
# SER-287 Phase 1b topline study results in patients with mild-to-moderate Ulcerative Colitis

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SERES THERAPEUTICS™

Leading the Microbiome Revolution

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# Seres Overview

| | |
|---|---|
| **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 |

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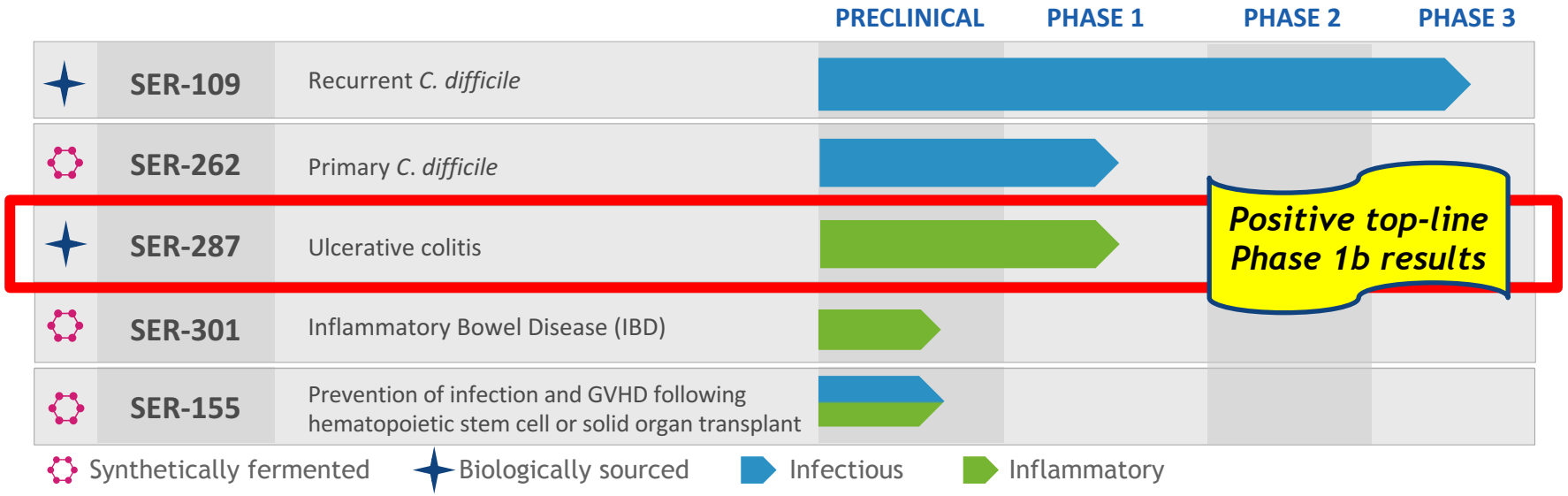
# Robust Microbiome Therapeutics Pipeline




| 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 |

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

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# SER-287 Overview

- Biologically sourced consortium of bacterial spores
- Orally administered
- Strong intellectual property protection supported by multiple patent claims covering Ulcerative Colitis, as well as regulatory data protection
- Hypothesized to act by modulating the dysbiotic microbiome, reducing inflammation without immunosuppression effects[1,2]
- Rationale for development supported by:
  - Preclinical results from microbiome modification in animal models of colitis
  - Multiple randomized, placebo controlled clinical studies examining the the treatment effects of multiple fecal microbiota transplantation in patients with Ulcerative Colitis

1. Blander JM et al., Regulation of inflammation by microbiota interactions with the host, Nature Immunology, 2017. Lynch S and Pedersen O, The Human Intestinal Microbiome in Health and Disease, The New England Journal of Medicine, 2016.
2. Costello et al. Systematic review with meta-analysis: faecal microbiota transplantation for the induction of remission for active ulcerative colitis, *Alimentary Pharmacology & Therapeutics*, 2017.

# SER-287 Opportunity in Ulcerative Colitis

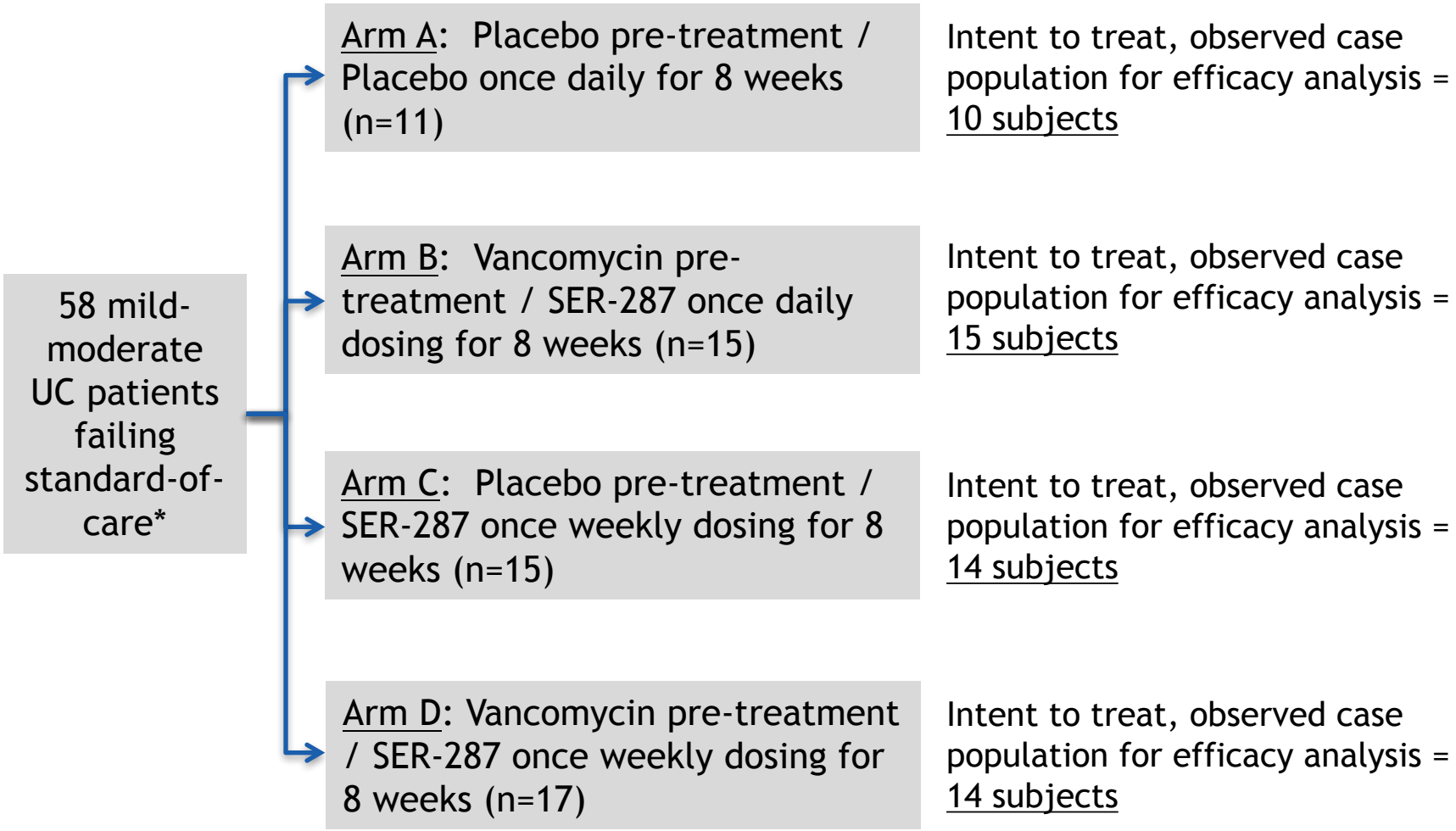
**Significant need for improved Ulcerative Colitis therapies**

- Large population: ~700K ulcerative colitis (US figures)
- Many ulcerative colitis patients do not respond to current therapies, both during induction and maintenance, and there is need for new treatment modalities
- Several leading ulcerative colitis therapies are immunosuppressive, increasing the risk of opportunistic infections and certain cancers, and limiting widespread use

**SER-287 target profile:**

- Oral
- Alternative mechanistic approach, potential as a mono or combination therapy
- Potential highly favorable safety profile

# SER-287 Phase 1b Ulcerative Colitis Study Design




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

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# SER-287 Phase 1b Study Endpoints

## Primary Objectives

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

## Secondary Objectives

- Clinical remission, endoscopic improvement and response through measure of the total modified Mayo Score
- Change in serum and fecal biomarkers *
- Complement of microbiome metabolic pathways from stool, urine and blood *
- Immunological and pathologic changes in mucosal biopsies *

* Data expected in the coming months

# Phase 1b Study Patient Demographics

| Characteristic | Statistic | (Placebo/ Placebo) (N = 11) | (Vancomycin / SER-287 daily) (N = 15) | (Placebo/SER-287 weekly) (N = 15) | (Vancomycin / SER-287 weekly) (N = 17) | Ser-287 (N = 47) | Overall (N = 58) |
|---|---|---|---|---|---|---|---|
| Age (years) | n | 11 | 15 | 15 | 17 | 47 | 58 |
| | Mean (SD) | 45.8 (15.20) | 47.8 (18.59) | 46.5 (16.12) | 47.9 (11.18) | 47.4 (15.10) | 47.1 (15.00) |
| Sex | | | | | | | |
| Male | n (%) | 4 (36.4) | 7 (46.7) | 6 (40.0) | 10 (58.8) | 23 (48.9) | 27 (46.6) |
| Female | n (%) | 7 (63.6) | 8 (53.3) | 9 (60.0) | 7 (41.2) | 24 (51.1) | 31 (53.4) |
| Race | | | | | | | |
| White | n (%) | 8 (72.7) | 12 (80.0) | 12 (80.0) | 15 (88.2) | 39 (83.0) | 47 (81.0) |
| Asian | n (%) | 1 (9.1) | 0 | 0 | 1 (5.9) | 1 (2.1) | 2 (3.4) |
| Black or African American | n (%) | 1 (9.1) | 2 (13.3) | 3 (20.0) | 1 (5.9) | 6 (12.8) | 7 (12.1) |
| Other - Indian | n (%) | 1 (9.1) | 1 (6.7) | 0 | 0 | 1 (2.1) | 2 (3.4) |
| Montreal Classification | | | | | | | |
| Ulcerative Proctitis | n (%) | 0 | 4 (26.7) | 0 | 2 (11.8) | 6 (12.8) | 6 (10.3) |
| Left-sided UC (distal UC) | n (%) | 8 (72.7) | 5 (33.3) | 10 (66.7) | 10 (58.8) | 25 (53.2) | 33 (56.9) |
| Extensive UC (pancolitis) | n (%) | 3 (27.3) | 6 (40.0) | 5 (33.3) | 5 (29.4) | 16 (34.0) | 19 (32.8) |
| Severity of UC | | | | | | | |
| Mild | n (%) | 3 (27.3) | 6 (40.0) | 6 (40.0) | 9 (52.9) | 21 (44.7) | 24 (41.4) |
| Moderate | n (%) | 8 (72.7) | 9 (60.0) | 9 (60.0) | 7 (41.2) | 25 (53.2) | 33 (56.9) |
| Receiving Current UC Treatment Prior to or On Date of 1st Pretreatment Dose | | | | | | | |
| No | n (%) | 1 (9.1) | 3 (20.0) | 2 (13.3) | 6 (35.3) | 11 (23.4) | 12 (20.7) |
| 5-ASA | n (%) | 7 (63.6) | 11 (73.3) | 11 (73.3) | 9 (52.9) | 31 (66.0) | 38 (65.5) |
| Immunomodulator | n (%) | 2 (18.2) | 1 (6.7) | 4 (26.7) | 2 (11.8) | 7 (14.9) | 9 (15.5) |
| Steroid | n (%) | 3 (27.3) | 3 (20.0) | 2 (13.3) | 0 | 5 (10.6) | 8 (13.8) |
| Other | n (%) | 1 (9.1) | 0 | 0 | 1 (5.9) | 1 (2.1) | 2 (3.4) |
| Time since first UC diagnosis (months) | n | 11 | 15 | 15 | 17 | 47 | 58 |
| | Mean (SD) | 138.2 (85.91) | 152.9 (143.77) | 149.1 (141.34) | 142.1 (105.41) | 147.8 (127.51) | 146.0 (120.12) |

# SER-287 Phase 1b Study Clinical Efficacy Endpoints

| Endpoint | Intent to Treat Population, Observed Case: Treatment Group | | | |
|---|---|---|---|---|
| | Placebo / Placebo (N = 10) (%) | Vancomycin / SER-287 daily (N = 15) (%) | Placebo / SER-287 weekly (N = 14) (%) | Vancomycin / SER-287 weekly (N = 14) (%) |
| **Clinical Remission** | | | | |
| | 1/10 (10.0) | **6/15 (40.0)** | 2/14 (14.3) | 3/14 (21.4) |
| Difference from placebo (SER-287 minus placebo) | | **30.0%** | 4.3% | 11.4% |
| **Endoscopic Improvement** | | | | |
| | 1/10 (10.0) | **6/15 (40.0)** | 5/14 (35.7) | 4/14 (28.6) |
| Difference from placebo (SER-287 minus placebo) | | **30.0%** | 25.7% | 18.6% |
| **Clinical Response** | | | | |
| | 6/10 (60.0) | 9/15 (60.0) | 6/14 (42.9) | 4/14 (28.6) |
| Difference from placebo (SER-287 minus placebo) | | 0.0% | -17.1% | -31.4% |

# Treatment-Emergent Adverse Events Incidence by Treatment and System Organ Class

| System Organ Class | Safety Population | | | | |
|---|---|---|---|---|---|
| | (Placebo / placebo) (N = 11) n (%) E | (Vancomycin / SER-287 daily) (N = 15) n (%) E | (Placebo / SER-287 weekly) (N = 15) n (%) E | (Vancomycin / SER-287 weekly) (N = 17) n (%) E | SER-287 (N = 47) n (%) E |
| Gastrointestinal disorders | 5 (45.5) 7 | 2 (13.3) 4 | 7 (46.7) 19 | 8 (47.1) 21 | 17 (36.2) 44 |
| General disorders and administration site conditions | 1 (9.1) 1 | 1 (6.7) 1 | 0 | 3 (17.6) 3 | 4 (8.5) 4 |
| Immune system disorders | 0 | 0 | 0 | 1 (5.9) 1 | 1 (2.1) 1 |
| Infections and infestations | 3 (27.3) 3 | 4 (26.7) 6 | 1 (6.7) 3 | 6 (35.3) 6 | 11 (23.4) 15 |
| Injury, poisoning and procedural complications | 2 (18.2) 3 | 0 | 0 | 0 | 0 |
| Investigations | 0 | 0 | 0 | 1 (5.9) 2 | 1 (2.1) 2 |
| Metabolism and nutrition disorders | 0 | 1 (6.7) 1 | 0 | 1 (5.9) 1 | 2 (4.3) 2 |
| Musculoskeletal and connective tissue disorders | 0 | 2 (13.3) 2 | 3 (20.0) 4 | 1 (5.9) 2 | 6 (12.8) 8 |
| Nervous system disorders | 0 | 3 (20.0) 4 | 0 | 1 (5.9) 1 | 4 (8.5) 5 |
| Psychiatric disorders | 1 (9.1) 1 | 1 (6.7) 1 | 0 | 0 | 1 (2.1) 1 |
| Reproductive system and breast disorders | 0 | 0 | 0 | 1 (5.9) 1 | 1 (2.1) 1 |
| Respiratory, thoracic and mediastinal disorders | 0 | 1 (6.7) 1 | 1 (6.7) 1 | 2 (11.8) 2 | 4 (8.5) 4 |
| Skin and subcutaneous tissue disorders | 0 | 3 (20.0) 3 | 0 | 1 (5.9) 1 | 4 (8.5) 4 |

# SER-287 Phase 1b Overall Safety: Most Common (>5%) Adverse Events by Treatment Group

| Safety Population | | | | | |
|---|---|---|---|---|---|
| Preferred Term | Placebo / Placebo (N = 11) n (%) | Vancomycin / SER-287 daily (N = 15) n (%) | Placebo / SER-287 weekly (N = 15) n (%) | Vancomycin / SER-287 weekly (N = 17) n (%) | SER-287 (N = 47) n (%) |
| Treatment-Emergent Adverse Events (All) | 7 (63.6) | 8 (53.3) | 9 (60.0) | 14 (82.4) | 31 (66.0) |
| Abdominal pain | 1 (9.1) | 0 | 3 (20.0) | 4 (23.5) | 7 (14.9) |
| Nausea | 0 | 1 (6.7) | 3 (20.0) | 1 (5.9) | 5 (10.6) |
| Back pain | 0 | 1 (6.7) | 3 (20.0) | 1 (5.9) | 5 (10.6) |
| Diarrhoea | 2 (18.2) | 0 | 2 (13.3) | 2 (11.8) | 4 (8.5) |
| Headache | 0 | 3 (20.0) | 0 | 1 (5.9) | 4 (8.5) |
| Constipation | 0 | 2 (13.3) | 1 (6.7) | 0 | 3 (6.4) |
| Flatulence | 0 | 0 | 0 | 3 (17.6) | 3 (6.4) |
| Upper Respiratory Tract Infection | 0 | 2 (13.3) | 0 | 1 (5.9) | 3 (6.4) |

# Advancing SER-287 Clinical Development

- Phase 1b top line results summary:
  - SER-287 microbiome treatment resulted in a benefit in clinical remission rates, as well as an improvement in endoscopic scores
  - No clinically significant safety or tolerability findings were observed
  - Microbiome results are expected in the coming months
- Company expects to meet with with the FDA as soon as possible to determine the most accelerated path to advance SER-287 development in mild, moderate and severe forms of Ulcerative Colitis, and in maintenance after induction therapy
- Company also intends to assess future development in Crohn's disease, and pediatric forms of inflammatory bowel disease