



Corporate Overview



SERES
THERAPEUTICS™

Leading the Microbiome Revolution

March 16, 2017

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.

Investor highlights

Opportunity

Expansive therapeutic opportunity utilizing the microbiome, a highly promising new area of medicine

Platform

Seres is a 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

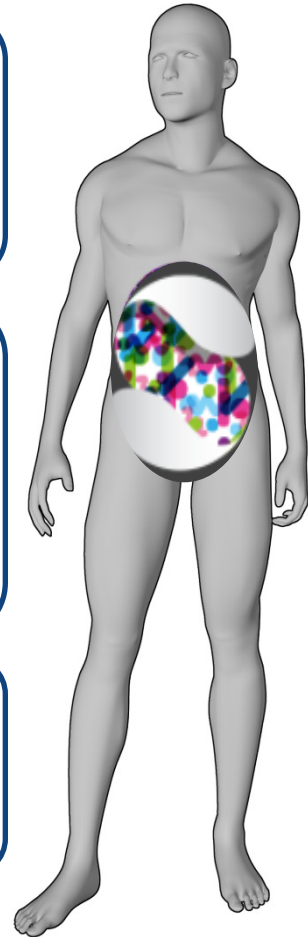
- A diverse microbiome resists colonization by exogenous pathogens
- Exposure to broad spectrum antibiotics, and resulting gut microbiome dysbiosis, increase risk for *C. difficile* infection and colonization / infection by multi-drug resistant organisms

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 microbiome composition has been demonstrated to impact the efficacy and safety of immuno-oncology checkpoint inhibitors

Metabolic Disease

- Effects on liver function, glucose utilization, and caloric availability
- Microbiome, and bacterial bile acid metabolism, 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



MASSACHUSETTS
GENERAL HOSPITAL



Memorial Sloan Kettering
Cancer Center







MAYO CLINIC



St. Joseph's
Healthcare Hamilton

Robust microbiome therapeutics pipeline

			PRECLINICAL	PHASE 1	PHASE 2
★	SER-109	Recurrent <i>C. difficile</i>	Potentially Pivotal Study ¹		
⦿	SER-262	Primary <i>C. difficile</i>			
★	SER-287	Ulcerative colitis			
⦿	SER-301	Inflammatory Bowel Disease (IBD)			
⦿	SER-155	Prevention of infection and GVHD following hematopoietic stem cell or solid organ transplant			

 Synthetically fermented
  Biologically sourced
  Infectious
  Inflammatory

DISCOVERY EFFORTS

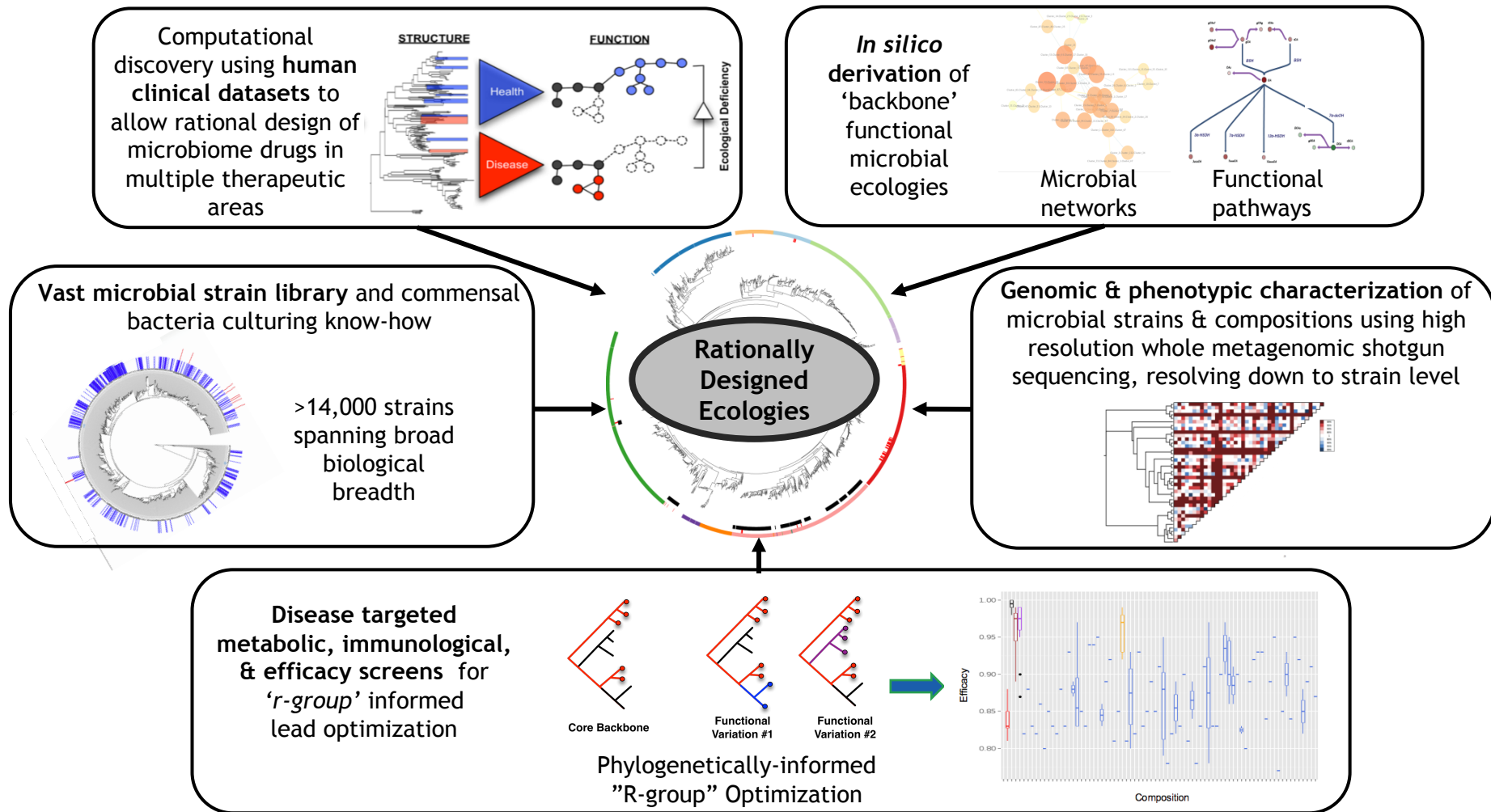
ACADEMIC COLLABORATOR

Immuno-oncology and hematopoietic stem cell transplant	 Memorial Sloan Kettering Cancer Center
Inflammatory bowel diseases	 Penn  St. Joseph's Healthcare Hamilton
Primary sclerosing cholangitis, NASH and other liver diseases	 MAYO CLINIC
Obesity/metabolic syndrome	 MASSACHUSETTS GENERAL HOSPITAL
Genetic metabolic diseases	 Penn

1. FDA has agreed that ECOSPOR III may qualify as pivotal study with achievement of a persuasive clinical effect and addressing FDA requirements, including clinical and statistical factors, an adequately sized safety database, and certain CMC parameters (See March 16, 2017 press release).

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

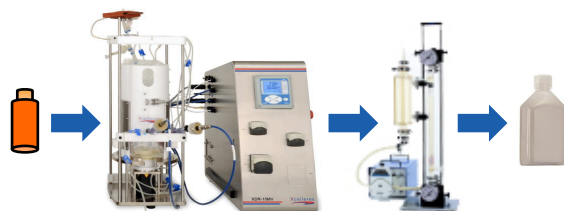
Differentiated microbiome R&D platform



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

Synthetic candidates



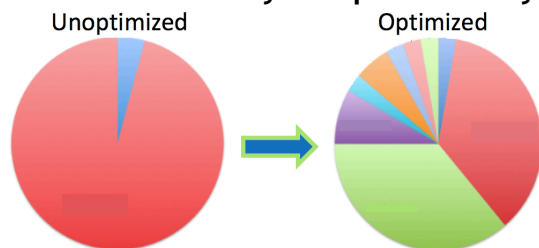
Fermentation of anaerobic and spore-forming microbes

cGMP Isolation of spores from complex biological materials



Biologically sourced

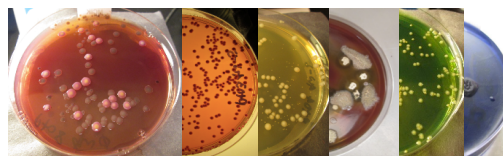
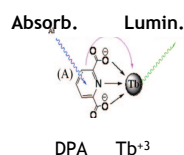
Novel germination, cultivation, and sporulation strategies enabling increased culture diversity and productivity



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
- Infection caused by two-hit process: Disruption of gut microbiome and exposure to pathogenic spores
- ~25% of patients with primary CDI 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"> • Invasive procedures (colonoscopy or NG-tube) • Potential for transmission of human pathogens • No FDA approved products
Antibodies 	<ul style="list-style-type: none"> • Limited efficacy in Phase 3 studies • Does not address underlying microbiome dysbiosis • Complex administration, not patient-friendly
Vaccines 	<ul style="list-style-type: none"> • Unproven efficacy until Phase 3 is complete • Complex to identify and vaccinate elderly at-risk groups

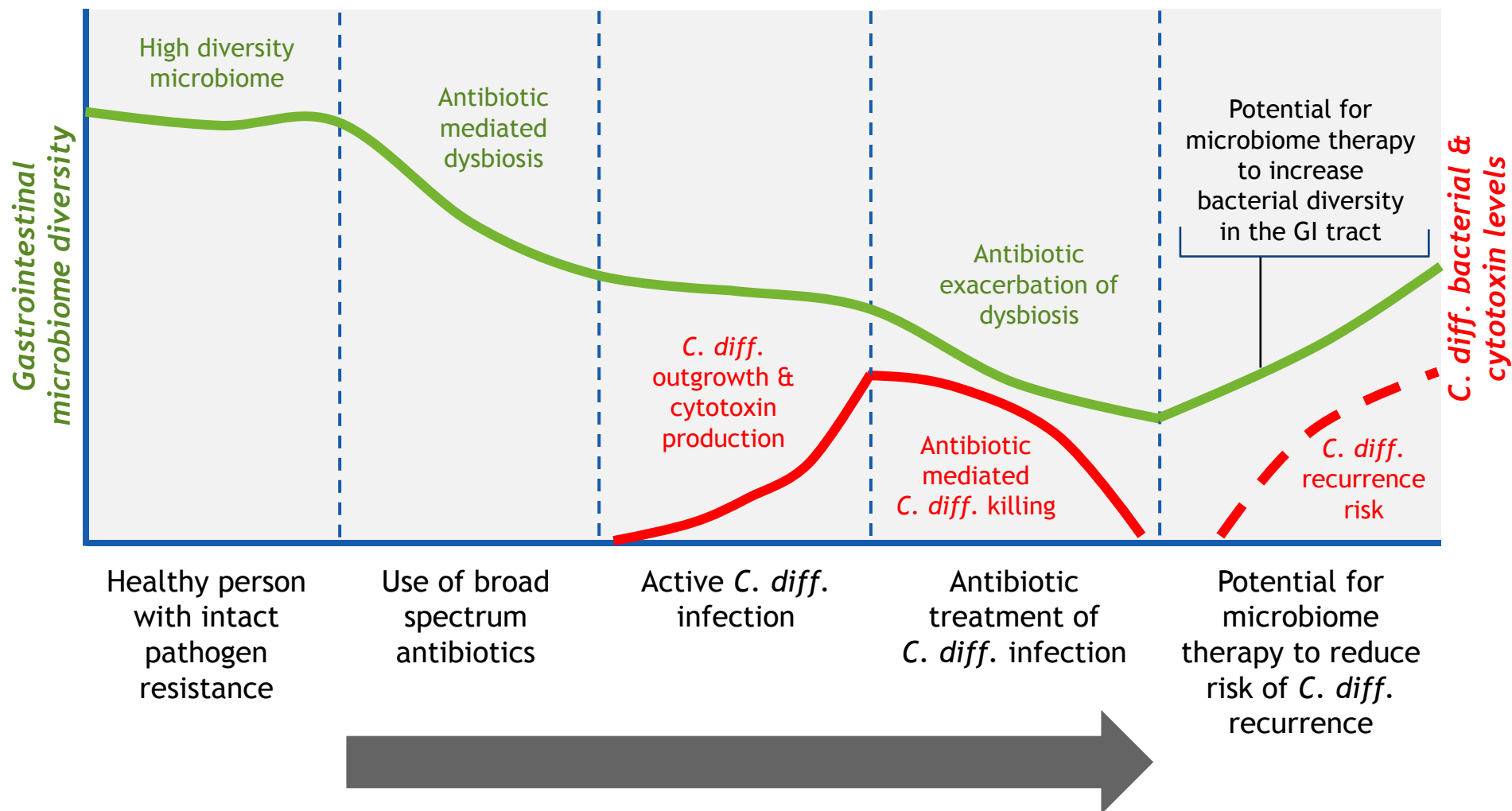
High Unmet
Medical Need

- Economic burden as high as \$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"> 13% 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: 44% (26 of 59) recurrence Placebo: 53% (16 of 30) 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 data• Investigation 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 handling• Phase 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

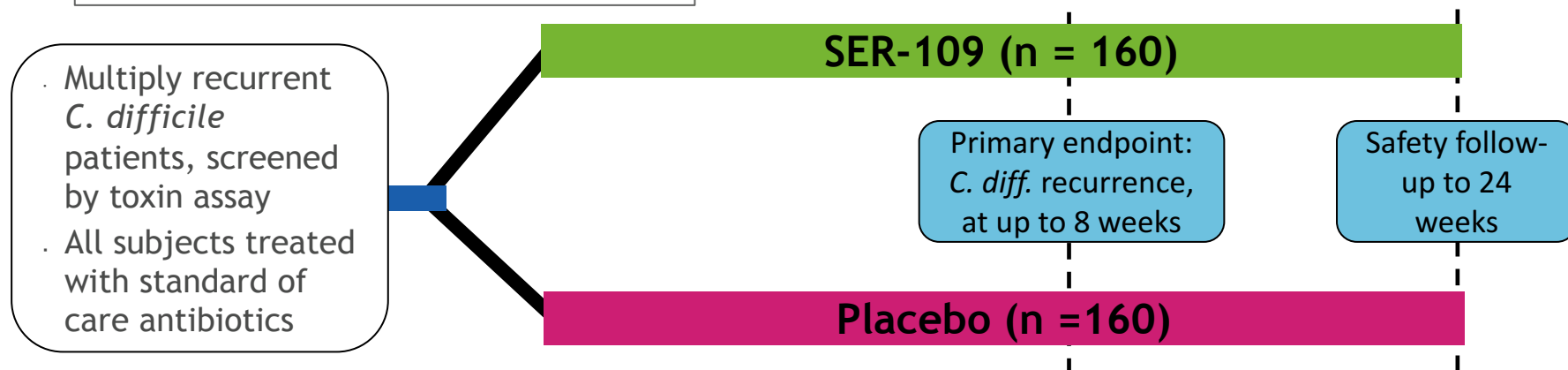
Diagnosis - Misdiagnoses may have occurred both in some patients entering the trial, as well as for recurrences diagnosed during the study

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

SER-109 ECOSPOR III: Potential Pivotal Study

- Positive Type B FDA meeting held to discuss available SER-109 data and proposed plans for further development
- Seres and FDA reach agreement on key design elements of a new SER-109 clinical study
- New trial may qualify as a Pivotal Study with achievement of a persuasive clinical effect and addressing FDA requirements, including clinical and statistical factors, an adequately sized safety database, and certain CMC parameters
- ECOSPOR III will utilize a SER-109 dose approximately 10-fold higher than the SER-109 dose used in the prior ECOSPOR study, administered over three days.

ECOSPOR III (SERES-012) study design



SER-262: Synthetic Ecobiotic® drug 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

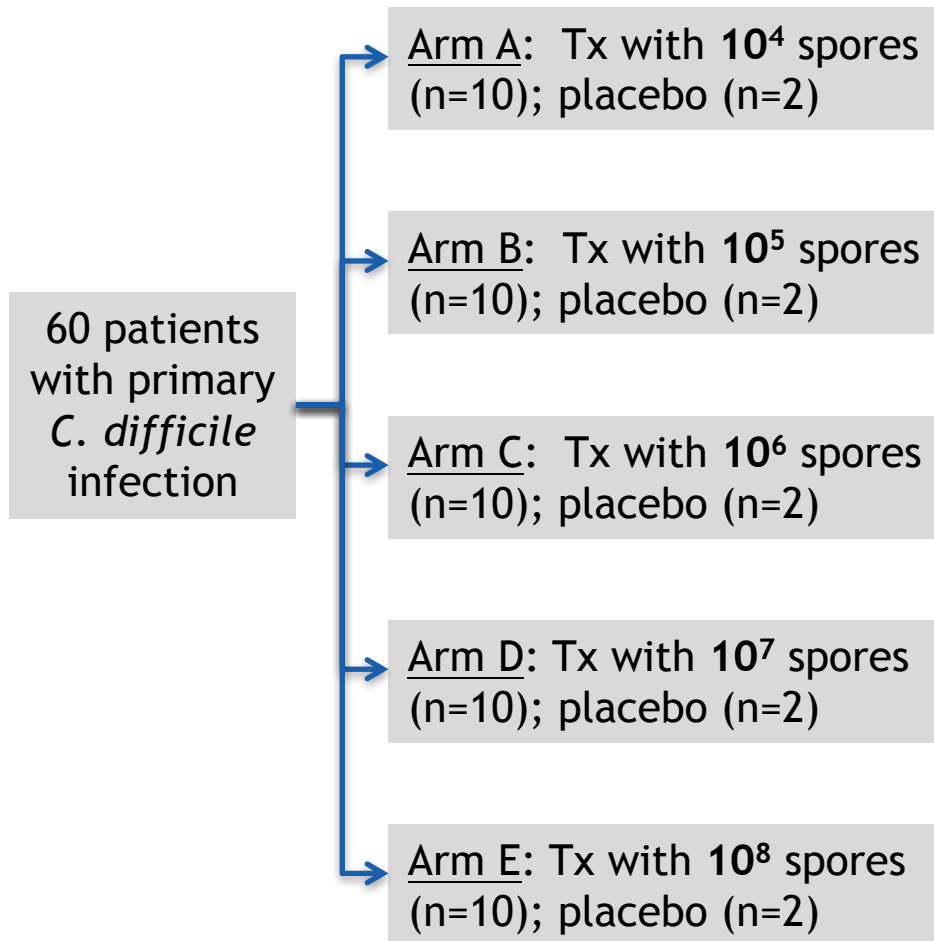
SER-262 strains utilize multiple carbon sources

Strain Designation	Sugars, sugar alcohols, glucosides														Carboxylic acids	
	f r u	g l u	m a n	r h a	r r b	x y l	c e l	s t r	t m e	p e c	m t l	s o r	N A G	g l a	s a f	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 to provide insight into efficacy and safety in patients with primary *C. difficile* infection



Primary Objective

- Safety and tolerability at 24 weeks
- Relative risk of *C. difficile* recurrence compared to placebo at up to 8 weeks

Secondary Objectives

- 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.

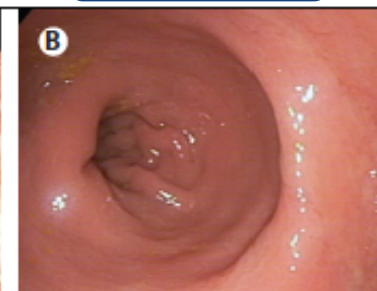
†Combined Mayo subscores of ≤1 for rectal bleeding plus stool frequency. ‡Decrease of ≥3 points or ≥50% reduction from baseline (or both) in combined Mayo subscores for rectal bleeding plus stool frequency. §Mayo endoscopy subscore 0. ¶Mayo endoscopy subscore ≤1, with ≥1 point reduction from baseline.

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 unmet need for improved therapies for IBD

- Large US population: ~700K ulcerative colitis, ~700K Crohn's
- Only ~30% of patients respond to currently approved therapies
- 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 to provide insight into efficacy and mechanism in UC patients

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 placebo 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

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

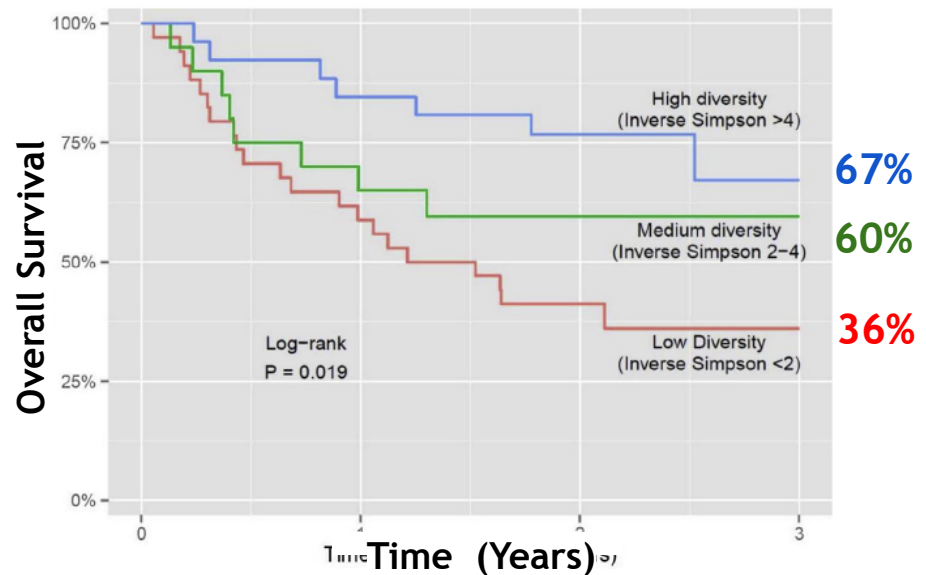


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SER-155: Synthetic Ecobiotic® therapeutic candidate to improve transplantation outcomes

- 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 Karpnits, 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 Waldschmidt...

+ See all authors and affiliations

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

Science




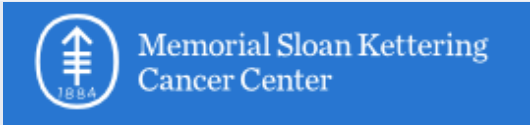
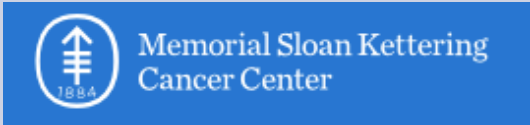




Commensal *Bifidobacterium* promotes antitumor immunity and facilitates anti-PD-L1 efficacy

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 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

16 Families of Applications

9 Nationalized

2 Pending PCT

5 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

Strong Financial Position

Resources to operate through 2018

Balance Sheet	As of Dec. 31, 2016
Cash, cash equivalents and investments	\$230 M

Income Statement	Latest Quarter, as of Dec. 31, 2016
R&D	(\$20 M)
G&A	(\$8 M)
Net loss	(\$25 M)

Common shares outstanding	40.4 M, as of Dec. 31, 2016
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Upcoming value-driving milestones

SER-109: Initiation of further clinical development

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

SER-262: Primary *C. difficile* infection - Phase 1b read-out (H2 2017)

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