Seres Health Presents Final Data for Study of SER-109 in Recurrent Clostridium difficile Infection at ICAAC 2014 Conference

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Phase I/II study also demonstrated SER-109 restoration of a diverse, healthy microbiome

CAMBRIDGE, Mass., Sept. 8, 2014 /PRNewswire/ -- Seres Health, a clinical-stage therapeutics company developing novel treatments for diseases related to the human microbiome, today announced final data for its single-arm, open-label clinical trial of SER-109, its first-in-field, oral microbiome therapeutic. SER-109, a mixture of bacterial spores, is designed for the treatment of recurrent *Clostridium difficile* Infection (CDI). The data presented at the 2014 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) show that in patients with recurrent CDI, SER-109 resulted in clinical cures, with 29 of the trial's 30 patients (97 percent) reaching the 8-week endpoint free of infection.

This Phase I/II study characterized the safety and efficacy profile of SER-109 for recurrent CDI and its impact on the gut microbiome. The study was designed in two, 15-patient cohorts. Cohort 1 evaluated a mean dose of $1.5x10^9$ spores and cohort 2 evaluated a dose of $1x10^8$ spores. Efficacy was assessed by the absence of CDI over an 8-week period. Safety was assessed by phone contact on day 4 and weeks 1, 2 and 4, and by in-person physical exams on weeks 8 and 24. Stool was collected on day 4 and weeks 1, 2, 4, 8 and 24.

Patients included in the study were between 18 and 90 years old, had greater than or equal to 3 laboratory-confirmed CDI episodes over 1 year, had a life expectancy >3 months and were able to give informed consent. Patients excluded from the study were those that had immunosuppression (acute leukemia, history of hematopoietic stem cell transplantation, cytotoxic chemo within 2 months, or neutrophil count <1000/uL), a history of irritable bowel disease or irritable bowel syndrome with diarrhea, a total colectomy, liver cirrhosis, the need for antibiotics within 6 weeks, prior fecal microbiota transplantation or Intensive Care Unit admission or were pregnant or nursing.

In cohort 1, 13 of the 15 patients (87 percent) achieved the protocol-defined endpoint. In addition, two patients had transient, self-limited diarrhea with a positive *C. diff* test, but both reached the week 8 endpoint without needing antibiotic therapy for CDI. Thus, in cohort 1, the clinical cure rate was 15 out of 15 (100 percent). In cohort 2, 14 of the 15 patients achieved the 8-week endpoint CDI free. One patient failed per protocol. There have been no drug-related serious adverse events.

Analysis of the microbiome using next-generation sequencing technology demonstrated that a single oral dose of SER-109 was capable of generating long-term changes in the microbiome, including the restoration of microbial diversity in the gastrointestinal (GI) tract of patients. Evidence for this was the engraftment of spore forming commensal bacteria from SER-109 in the patient's gut microbiota over the 8-week period. Unexpectedly, it was also determined that SER-109 catalyzed the outgrowth of other healthy non-spore forming organisms in the GI tract. This included critical genera that were missing in patients due to long term exposure to antibiotics.

Genomic and microbiological analysis demonstrated that prior to dosing with SER-109, multiple patients were colonized with *Klebsiella*, Vancomycin-resistant *Enterococci*, or imipenem resistant *Enterobacteriacea*. This is consistent with the general dysbiosis observed in these heavily antibiotic treated patients. Colonization with these organisms was rapidly reduced by up to 100,000-fold in the period following SER-109 dosing, consistent with the shift of the microbiome to a healthy state. This clinical data suggests that microbiome therapeutics may have utility in broader infectious disease indications.

"The scientific and medical implications of this work demonstrate that true drugs can be derived from rational design using commensal organisms normally found in the human microbiome," said Dr. Roger J. Pomerantz, President, CEO and Chairman of Seres Health.

"The study offers hope that a breakthrough oral drug for preventing recurrent *C. difficile* infection is on the horizon, which

can replace invasive fecal transplants," said Dr. Darrell S. Pardi, gastroenterologist at Mayo Clinic and one of the study investigators. "It suggests that Ecobiotic® drugs that repair the microbiome may be a way to treat other gut infections and could complement antibiotics by restoring microbial diversity after antibiotic therapy."

About SER-109

SER-109 is the lead Seres Health Ecobiotic® microbial therapeutic in clinical testing for the treatment of recurrent *Clostridium difficile* infection (CDI). SER-109 was developed utilizing the Seres Health Microbiome Therapeutics™ platform that provides deep insight into the ecologies of disease and then identifies microbial compositions that can catalyze a shift to health. CDI is a rapidly growing problem associated with antibiotic use. Approximately 100,000 - 150,000 of CDI patients in the U.S. have more than one recurrence. Multiple recurrent CDI has recently been designated as an Orphan Drug Indication by the FDA.

About Seres Health

Seres Health is a clinical-stage therapeutics company focused on discovering and developing Ecobiotic® therapeutic products, novel drugs to treat important diseases by targeting the underlying biology of the human microbiome. Founded by Flagship VentureLabs™, Seres is pioneering the first therapeutics that catalyze a shift to health by augmenting the biology of the microbiome. Current candidates span infectious, metabolic, and inflammatory diseases. Seres recently announced a research alliance with Mayo Clinic and has received over $20 million in funding to date. For more information, please visit www.sereshealth.com.

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