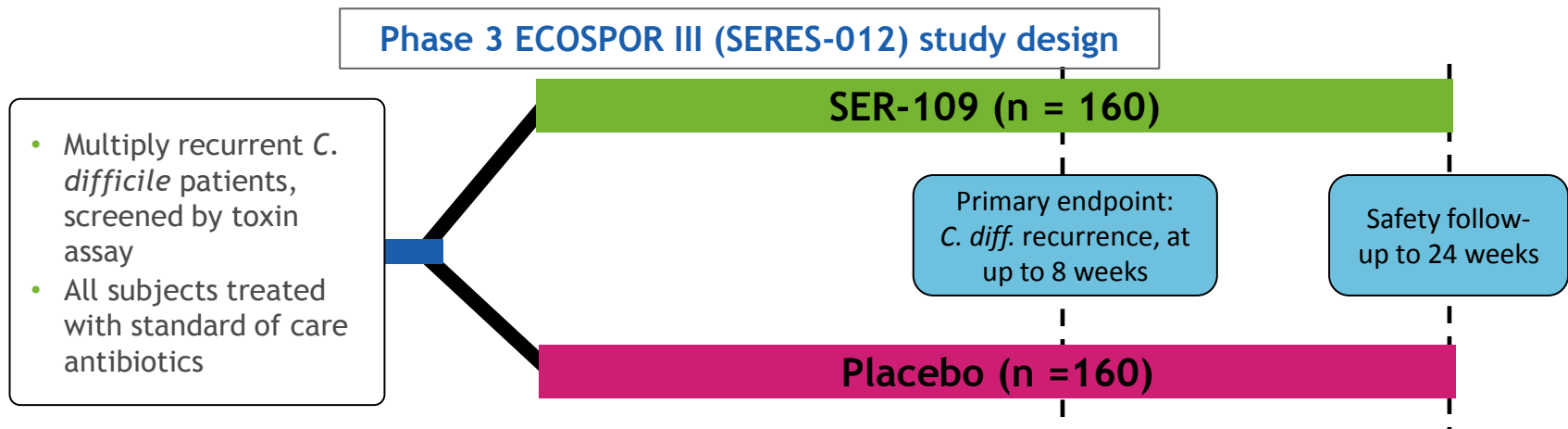
Microbiome therapeutic intervention - Race to Repair

Hypothetical patient course



Phase 3 SER-109 ECOSPOR III study 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 efforts:
 - 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: Synthetic, fermented Ecobiotic® therapeutic candidate for primary *C. difficile* infection

- Oral, microbiome therapeutic candidate comprising twelve strains of fermented, rationally-selected bacterial spores
- Bacterial species selected based on analysis of SER-109 Phase 1b microbiome data, biological and phylogenetic heterogeneity, and preclinical efficacy in *C. difficile* infection mouse model
- Data support a mechanism of action in which SER-262 strains compete for *C. difficile* preferred carbon sources

SER-262 strains utilize multiple carbon sources

Strain Designation	Sugars, sugar alcohols, glucosides													Carboxylic acids					
	f r u	g l u	m a n	r h a	r i b	x y l	c e l	s c r	t r e	m e l	p m t	s o r	N A G	m	s a l	f o r	s u c	p y r	
<i>C. difficile</i>																			
1																			
2																			
3																			
4																			
5																			
6																			
7																			
8																			
9																			
10																			
11																			
12																			

In vitro fermentation



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

- First rationally designed fermented microbiome drug ever tested in humans
- Preliminary unblinded clinical data available from seven of eight patient cohorts
- No drug related serious adverse events observed
- No relative differences were observed in the risk of recurrence rates in patients administered SER-262 as compared to placebo
 - Study was not powered to detect statistically significant difference in recurrence rates
 - A small group of placebo treated patients were included in the study and, in this group, no recurrences were observed
 - Low *C. diff.* recurrence rate observed in patients treated with vancomycin and SER-262, as compared to those treated with metronidazole and SER-262, 4% versus 31%, respectively (p value = 0.0049). Medical literature suggests a recurrence rate of about 25% in patients treated solely with Vancomycin for primary *C. diff.* infection. Data suggest that treatment with vancomycin, followed by SER-262, results in more robust and kinetically more rapid engraftment, and thus may lead to corresponding clinical efficacy
- First ever demonstration of engraftment of a rationally-designed, fermented microbiome therapeutic candidate based on available data from the first five, lowest dose cohorts
 - 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 drugs or with FMT.
 - In subjects where SER-262 engraftment was observed, broader global changes to the microbiome were also observed
 - Vancomycin lead to more rapid and robust engraftment of SER-262 bacterial strains, as compared to metronidazole

SER-287 and Ulcerative Colitis



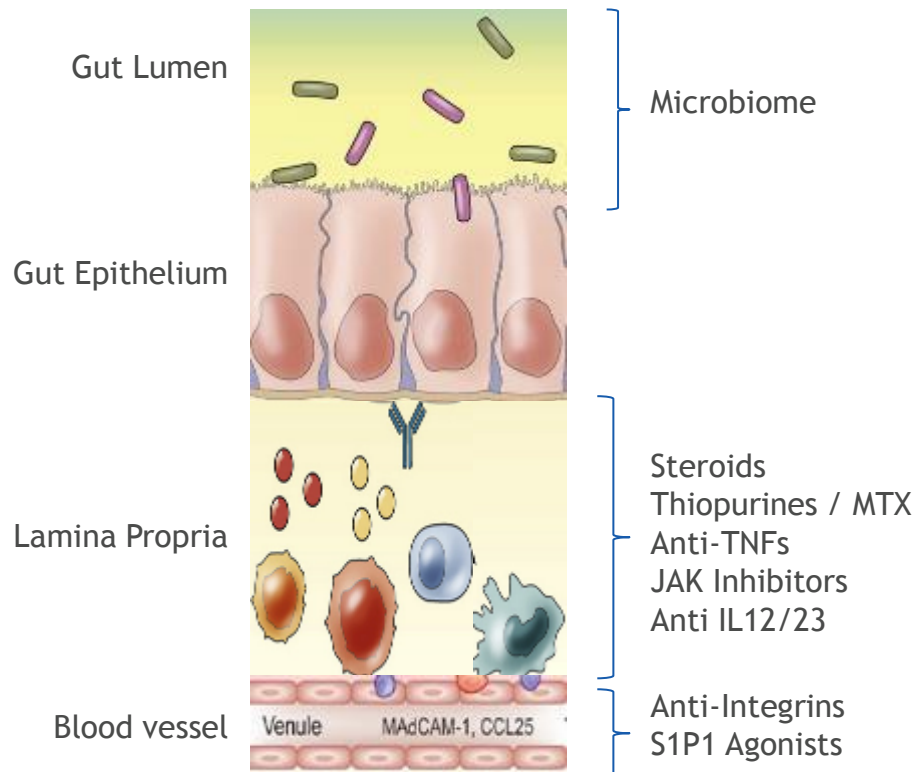
Leading the Microbiome Revolution

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

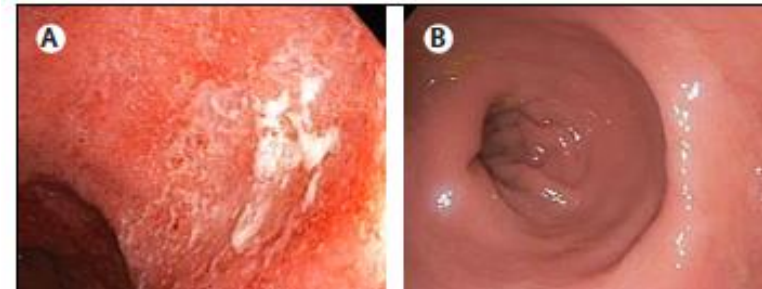
THE LANCET

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

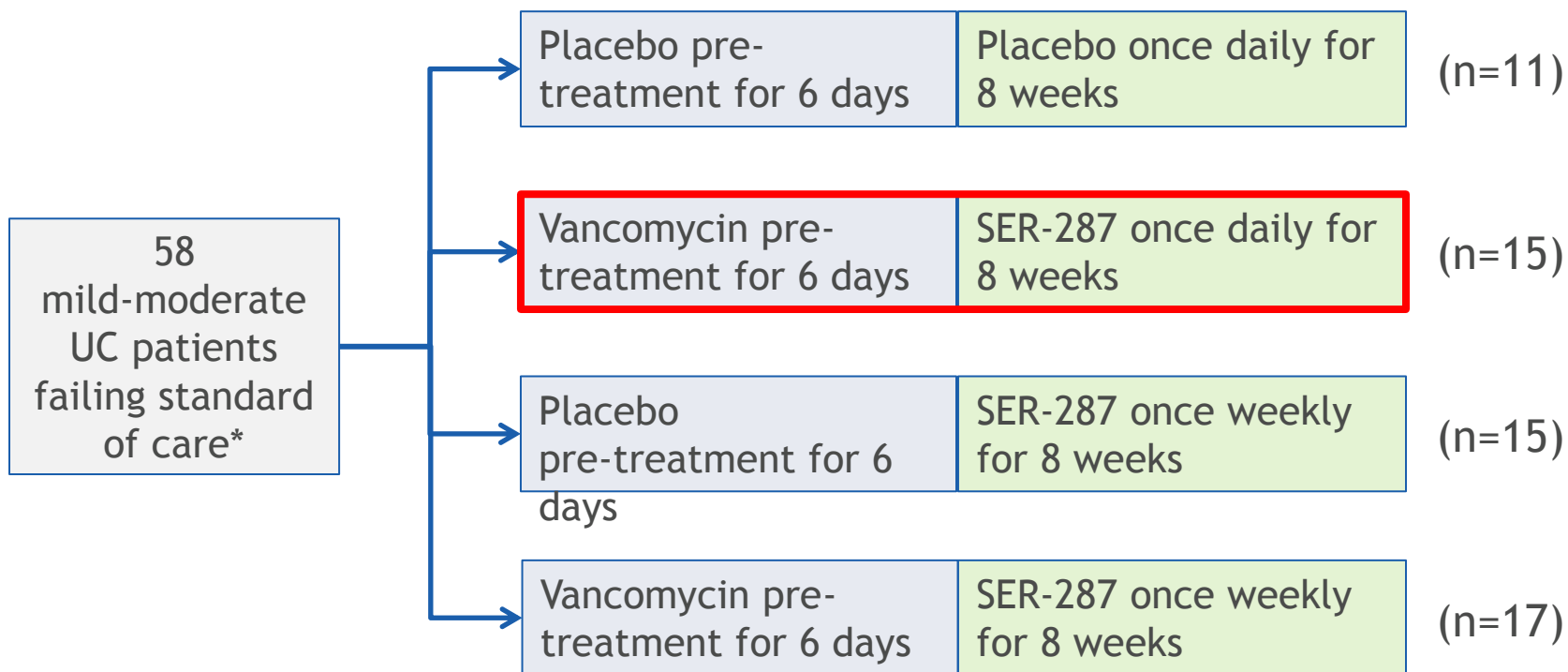
Subject A,
Baseline

Subject A,
8-wk post FMT



	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

SER-287 Phase 1b study endpoints

Primary Objectives

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

Secondary Objectives

- Remission, endoscopic improvement, and response through measure of the total modified Mayo Score
- Change in serum and fecal biomarkers
- Pathologic changes in mucosal biopsies (i.e., histology)

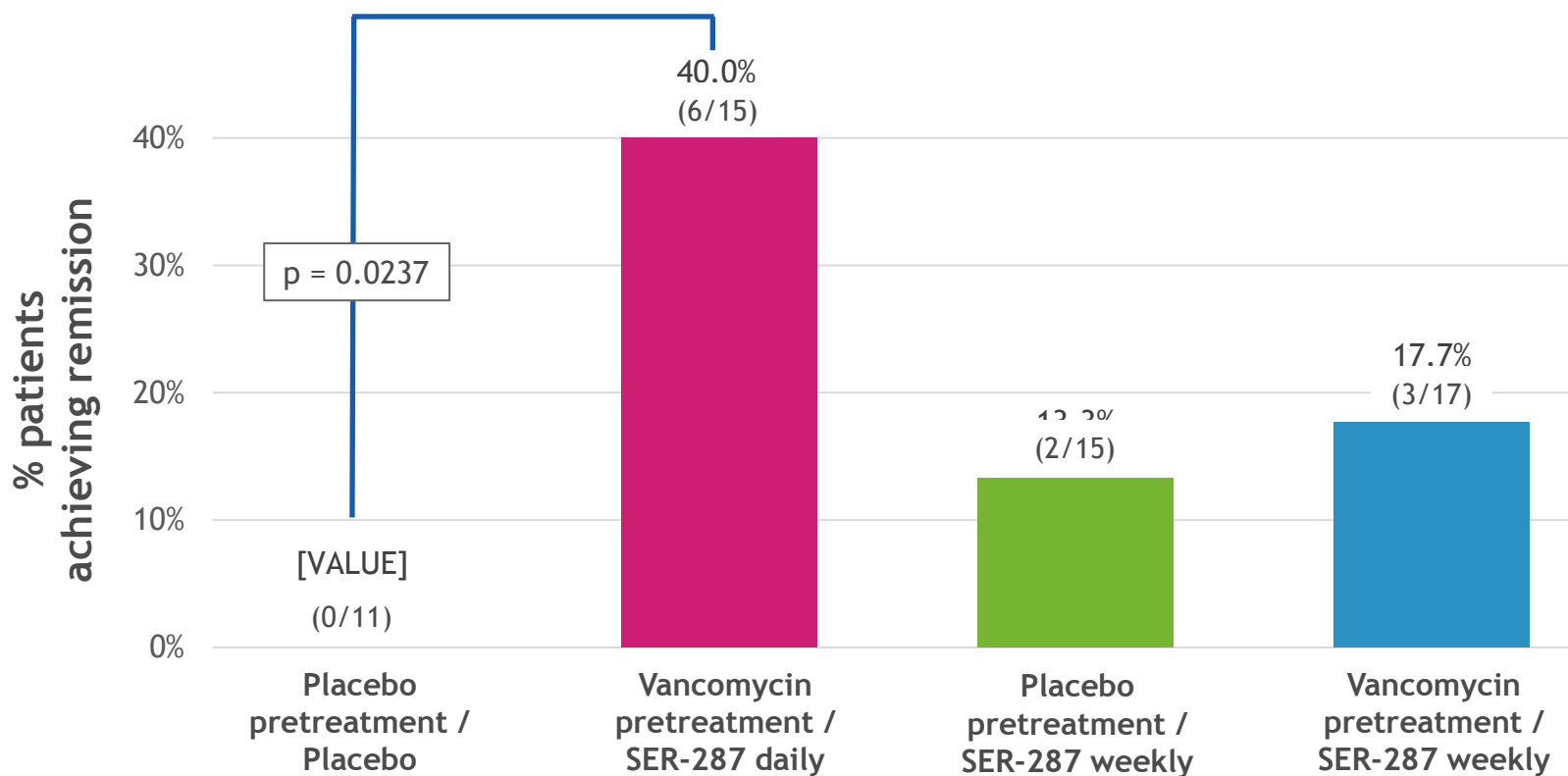
Clinical efficacy endpoints

Modified Mayo score components

1. Mucosal Appearance by endoscopy (***Most objective***)
2. Stool Frequency
3. Rectal Bleeding
4. Physician Rating of Disease Activity

Endpoint	Protocol Definition
Remission	Total Modified Mayo Score ≤ 2 and an endoscopic subscore of 0 or 1
Endoscopic Improvement	Decrease in endoscopic subscore of ≥ 1
Response	Decrease of ≥ 3 points in Total Modified Mayo Score from baseline, along with either a decrease of ≥ 1 point in rectal bleeding subscore or absolute rectal bleeding subscore of 0 or 1

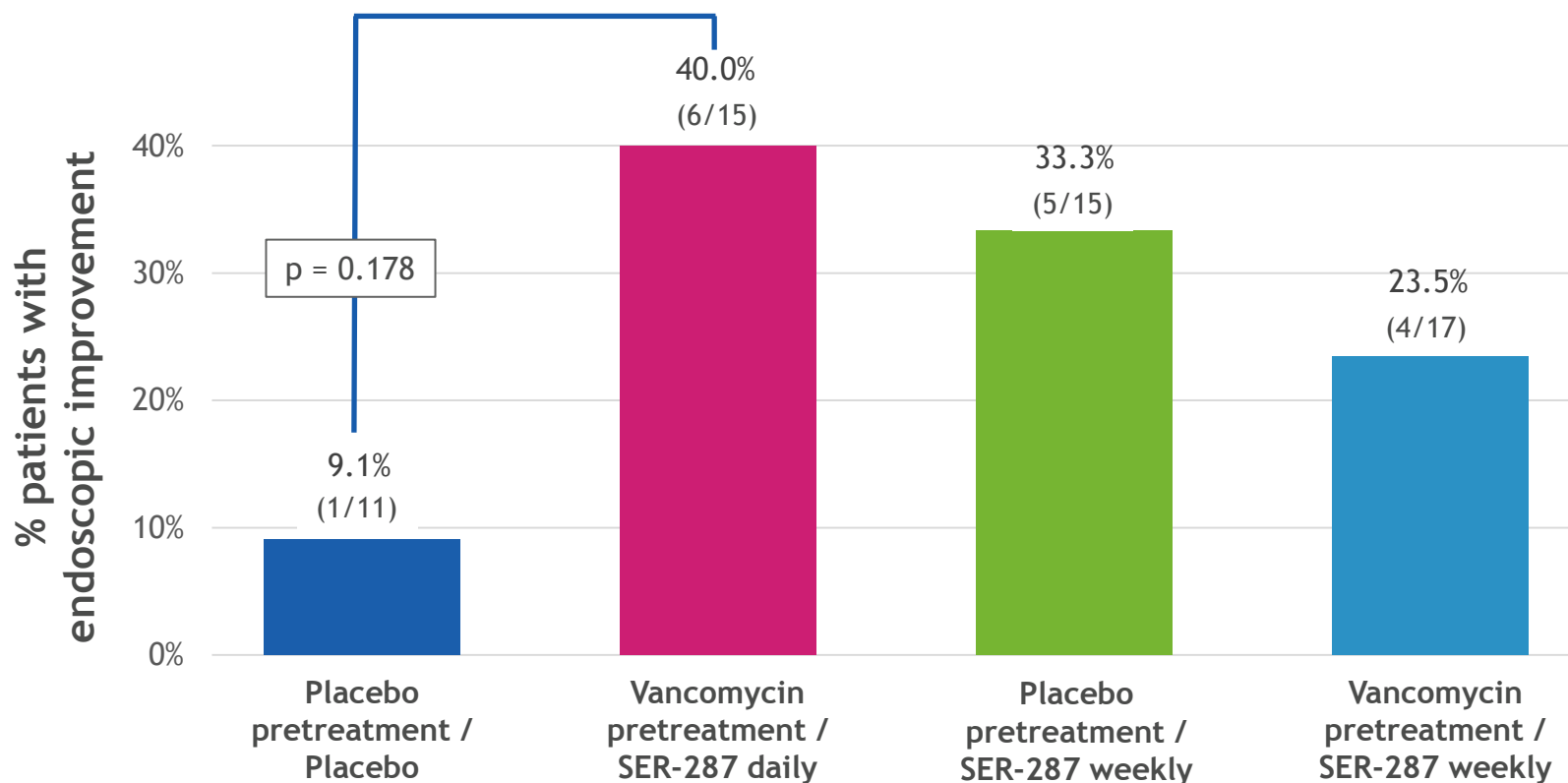
Significant and dose dependent impact on remission



Endoscopy readings were centrally read by blinded readers.

Data based on an intent to treat missing data counted as a failure analyses. Under observed data analysis, 1/10 (10%) and 6/15 (40%) patients in the placebo pretreatment / placebo and vancomycin pretreatment / SER-287 daily treatment arms, respectively, achieved remission and endoscopic improvement ($p=0.1794$). The observed analysis includes a patient in the placebo study arm who experienced a disease flare and was treated with corticosteroids (a protocol violation) prior to the end of treatment endoscopy

Dose dependent impact on endoscopic improvement

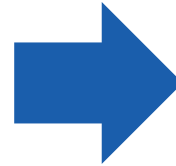


Endoscopy readings were centrally read by blinded readers.

Data based on an intent to treat missing data counted as a failure analyses. Under observed case analysis, 1/10 (10%) and 6/15 (40%) patients in the placebo pretreatment / placebo and vancomycin pretreatment / SER-287 daily treatment arms, respectively, achieved endoscopic improvement ($p=0.1794$). The observed analysis includes a patient in the placebo study arm who experienced a disease flare and was treated with corticosteroids (a protocol violation) prior to the end of treatment endoscopy

Illustrative endoscopy improvement findings from patient in SER-287 daily treatment arm

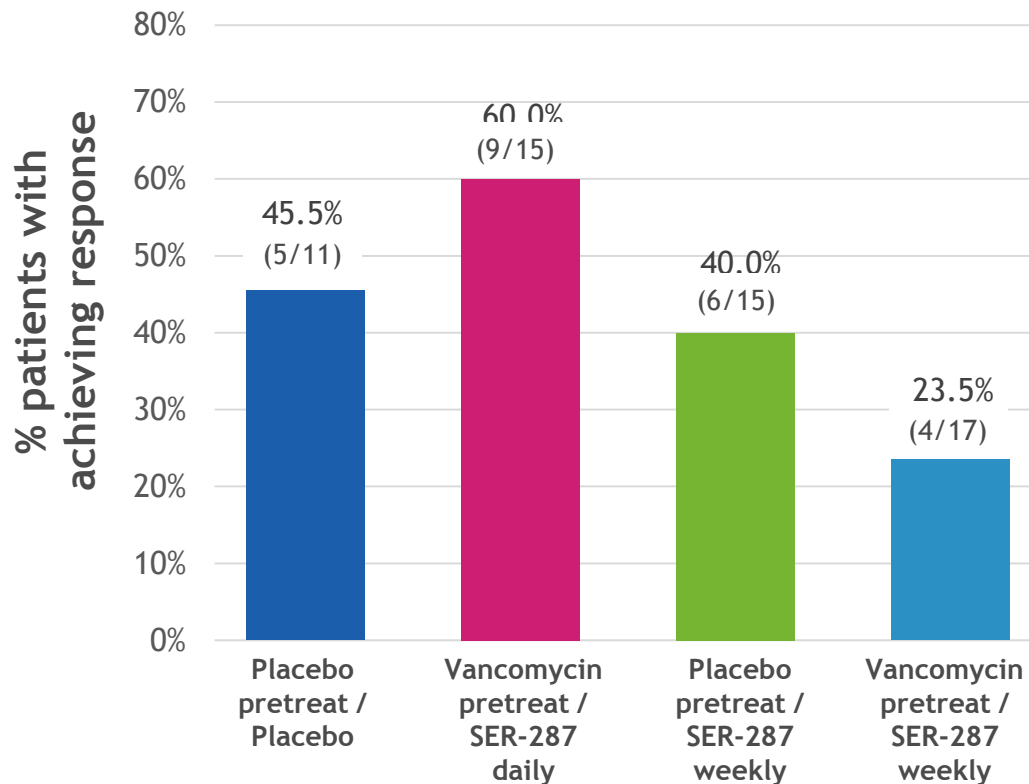
Pre-treatment endoscopy showing the sigmoid colon with spontaneous bleeding and ulceration



Post-treatment day 64 endoscopy



Response rate is less reliable endpoint; Not recommend by FDA as a primary endpoint for UC



High placebo response rate reported in other UC clinical studies using drugs with diverse mechanisms¹

Ulcerative Colitis: Clinical Trial Endpoints Guidance for Industry²

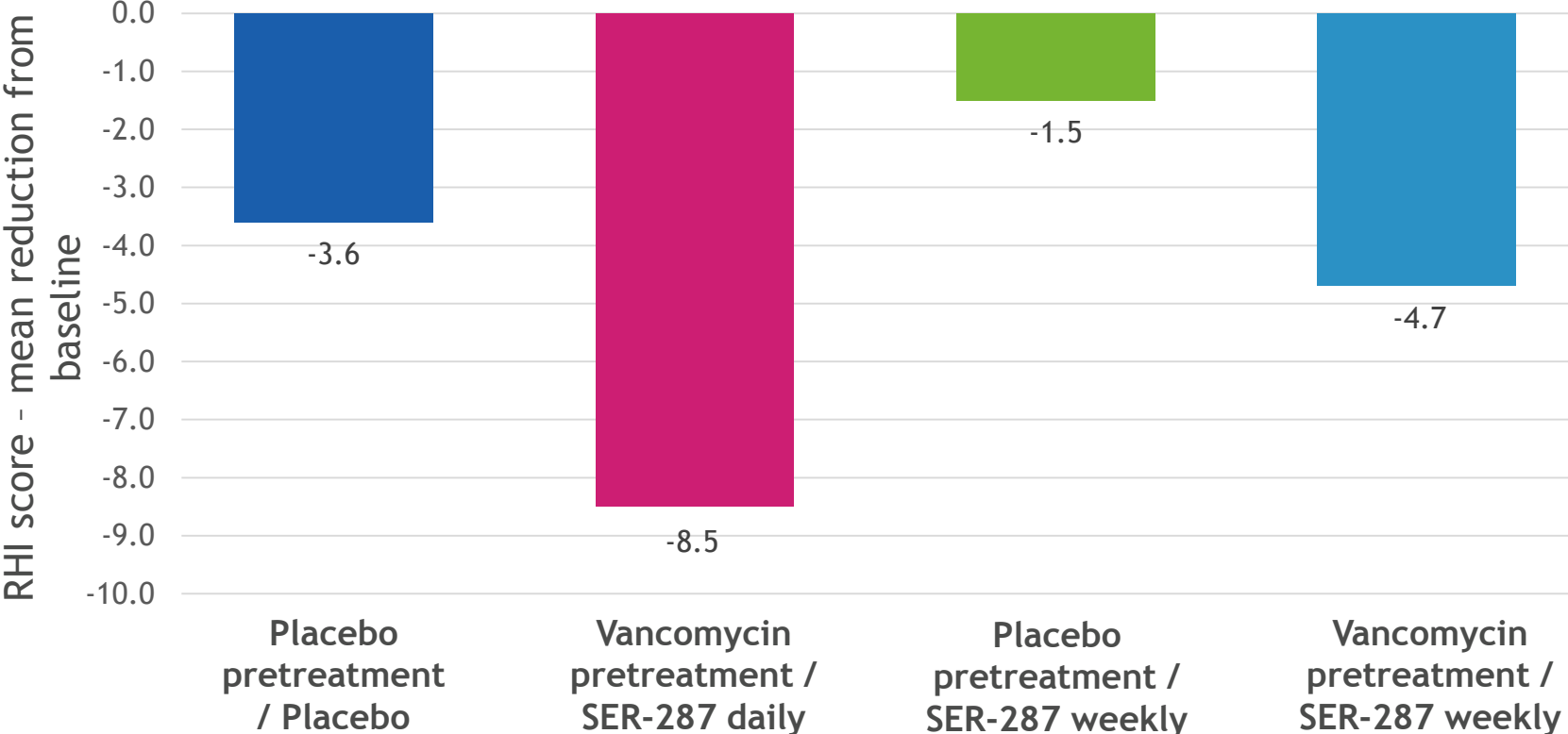
“We currently recommend a primary endpoint of clinical remission (responder definition based on Stool Frequency, Rectal Bleeding, and Endoscopy scores).”

1. Jairath V. et al., *Journal of Crohn's and Colitis*, 2016

2. August 2016 FDA draft guidance

Data based on an intent to treat missing data counted as a failure analyses. Under observed case analysis, 6/10 (60%) and 6/10 (60%) patients in the placebo pretreatment/placebo and vancomycin pretreatment/SER-287 daily treatment arms, respectively, achieved response (p=0.99). The observed analysis includes a patient in the placebo study arm who experienced a disease flare and was treated with corticosteroids (a protocol violation) prior to the end of treatment endoscopy

Histological healing RHI score change 8 weeks post SER-287 administration



Note: Intent to treat population, missing data equal failure
Subjects with normal histology at Baseline were excluded. Seres also evaluated potential biomarkers serum CRP and fecal calprotectin and observed no statistically significant impact.

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%)

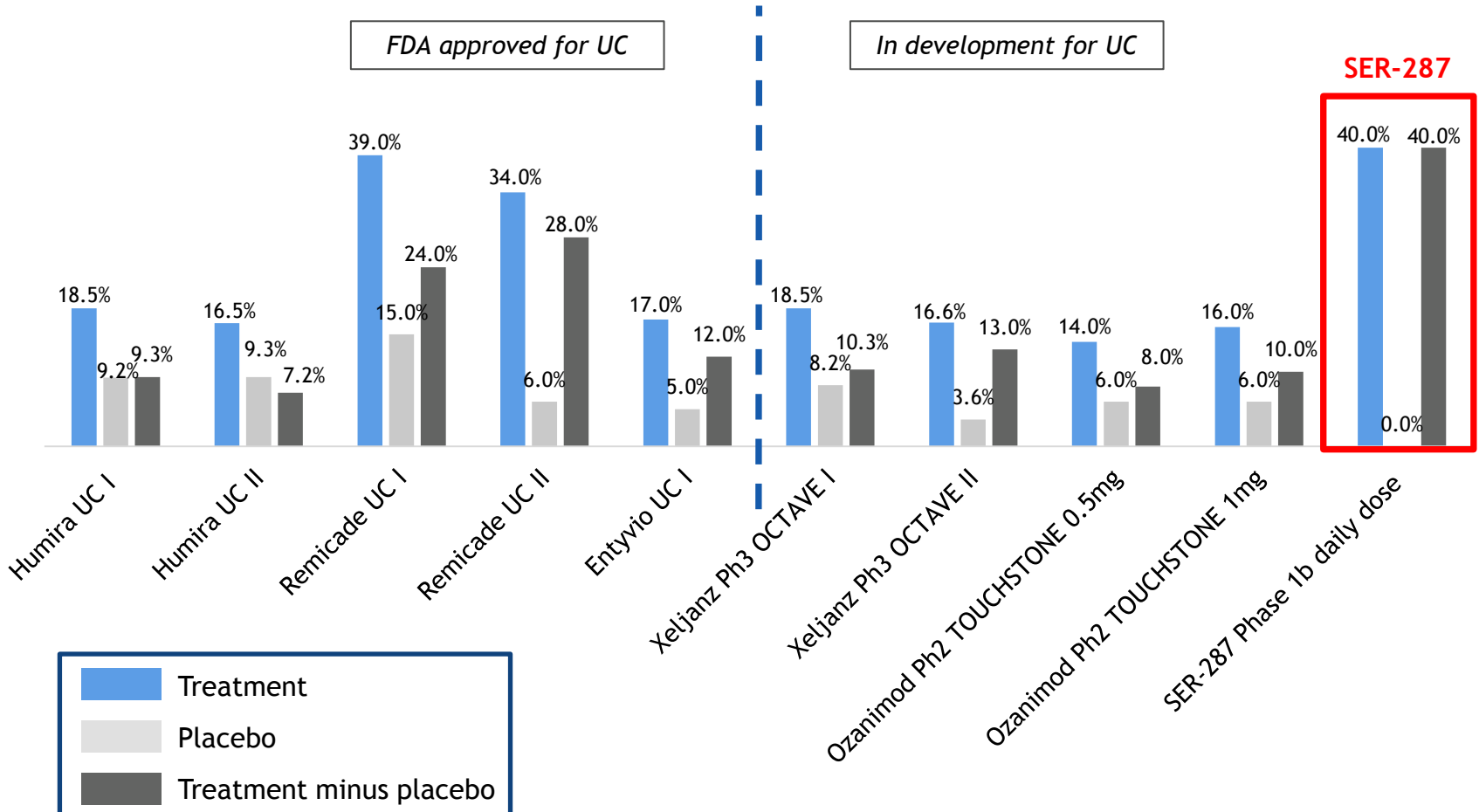
Analyses of post SER-287 treatment impact on disease activity

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)

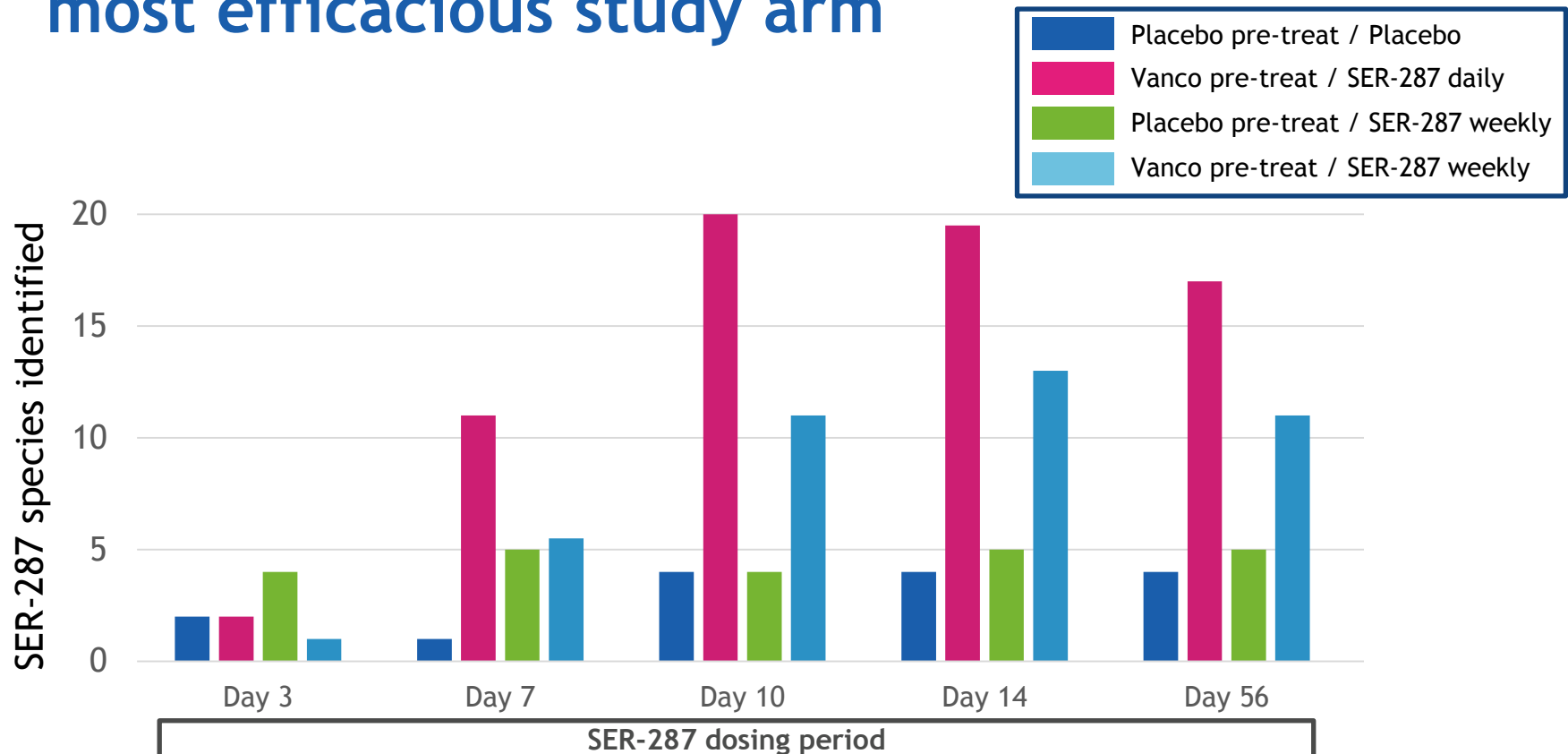
Favorable SER-287 efficacy relative to selected approved and development stage UC drugs

Remission Rates for Induction in Active UC



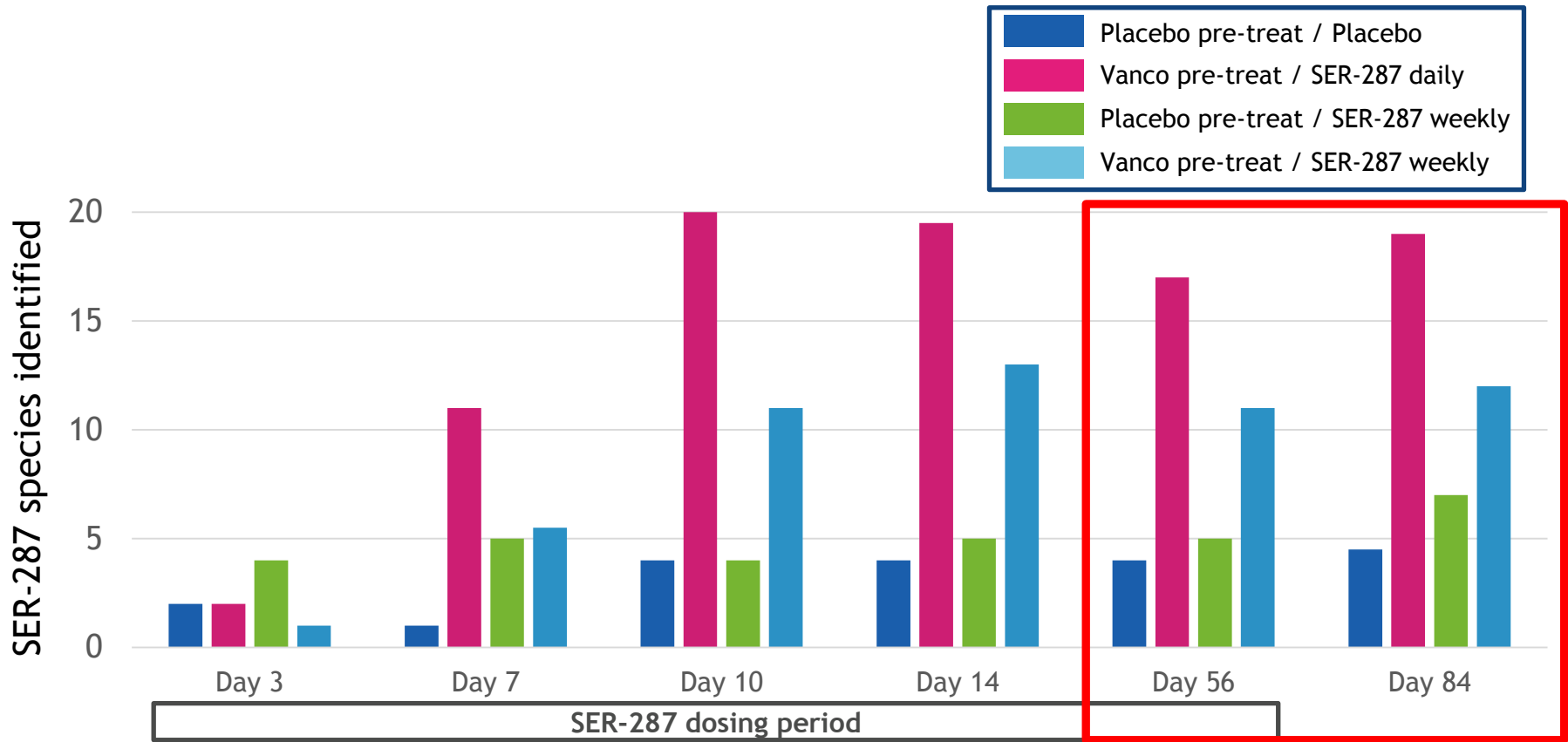
Adapted from Leerink Nov. 27 2017 report: Future of IBD: Category should double by 2023 despite GED-0301 disappointment; Note that study-to-study differences limit the ability to directly compare results.

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



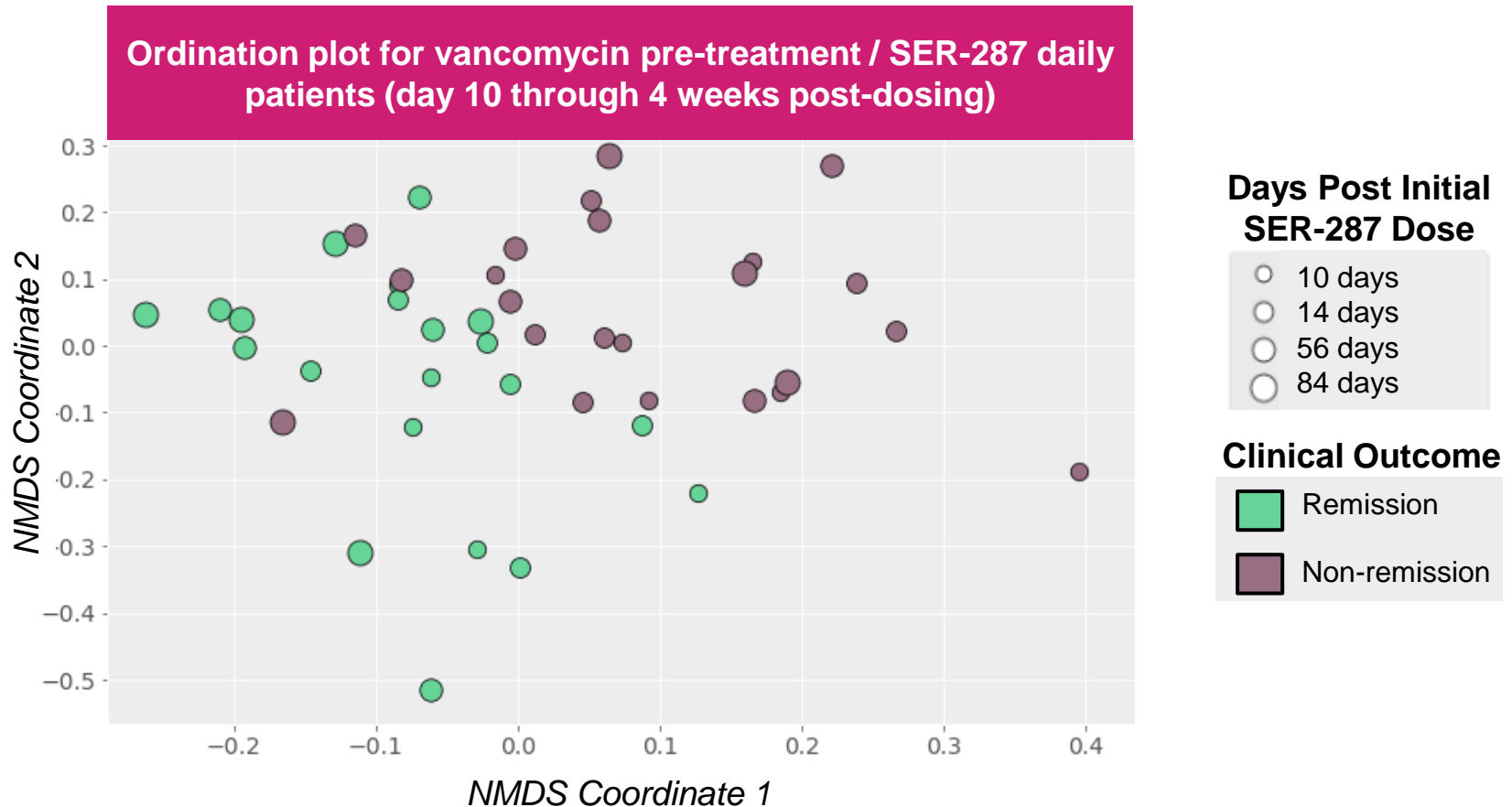
- Statistically significant engraftment in vanco pre-treat / SER-287 daily arm, versus placebo pre-treat / placebo arm, beginning at day 7 and maintained throughout the dosing period
- Statistically significant and dose-dependent engraftment in study arms with vanco pre-treatment / SER-287 versus placebo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

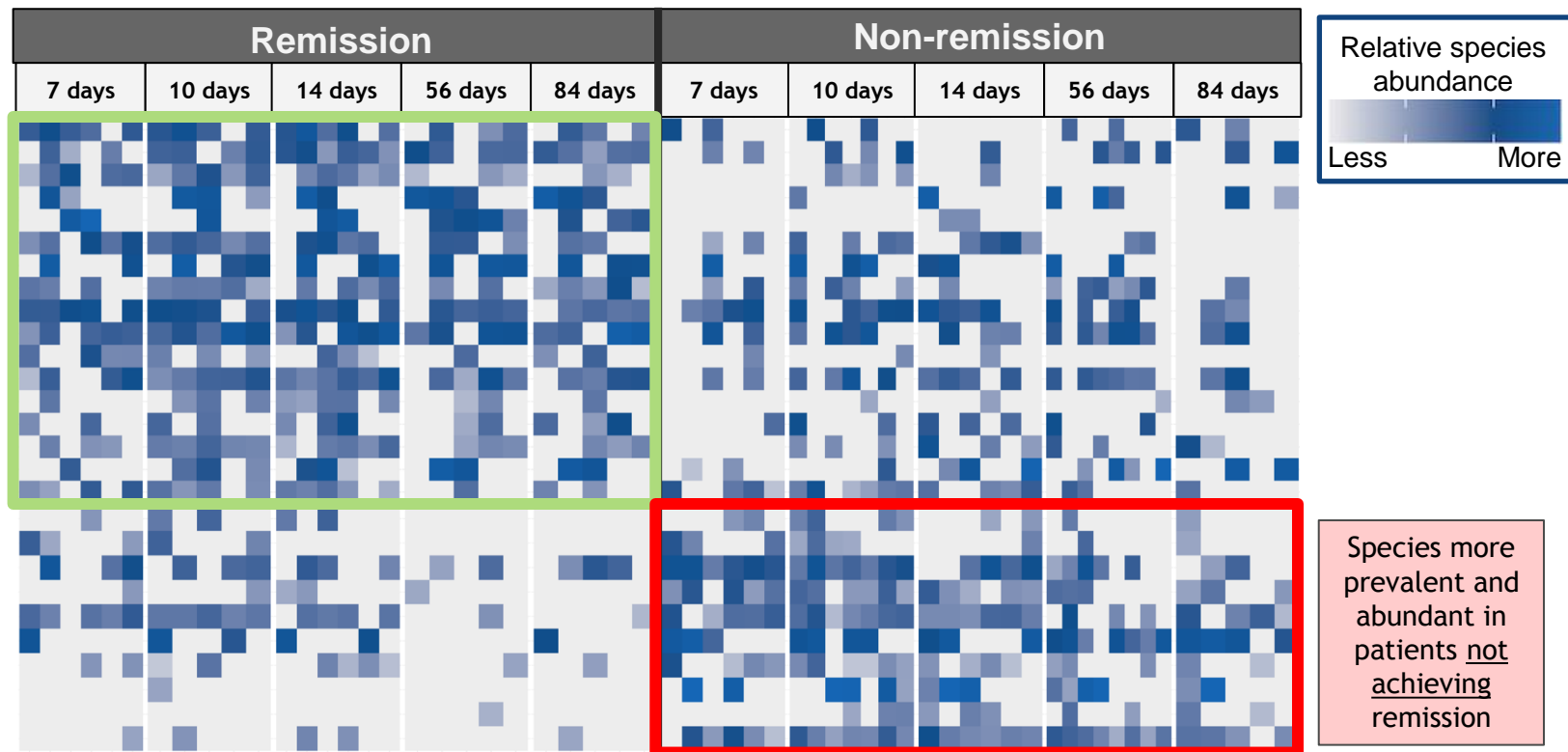
Microbiome composition is distinct in patients achieving remission



Non-metric multidimensional scaling plot shows ecological distance between microbiome compositions of 15 subjects (6 remission, 9 non-remission) at different timepoints; microbiome samples not available for all timepoints of each subject. Ecological distance is calculated using the Binary Jaccard metric which computes the similarity between any two samples based on the presence and absence of species.

Specific bacterial species linked with remission

- Identified 27 species ecology statistically significantly correlated with remission
- Species include both SER-287 bacteria and others augmented by treatment



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

Advancing SER-287 clinical development

- Compelling Phase 1b results:
 - Beneficial impact on remission and endoscopic improvement
 - Favorable safety and tolerability profile
 - Microbiome data provide mechanistic support for clinical results and demonstrate species-level bacterial signatures associated with efficacy
- Obtained FDA Orphan Designation for Pediatric Ulcerative Colitis
- Rapidly advancing SER-287 clinical development:
 - Obtain FDA guidance
 - Expect to start next Ulcerative Colitis clinical study - mid-2018
 - Evaluate other opportunities (e.g. Crohn's disease, UC combination therapy)

SER-287 Phase 1b study results presented at 13th European Crohn's and Colitis Organisation congress (Feb 14-17, 2018)

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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Gut microbiome composition impacts efficacy of checkpoint inhibitors in oncology patients

Science AAAS

Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota

Marie Vétizou^{1,2,3}, Jonathan M. Pitt^{1,2,3}, Romain Daillière^{1,2,3}, Patricia Lepage⁴, Nadine Waldschmit...

+ See all authors and affiliations

Science 27 Nov 2015:
Vol. 350, Issue 6264, pp. 1079-1084
DOI: 10.1126/science.aad1329

Science AAAS

Commensal *Bifidobacterium* promotes antitumor immunity and facilitates anti-PD-L1 efficacy

Ayelet Sivan^{1*}, Leticia Corrales^{1*}, Nathaniel Hubert², Jason B. Williams¹, Keston Aquino-Michaels³, Zachary...

+ See all authors and affiliations

Science 27 Nov 2015:
Vol. 350, Issue 6264, pp. 1084-1089

Science AAAS

Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors

Bertrand Routy^{1,2,3}, Emmanuelle Le Chatelier⁴, Lisa Derosa^{1,2,3}, Connie P. M. Duong^{1,2,5}, Maryam Tidjani Alou^{1,2,3}, Romain D...

+ See all authors and affiliations

Science 02 Nov 2017:
aan3706
DOI: 10.1126/science.aan3706

Science AAAS

Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients

V. Gopalakrishnan^{1,2,*}, C. N. Spencer^{2,3,*}, L. Nezi^{3,*}, A. Reuben¹, M. C. Andrews¹, T. V. Karpinets³, P. A. Prieto^{1†}, D. Vicente^{1...}

+ See all authors and affiliations

Science 02 Nov 2017:
aan4236
DOI: 10.1126/science.aan4236

November 2017 Collaboration

MDAnderson
Cancer Center



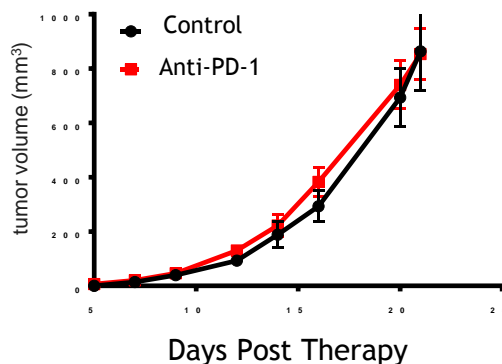
PARKER
INSTITUTE
for CANCER IMMUNOTHERAPY



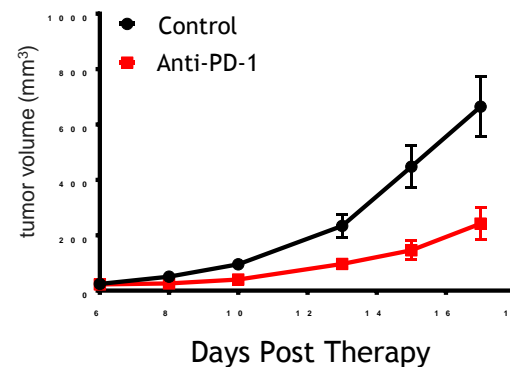
Modulation of the microbiome restores anti tumor efficacy and immune infiltration to anti-PD-1 therapy

Anti-tumor efficacy following anti-PD-1 administration into colonized mice

Tumor Growth Curves - Germ free

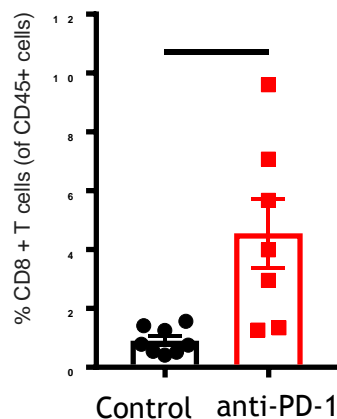


Tumor Growth Curves - Colonized

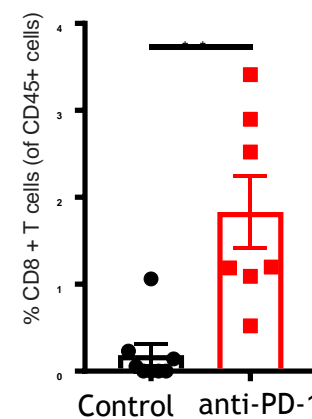


Immune cell infiltration into tumor following anti-PD-1 administration

CD8+ T cells



Dendritic cells



Collaboration to advance microbiome therapeutic into immuno-oncology



- Planned placebo-controlled 3 arm clinical study to evaluate impact of checkpoint inhibitors plus adjunctive microbiome therapeutics on clinical outcomes in patients with advanced metastatic melanoma
- Planned start study in 2018
- Seres option to license foundational intellectual property from MD Anderson related to the use of bacteria in combination with checkpoint inhibitors

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 (mid-2018)

Immuno-oncology clinical study start (2018)

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

Resources to operate through Q1 2019

Balance Sheet	As of Dec. 31, 2017
Cash, cash equivalents and investments	\$150 M

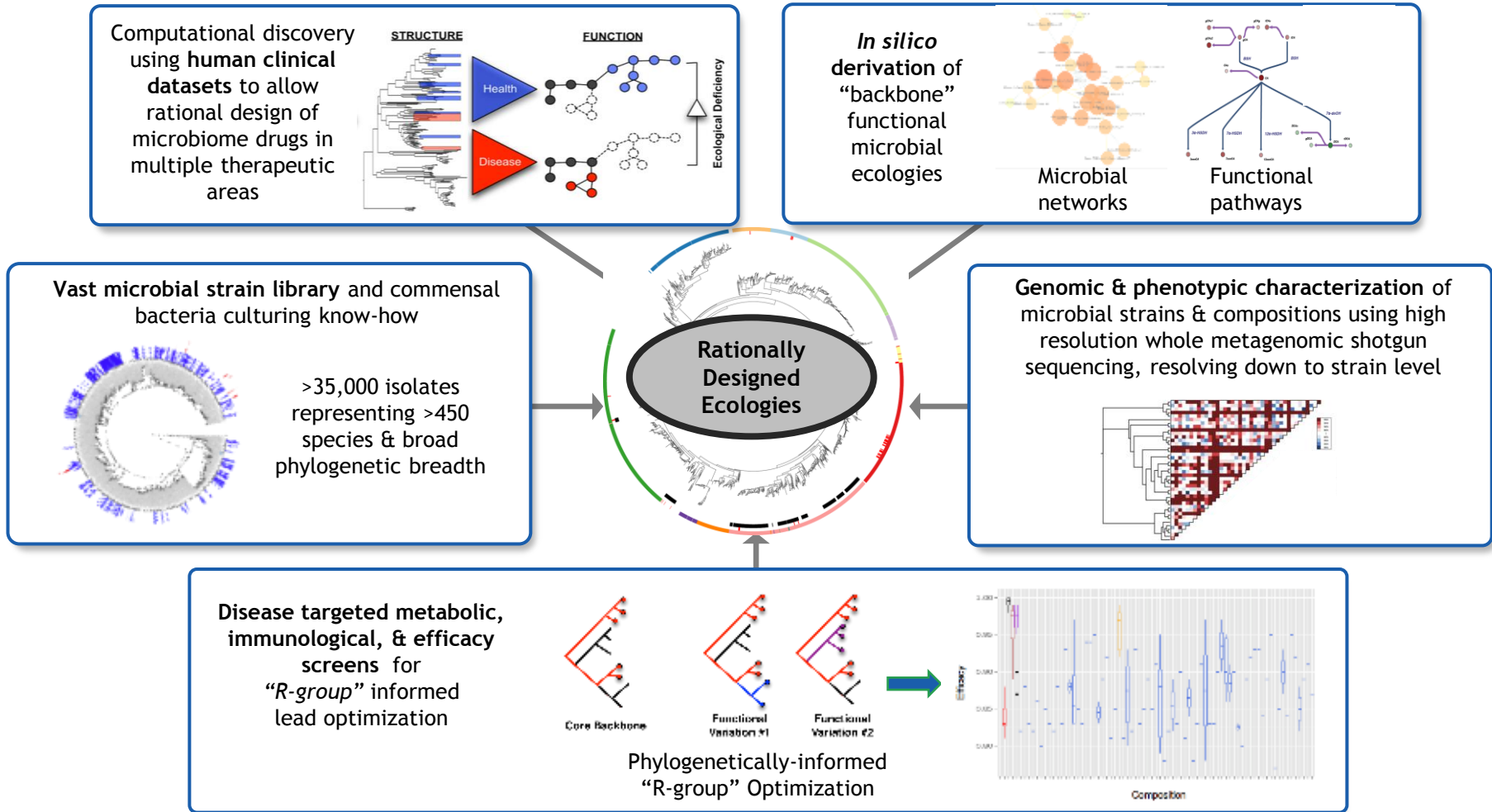
Appendix



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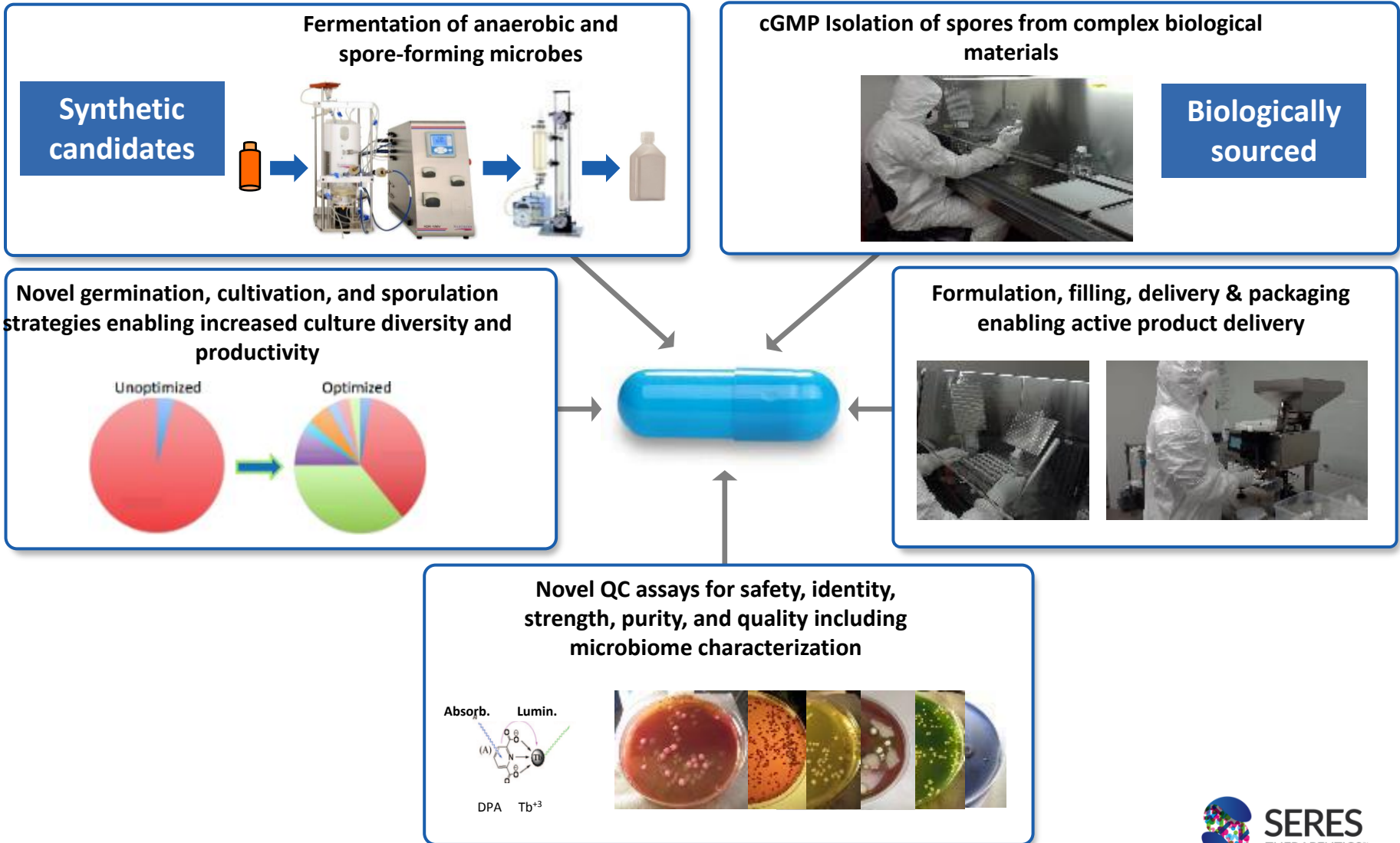
Leading the Microbiome Revolution

Differentiated microbiome R&D platform



Only company with clinical stage development programs giving insights into how to therapeutically alter the microbiome to treat multiple diseases

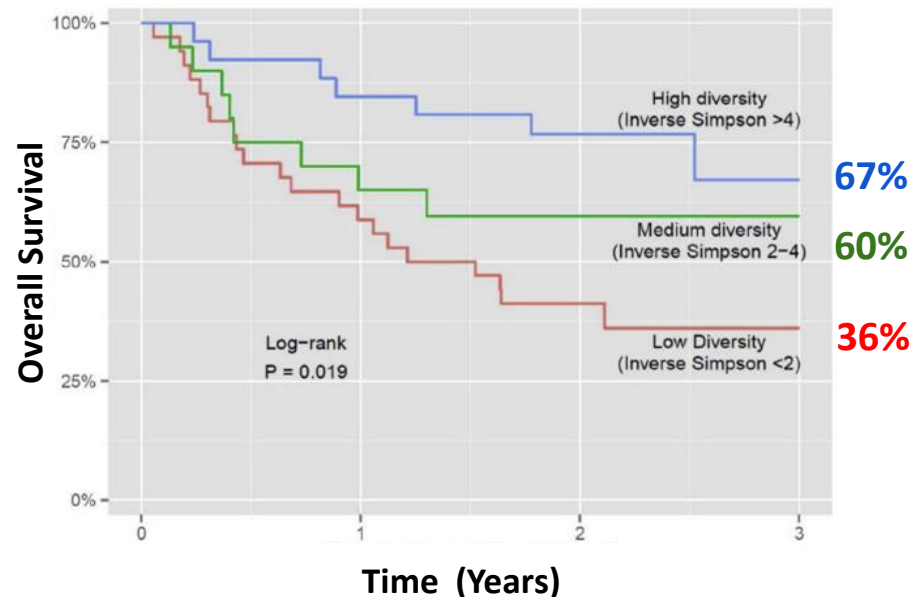
CMC platform enables manufacture of cGMP-compliant, oral, microbiome therapeutic candidates



SER-155: Ecobiotic[®] therapeutic candidate to improve transplantation outcomes

- Ecobiotic[®] therapeutic candidate to improve outcomes in patients receiving allogeneic hematopoietic stem cell transplantation (HSCT) or solid organ transplants
- Designed to reduce both infection risk, and Graft vs. Host Disease (GvHD)

Patient Microbiome Diversity Correlates with Mortality Risk³



CARB-X
Xccelerating global antibacterial innovation

Nov. 2017: CARB-X grant of up to \$5.6M obtained to support preclinical research and early development work for SER-155