



Baird 2017 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. Such statements are subject to factors, risks and uncertainties (such as those detailed in the Company’s periodic 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

Pipeline

Broad pipeline in infectious, inflammatory and immune, metabolic and liver diseases

Team

Experienced, accomplished leadership team

Runway

Strong cash and strategic position

The microbiome is essential to human health

Infectious Disease

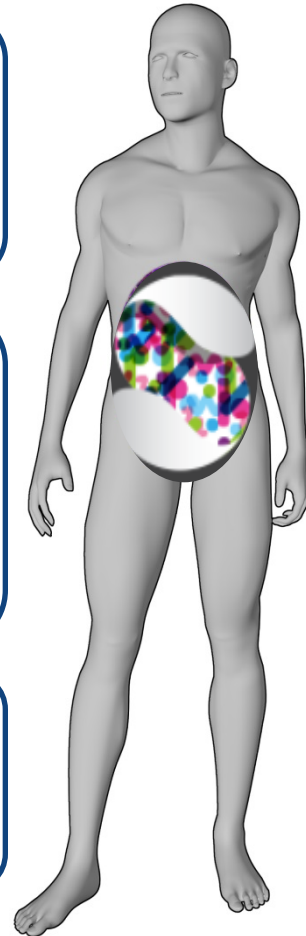
- A diverse microbiome resists colonization by exogenous pathogens
- Exposure to broad spectrum antibiotics, and resulting gut microbiome dysbiosis, increase risk for *C. difficile* infection and colonization / infection by multi-drug resistant organisms

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)



Business strategy

Focused clinical efforts

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

C. difficile
infection

Inflammatory
bowel disease

World class, differentiated, microbiome expertise

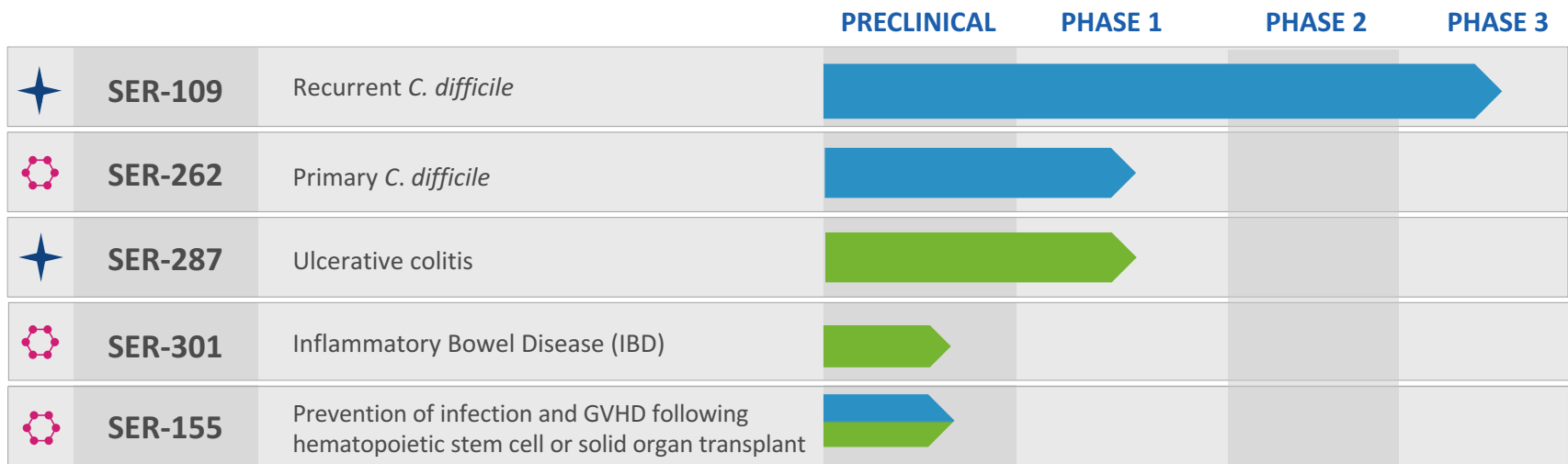
- Computational biology
- Basic microbiome research
- Microbiology
- Translational science
- Clinical development
- Advanced manufacturing


Research in new therapeutic areas

- Collaborate with leading academic centers to advance research in promising therapeutic areas



Robust microbiome therapeutics pipeline



 Synthetically fermented
  Biologically sourced
  Infectious
  Inflammatory

DISCOVERY EFFORTS

ACADEMIC COLLABORATOR

Immuno-oncology and hematopoietic stem cell transplant



Inflammatory bowel diseases



St. Joseph's
Healthcare Hamilton

Primary sclerosing cholangitis, NASH and other liver diseases



Obesity/metabolic syndrome



Genetic metabolic diseases



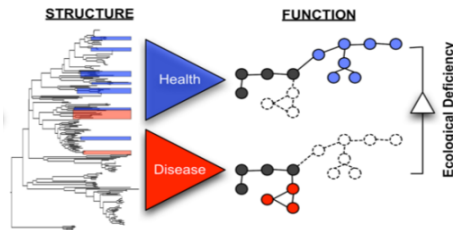
Based on interactions with the U.S. Food and Drug Administration, ECOSPOR III will be designated a Phase 3 trial and the company expects that this single pivotal study may support SER-109 registration and approval.

Collaboration with Nestlé Health Science regarding *C. difficile* and IBD programs for markets only outside of North America

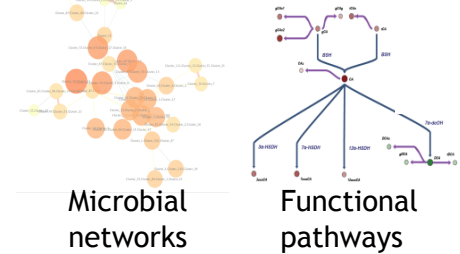


Differentiated microbiome R&D platform

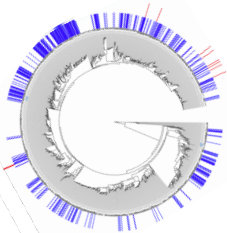
Computational discovery using human clinical datasets to allow rational design of microbiome drugs in multiple therapeutic areas



In silico derivation of 'backbone' functional microbial ecologies

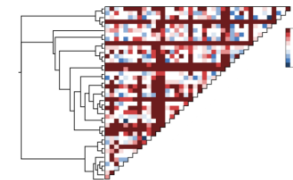


Vast microbial strain library and commensal bacteria culturing know-how



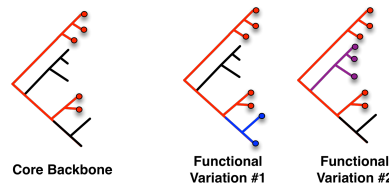
>14,000 strains spanning broad biological breadth

Genomic & phenotypic characterization of microbial strains & compositions using high resolution whole metagenomic shotgun sequencing, resolving down to strain level

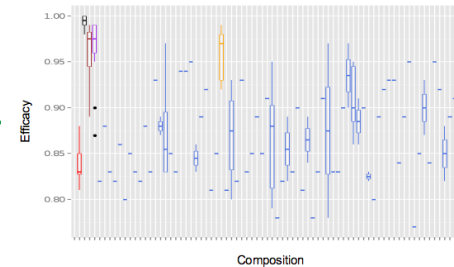


Rationally Designed Ecologies

Disease targeted metabolic, immunological, & efficacy screens for 'r-group' informed lead optimization



Phylogenetically-informed "R-group" Optimization

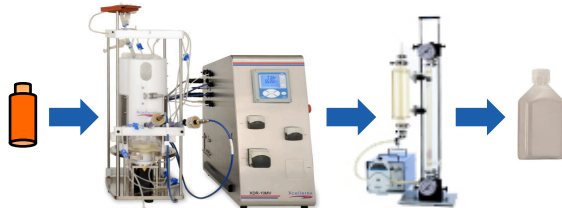


Only company with clinical stage microbiome development programs, human microbiome datasets, and clinical datasets before and after treatment

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

Fermentation of anaerobic and spore-forming microbes

Synthetic candidates



cGMP Isolation of spores from complex biological materials



Biologically sourced

Novel germination, cultivation, and sporulation strategies enabling increased culture diversity and productivity

Unoptimized

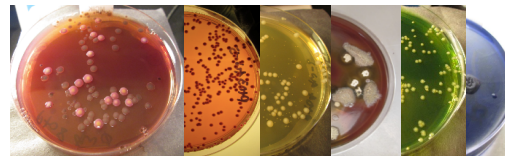
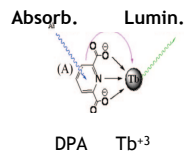
Optimized



Formulation, filling, delivery & packaging enabling active product delivery



Novel QC assays for safety, identity, strength, purity, and quality including microbiome characterization



Clostridium difficile Infection

Overview and R&D Programs



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C. difficile infection overview

- Infectious disease caused by toxin producing anaerobic, spore-forming bacteria, resulting in diarrhea, abdominal pain, fever, and nausea
- Leading cause of hospital-acquired infection in the US
 - Approximately 29,000 deaths/year
 - Multiply recurrent *C. difficile* infection incidence increased 43% between 2001-2010
- ~25% of patients with primary *C. diff.* recur
- Risk of relapse increases with each recurrence



Treatment landscape & disease burden

Modality	Characteristics
Antibiotics 	<ul style="list-style-type: none"> • Perpetuates microbiome dysbiosis, creating <i>C. difficile</i> infection susceptibility • High recurrence rates, especially in recurrent cases
Fecal Transplant 	<ul style="list-style-type: none"> • Typically invasive procedure (colonoscopy or NG-tube) • Potential for transmission of human pathogens • No FDA approved products
Antibodies 	<ul style="list-style-type: none"> • Modest efficacy in Phase 3 studies • Does not address underlying microbiome dysbiosis • Complex administration, not patient-friendly

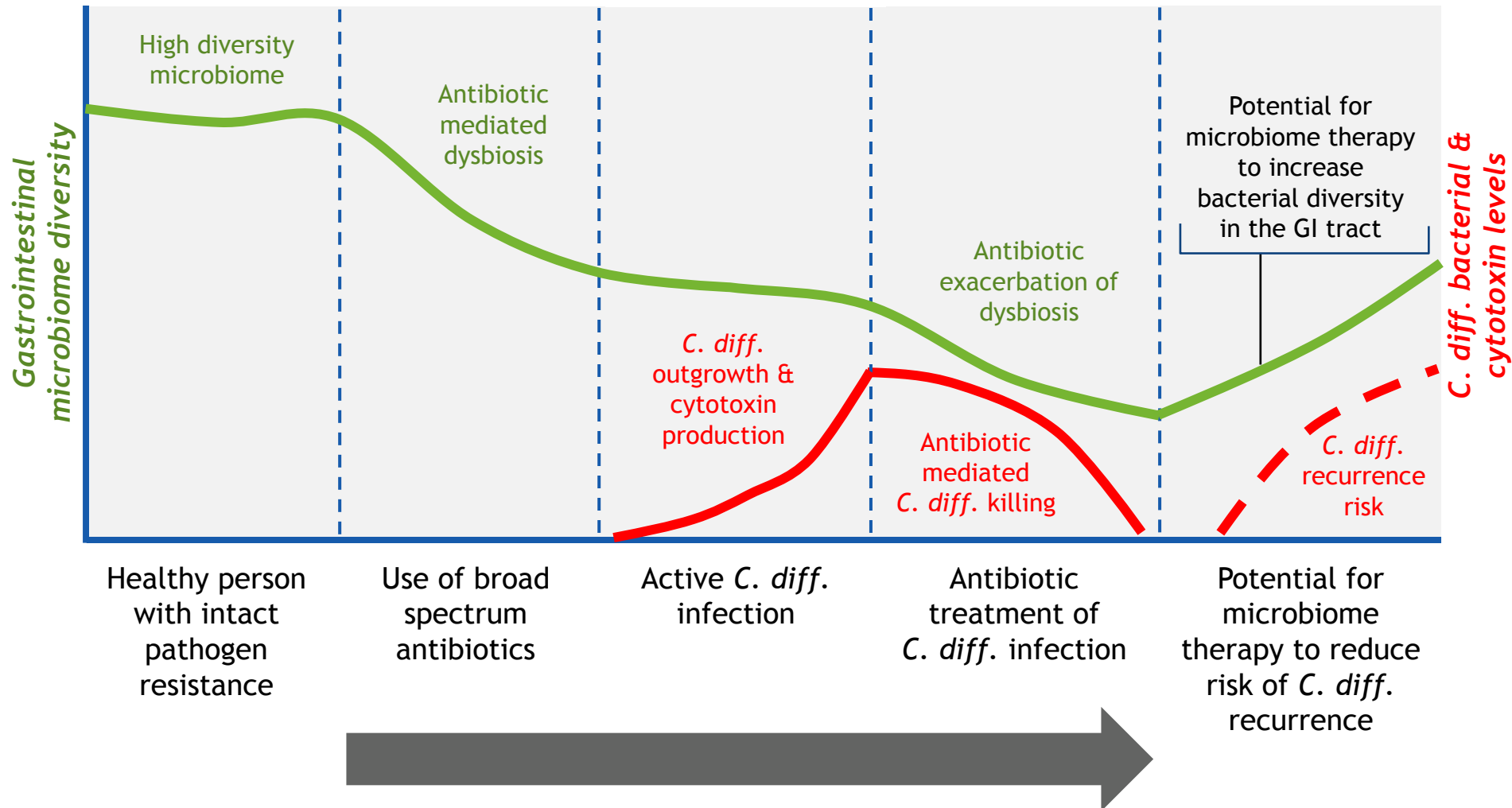
High Unmet Medical Need

- Economic burden of \$4.8B in U.S. acute-care facilities¹
- Recurrent CDI episode ~\$18K²; >\$50K for cycle of recurrences

High Treatment Costs

Dysbiosis and potential for therapeutic intervention

Hypothetical patient course



SER-109 Phase 1b and Phase 2 (8-week) study results

	Phase 1b Open Label, Single-Arm (n=30; 4 sites)	Phase 2 - Interim results Randomized, Placebo-Controlled (n=89; randomized 2:1; 28 sites)
Primary Endpoint	CDI recurrence up to 8 weeks defined by: >3 unformed stools over 1 day	CDI recurrence up to 8 weeks defined by: ≥ 3 unformed stools/day for ≥ 2 days
Efficacy	<ul style="list-style-type: none"> • 87% non recurrence, per protocol • 3 of 4 patients with recurrent transient diarrhea, did not require antibiotic treatment and tested negative for <i>C. diff.</i> at 8 weeks 	<ul style="list-style-type: none"> • SER-109: 59% (33 of 59) non recurrence • Placebo: 47% (14 of 30) non recurrence • Relative risk recurrence between arms not significant
Safety	<ul style="list-style-type: none"> • Most AEs were mild to moderate and transient • Most frequent AEs were gastrointestinal symptoms similar in nature to that seen in FMT trials or following CDI 	<ul style="list-style-type: none"> • SER-109 is well-tolerated with an acceptable safety profile, it was associated with a small increase in gastrointestinal adverse effects, particularly diarrhea, compared to placebo (25% vs 14%)

SER-109 Phase 2 study post read-out analyses and findings

SER-109 analyses	Key issues addressed
Clinical	<ul style="list-style-type: none">Detailed analyses of clinical dataInvestigation of <i>C. difficile</i> diagnostics
Pharmacodynamics / microbiome analyses	<ul style="list-style-type: none">Investigation of drug activity
Chemistry, Manufacturing and Controls (CMC)	<ul style="list-style-type: none">Drug product distribution and handlingPhase 1b to Phase 2 manufacturing and formulation changes, and potential impact on drug activity



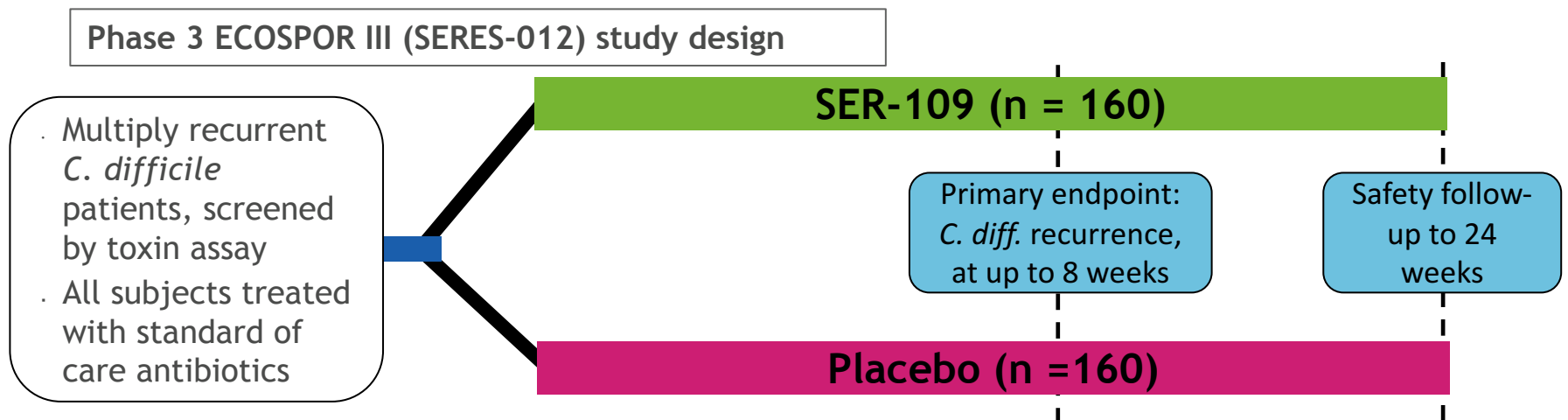
Key Findings: Factors contributing to SER-109 Phase 2 study result

Diagnosis - Misdiagnoses may have occurred both in some patients entering the trial, as well as for recurrences diagnosed during the study

Dose - The dose used in the Phase 2 study may have been suboptimal in certain patients

Phase 3 SER-109 ECOSPOR III study underway

- Based on FDA feedback, ECOSPOR III designated as a Phase 3 study
- The ECOSPOR III Phase 3 study is the first pivotal trial in the emerging field of oral microbiome therapeutics
- ECOSPOR III to utilize a SER-109 dose approximately 10-fold higher than the dose used in the prior Phase 2 study, administered over three days



SER-262: Synthetic Ecobiotic® therapeutic candidate for primary *C. difficile* infection

- Oral, microbiome therapeutic candidate comprising twelve strains of fermented, rationally selected bacterial spores
- Bacteria 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 a b	r i b	x y l	c e l	s t r	t r e	m e l	p e l	m t r	s a G	N g m	a s a	f o r	s p y	
<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

60+ patients with primary *C. difficile* infection

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

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

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

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

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

Multi Dose Cohorts: Tx spores (n=10); placebo (n=2); Dosing provided over three 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

Inflammatory Bowel Disease

Overview and R&D Programs



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Multiple FMT studies provide proof of concept for microbiome therapy 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

	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
Secondary outcomes				
Steroid-free clinical remission†	18 (44%)	8 (20%)	2.2 (1.1-4.5)	0.021
Steroid-free clinical response‡	22 (54%)	9 (23%)	2.4 (1.3-4.5)	0.004
Steroid-free endoscopic remission§	5 (12%)	3 (8%)	1.6 (0.4-6.4)	0.48
Steroid-free endoscopic response¶	13 (32%)	4 (10%)	3.2 (1.1-8.9)	0.016

*Total Mayo score ≤ 2 , with all subscores ≤ 1 , and ≥ 1 point reduction from baseline in endoscopy subscore.

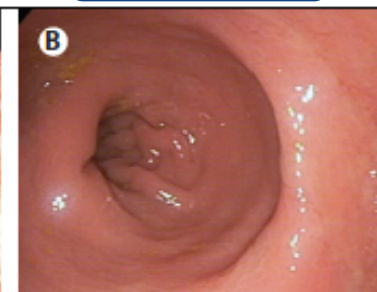
†Combined Mayo subscores of ≤ 1 for rectal bleeding plus stool frequency. ‡Decrease of ≥ 3 points or $\geq 50\%$ reduction from baseline (or both) in combined Mayo subscores for rectal bleeding plus stool frequency. §Mayo endoscopy subscore 0. ¶Mayo endoscopy subscore ≤ 1 , with ≥ 1 point reduction from baseline.

Table 2: Primary and secondary outcomes at week 8

Subject A, Baseline



Subject A, 8-wk post FMT



SER-287 Inflammatory Bowel Disease (IBD) opportunity

Significant need for improved therapies

- Large US population: ~700K ulcerative colitis, ~700K Crohn's
- Many patients do not respond to current therapies, both for induction and maintenance
- Many therapies are immunosuppressive, limiting widespread use

SER-287 target profile:

- Oral
- Alternative mechanistic approach, potential mono or combo therapy
- Not expected to be immunosuppressive

SER-287 development opportunity:

- Initial development as induction therapy for ulcerative colitis
- Potential development as UC maintenance therapy, Crohn's disease

SER-287 Phase 1b ulcerative colitis study is fully enrolled

55 mild-moderate UC patients failing standard-of-care*

Arm A (n~15): Placebo pre-treatment / SER-287 once weekly dosing for 8 weeks

Arm B (n~10): Placebo pre-treatment / Placebo once daily for 8 weeks

Arm C (n~15): Vancomycin pre-treatment / SER-287 once daily dosing for 8 weeks

Arm D (n~15): Vancomycin pre-treatment / SER-287 once weekly dosing for 8 weeks

Primary Objective

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

Secondary Objectives

- Clinical responses, including complete remission, and endoscopic improvement
- Change in serum and fecal biomarkers
- Complement of microbiome metabolic pathways from stool, urine and blood
- Immunological and pathologic changes in mucosal biopsies

* Study enrollment completed with 58 subjects

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

- Follow-on therapeutic candidate to SER-287 in preclinical development for inflammatory bowel disease
- Oral, microbiome therapeutic candidate comprising fermented, rationally selected bacteria
- Selection of SER-301 bacterial composition to be based on:
 - SER-287 study data (clinical and microbiome analysis)
 - Existing collaborations evaluating analysis of FMT ulcerative colitis clinical study data
 - Preclinical screening for microbial function, immunological assay, and animal models

Additional R&D Opportunities

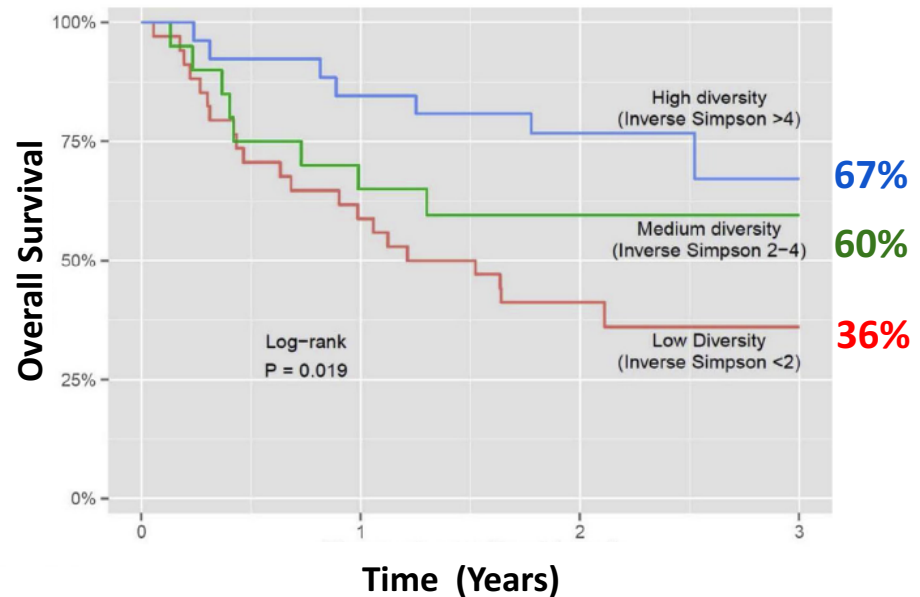


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SER-155: Synthetic Ecobiotic® therapeutic candidate to improve transplantation outcomes

- Ecobiotic® synthetically derived 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)

HSCT Patient Microbiome Health Correlates with Overall Mortality Risk³



Immuno-oncology microbiome therapeutic opportunity

Therapeutic Objectives

- **To improve efficacy:** Modulate immune response, improve clinical response to therapeutic checkpoint inhibitors
- **To improve safety:** Reduce anti-CTLA4 induced colitis by providing microbial ecologies correlated with improved patient outcomes

ASCO-SITC Clinical Immuno-Oncology Symposium

February 23-25, 2017 | Hyatt Regency Orlando | Orlando, FL | #Immunosym



Association of diversity and composition of the gut microbiome with differential responses to PD-1 based therapy in patients with metastatic melanoma.

Citation:

J Clin Oncol 35, 2017 (suppl 7S; abstract 2)

Author(s):

Vancheswaran Gopalakrishnan, Christine Spencer, Alexandre Reuben, Tatiana Karpinetz, Diane Hutchinson, Kristi Hoffman, Peter A. Prieto, Michael T. Tetzlaff, Alexander Lazar, Michael A. Davies, Jeffrey E. Gershenwald, Robert R. Jenq, Patrick Hwu, Padmanee Sharma, James Patrick Allison, Andrew Futreal, Nadim Ajami, Joseph Petrosino, Carrie Daniel-MacDougall, Jennifer A. Wargo; UT MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; Baylor College of Medicine, Houston, TX; Memorial Sloan-Kettering Cancer Ctr, New York, NY



Intestinal microbiome analyses identify melanoma patients at risk for checkpoint-blockade-induced colitis

Krista Dubin^{1,2,3}, Margaret K. Callahan^{4,5}, Boyu Ren⁶, Raya Khanin⁷, Agnes Viale⁸, Lilan Ling², Daniel No², Asia Gobourne², Eric Littmann², Curtis Huttenhower^{6,9}, Eric G. Pamer^{1,2,10,*} & Jedd D. Wolchok^{4,5,10,11,*}

Science

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









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

Collaborations with leading institutes to advance R&D progress

Target Indication	Academic Collaboration
Inflammatory bowel disease	  
Immuno-oncology therapeutics	
Hematopoietic stem cell and solid organ transplantation	
Primary sclerosing cholangitis, NASH and Other liver diseases	
Obesity and metabolic syndrome	
Rare genetic metabolic diseases (e.g., urea cycle disorders, hepatic encephalopathy)	

Collaboration announcements: Mayo Clinic, see June 6, 2016 press release; Memorial Sloan Kettering, University of Pennsylvania, see May 12, 2016 press releases; Medical University of Graz and Research Institute of St. Joseph's Hamilton, see May 4, 2016 press release; Massachusetts General Hospital, see June 22, 2016 press release.

Broad IP portfolio and regulatory exclusivity

7 ISSUED US PATENTS + LICENSED IP*

- Demonstrates rationally designed ecologies of spores and microbes are patentable
- Composition of matter and method claims
- Claims related to SER-109/CDI & colitis lead candidates through **2033**

SERES PATENT PORTFOLIO

15 Families of Applications

9 Nationalized

2 Pending PCT

4 Pending Provisionals

REGULATORY EXCLUSIVITY



12 years for new biological composition



10 years for new drug

* Includes additional rights to intellectual property including 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

Well positioned for success

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

SER-287: Ulcerative colitis - Phase 1b read-out (H2 2017)

SER-262: Primary *C. difficile* infection - Phase 1b read-out (early 2018)

Advancing new pipeline programs in infectious diseases, inflammatory and immune diseases (including immuno-oncology), metabolic and liver diseases

Resources to operate through 2018

Balance Sheet	As of June 30, 2017
Cash, cash equivalents and investments	\$175.2 M

\$20.0 million milestone payment associated with the SER-109 Phase 3 study start from Nestlé Health Science has been received in the third quarter of 2017