Cowen and Company 37th Annual Health Care Conference

Roger J. Pomerantz, M.D.
President, Chief Executive Officer and Chairman

SERES THERAPEUTICS™

Leading the Microbiome Revolution

March 8, 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

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The microbiome is essential to human health

Infectious Disease

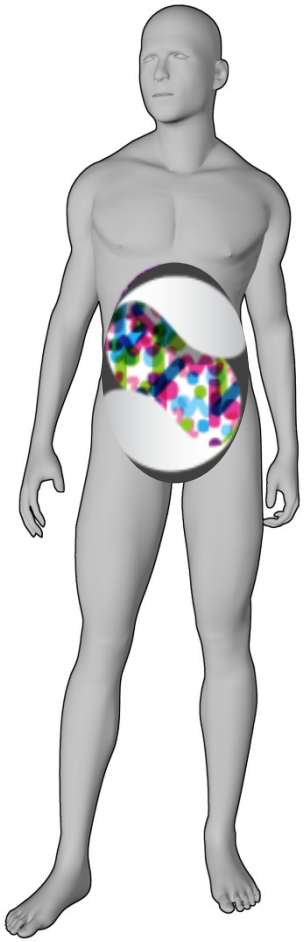
- A diverse microbiome resists colonization by exogenous pathogens
- Exposure to spectrum antibiotics, and resulting gut microbiome dysbiosis, increase risk for *C. difficile* infection and colonization / infection by multi-drug resistant organisms

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)



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.; Slvan A. et al., Science 2015.; Dubin et al., Nature, 2016. NASH: Le Roy et al., Hepatology, 2012. Metabolic syndrome: Perry et al. Nature, 2016, Ridaura VK et al., Science 2013. Primary sclerosing cholangitis Tabibian JH et al., Hepatology, 2016

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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
Penn
MAYO CLINIC
St. Joseph's Healthcare Hamilton

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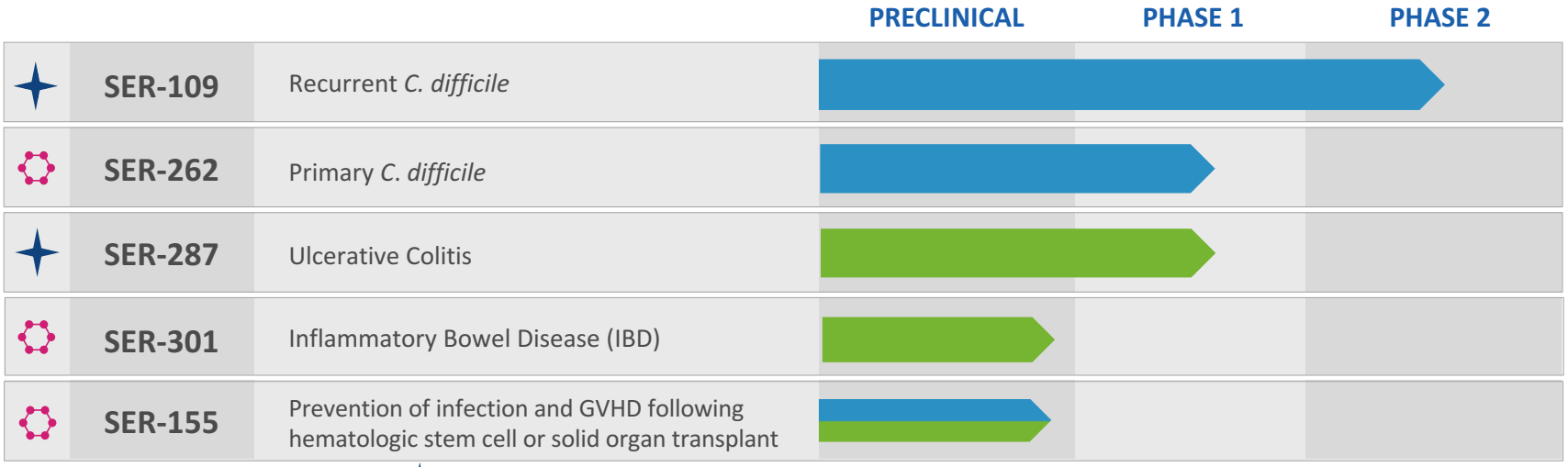
Robust microbiome therapeutics pipeline



DISCOVERY EFFORTS	ACADEMIC COLLABORATOR
Immuno-oncology and Hematologic 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

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

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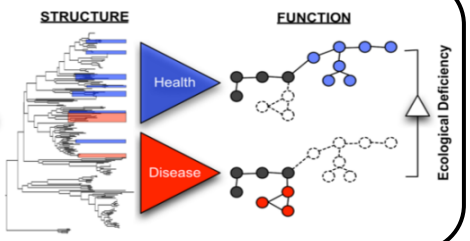
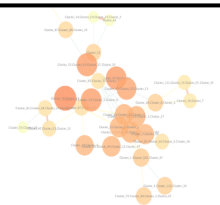
Differentiated microbiome R&D platform

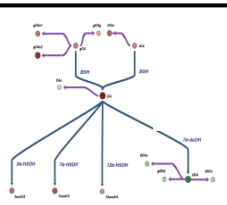
Computational discovery using **human clinical datasets** to allow rational design of microbiome drugs in multiple therapeutic areas



***In silico* derivation** of 'backbone' functional microbial ecologies

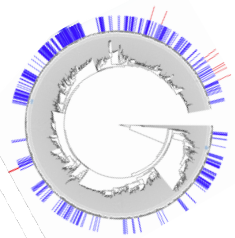


Microbial networks

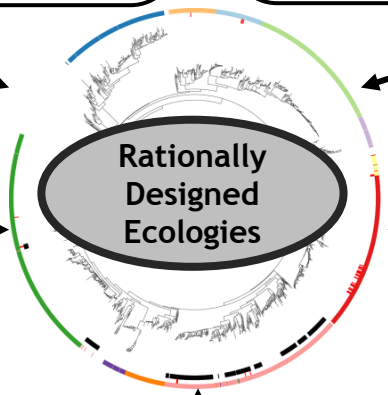


Functional pathways

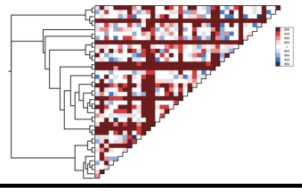
Vast microbial strain library and commensal bacteria culturing know-how



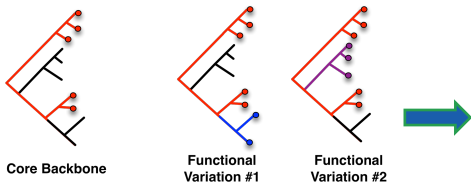
>14,000 strains spanning broad biological breadth



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



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



Phylogenetically-informed "R-group" Optimization

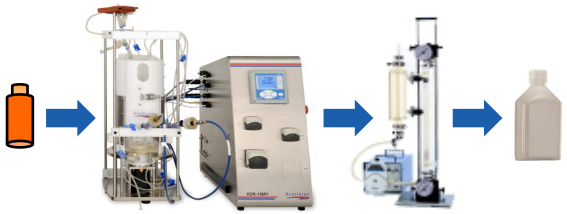
Only company with clinical stage microbiome development programs, human microbiome datasets, and clinical datasets before and after treatment

THERAPEUTICS

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

Synthetic candidates

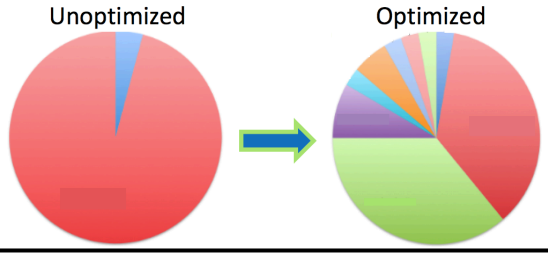
Fermentation of anaerobic and spore-forming microbes



Biologically sourced

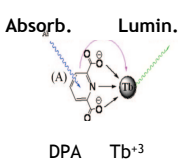
cGMP Isolation of spores from complex biological materials

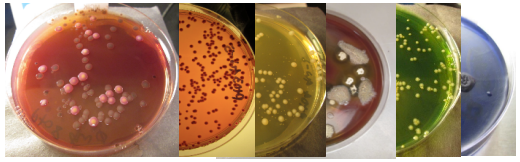
Novel germination, cultivation, and sporulation strategies enabling increased culture diversity and productivity



Formulation, Filling, Delivery & Packaging enabling active product delivery

Novel QC assays for Safety, Identity, Strength, Purity, and Quality including microbiome characterization





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Clostridium difficile Infection

Overview and R&D Programs

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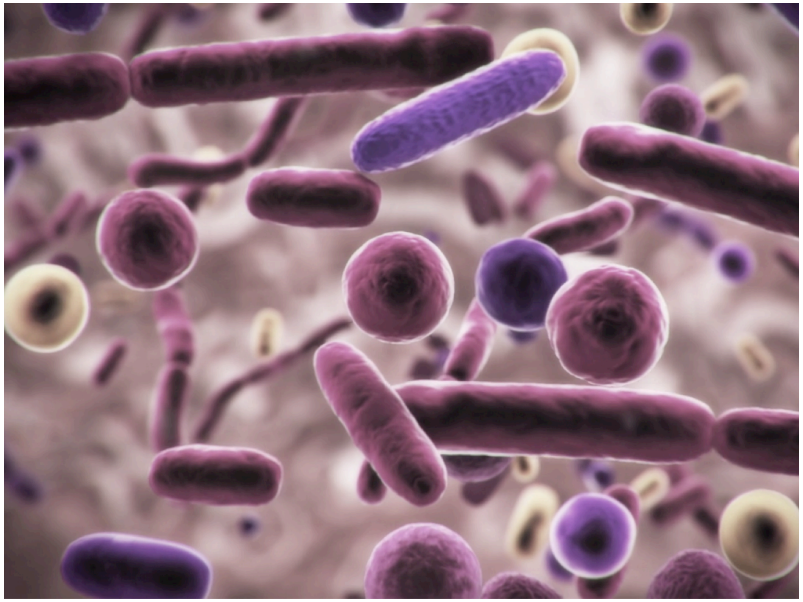
C. difficile infection overview

- 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



Leffler and Lamont, New England Journal of Medicine, 2015

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Treatment landscape & disease burden

Modality	Characteristics
Antibiotics 	• Perpetuates microbiome dysbiosis, creating *C. difficile* infection susceptibility • High recurrence rates, especially in recurrent cases
Fecal Transplant 	• Invasive procedures (colonoscopy or NG-tube) • Potential for transmission of human pathogens • No FDA approved products
Antibodies 	• Limited efficacy in Phase 3 studies • Does not address underlying microbiome dysbiosis • Complex administration, not patient-friendly
Vaccines 	• 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 facilities[1]**
- **Recurrent CDI episode ~$18K[2]; >$50K for cycle of recurrences**

High Treatment Costs

1. Dubberke and Olsen, Clinical Infectious Diseases 2012; 2. Ghantoji et al., Journal of Hospital Infection, 2010.

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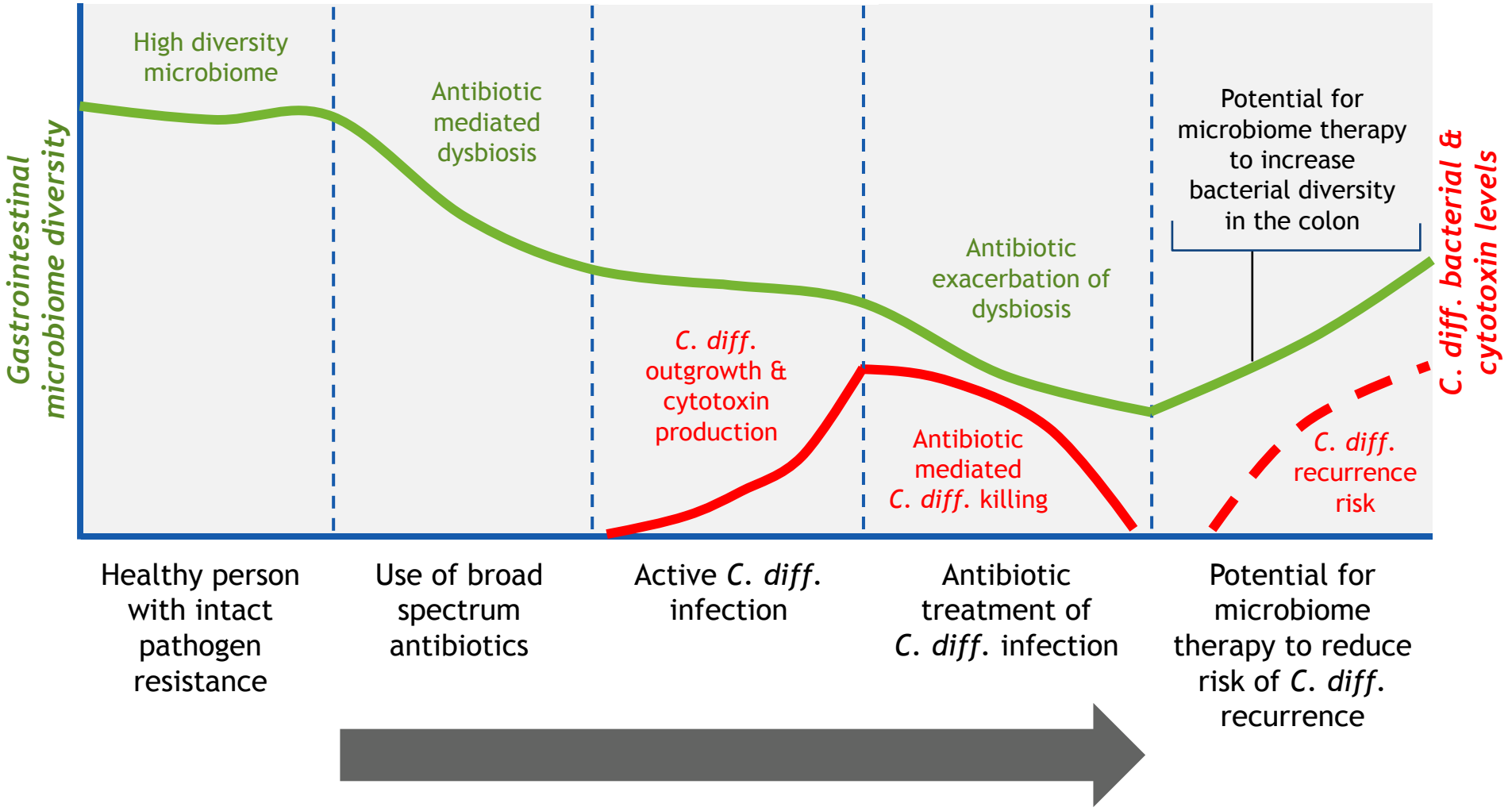
Dysbiosis and potential for therapeutic intervention

Hypothetical patient course



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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	• 13% recurrence per protocol • 3 of 4 patients with recurrent transient diarrhea, did not require antibiotic treatment and tested negative for *C. diff*. at 8 weeks	• SER-109: 44% (26 of 59) recurrence • Placebo: 53% (16 of 30) recurrence • Relative risk recurrence between arms not significant
Safety	• 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	• 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%)

Phase 1b study results: Khanna *et al. The Journal of Infectious Diseases; Phase 2 results: see July 31, 2016 press release (study results), and January 31, 2017 press release (Phase 2 study analyses)*

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

SER-109 analyses	Key issues addressed
Clinical	• Detailed analyses of clinical data • Investigation of *C. difficile* diagnostics
Pharmacodynamics / microbiome analyses	• Investigation of drug activity
Chemistry, Manufacturing and Controls (CMC)	• 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

See January 31, 2017 press release for additional information

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Further SER-109 clinical development

- FDA discussions regarding a new SER-109 clinical study in progress
- Anticipate completion of FDA dialogue in the near future

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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		
	fru	glu	man	rha	rlb	xyl	cel	scr	tre	mel	pec	mtl	sor	NAG	glm	sal	for	suc	pyr
C. difficile																			
1																			
2																			
3																			
4																			
5																			
6																			
7																			
8																			
9																			
10																			
11																			
12																			

***In vitro* fermentation**

For additional information, see 2016 American Society of Microbiology conference poster, available on Seres website under 'Our Science'

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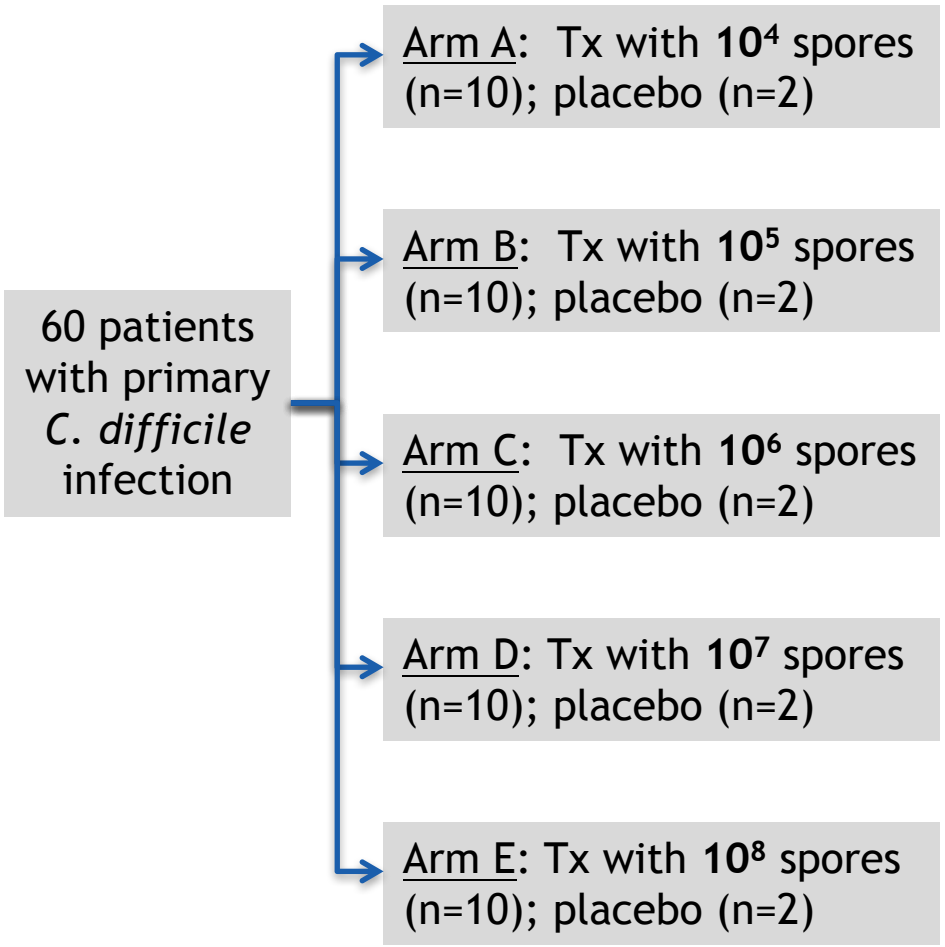
SER-262 Phase 1b to provide insight into efficacy and safety in patients with primary *C. difficile* infection



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

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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

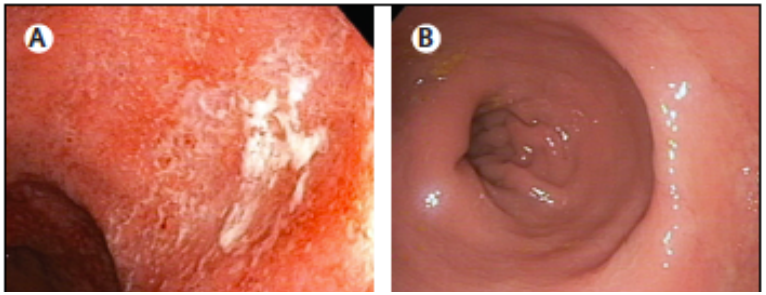
	Faecal microbiota transplantation (n=41)	Placebo (n=40)	Risk ratio (95% CI)	p value
Primary outcome				
Steroid-free clinical remission and endoscopic remission or response*	11 (27%)	3 (8%)	3·6 (1·1–11·9)	0·021
Secondary outcomes				
Steroid-free clinical remission†	18 (44%)	8 (20%)	2·2 (1·1–4·5)	0·021
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



Selected references: Paramsothy *et al*. Lancet, 2017; Moayyedi *et al*. Gastroenterology, 2015

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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

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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

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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

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Additional R&D Opportunities

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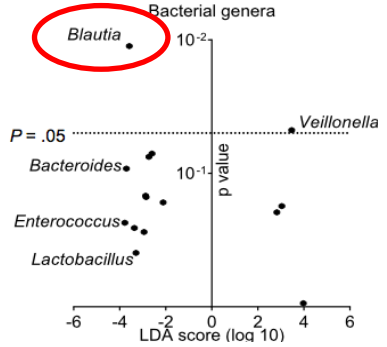
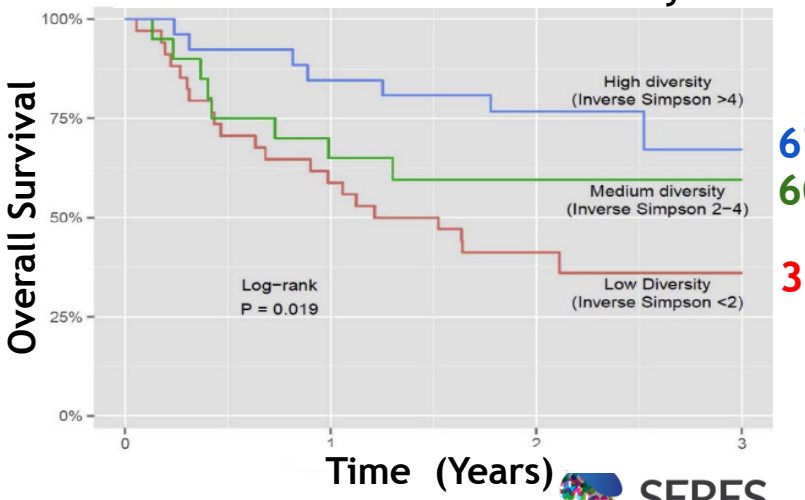
SER-155: To improve hematopoietic stem cell transplantation outcomes

SER-155 Overview	• Designed Ecobiotic® drug candidate for prevention of allogeneic HSCT associated infection and Graft vs. Host Disease (GvHD)
Prevention of HSCT Infection Supporting Data	• HSCT conditioning results in dysbiosis, and increased risk of bacteremia from gut pathogens • SER-109 Phase 1b demonstrated significant reduction of carriage of Gram(-) and Gram(+) pathogens[1]
Prevention of GvHD Supporting Data	• Increased microbiome diversity may improve intestinal barrier function and modulate inflammatory tone • GvHD mortality associated with immune dysregulation due to microbiome changes
Opportunity	• ~22,000 allo-HSCT per year with high hospitalization and treatment cost (US and EU data)

Microbiome Profile Correlates with GvHD Mortality Risk[2]



HSCT Patient Microbiome Health Correlates with Overall Mortality Risk[3]



[1] Khanna *et al*, Journal of Infectious Disease 2016 [2] Jenq, *et al*, Biology of Blood and Marrow Transplantation 2015, [3] Taur, *et al.*, Blood 2015.

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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 Karpinets, 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; Memor Sloan-Kettering Cancer Ctr, New York, NY

nature COMMUNICATIONS

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

Krista Dubin[1,2,3], Margaret K. Callahan[4,5], Boyu Ren[6], Raya Khanin[7], Agnes Viale[8], Lilan Ling[2], Daniel No[2], Asia Gobourne[2], Eric Littmann[2], 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 Daillère[1,2,3], Patricia Lepage[4], 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 Hubert[2], Jason B. Williams[1], Keston Aquino-Michaels[3], Zachary...
+ See all authors and affiliations

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

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Collaborations with leading institutes to advance R&D progress

Target Indication	Academic Collaboration
Inflammatory Bowel Disease	Penn; Medizinische Universität Graz; St. Joseph's Healthcare Hamilton
Immuno-oncology Therapeutics	Memorial Sloan Kettering Cancer Center
Hematopoietic Stem Cell Transplantation	Memorial Sloan Kettering Cancer Center
Primary Sclerosing Cholangitis, NASH and Other Liver Diseases	Mayo Clinic
Obesity and Metabolic Syndrome	MGH 1811 Massachusetts General Hospital
Rare genetic metabolic diseases (e.g., urea cycle disorders, hepatic encephalopathy)	Penn

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

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Upcoming value-driving milestones

SER-109: Completion of FDA dialogue regarding future development

SER-109: Initiation of further clinical development

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

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

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

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Thank you

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