Vedanta Biosciences Announces Successful Phase 1a/1b Data Demonstrating Safety, Tolerability, and Proof of Mechanism for Lead, Rationally Defined Bacterial Consortium Product Candidate, VE303

All doses were safe and well-tolerated

VE303 treatment resulted in rapid, durable, dose-dependent colonization and accelerated gut microbiota restoration after antibiotics

A Phase 2 study in recurrent C. difficile infection is expected to begin in the fourth quarter of 2018

Three other programs in immuno-oncology, allergy, and inflammatory bowel disease are expected to enter the clinic within the next nine months

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CAMBRIDGE, Mass.--(BUSINESS WIRE)--Vedanta Biosciences, a clinical-stage company developing a new category of therapies for immune-mediated diseases based on rationally defined consortia of human microbiome-derived bacteria, today announced preliminary results from the Phase 1a/1b clinical study in healthy volunteers for its lead, orally-administered live biotherapeutic product (LBP) candidate for recurrent Clostridium difficile infection (rCDI), VE303. With these Phase 1 data to support dosage selection, Vedanta Biosciences expects to begin a Phase 2 study before the end of the year to evaluate the safety and efficacy of VE303 in patients with rCDI. Additional exploration of VE303 in healthy volunteers to inform dose selection in other indications is ongoing.

This study was designed to evaluate safety and tolerability of a range of doses of VE303 in healthy adult volunteers. The study also evaluated pharmacokinetics of intestinal colonization by the VE303 strains and pharmacodynamics of recovery of the gut microbiota after administration of antibiotics followed by a course of VE303.

Summary of Key Findings:

1. Single and multiple doses of VE303, after vancomycin administration, ranging up to 1.1 x 1011 total colony forming units (CFU), were safe and well-tolerated. Adverse events related to VE303 administration occurred in less than one third of study volunteers and all were Grade 1.
2. Abundant colonization of VE303 strains that lasted for at least 12 weeks was detected at all doses.

3. Repeated dosing led to increased robustness of strain colonization (i.e., a majority of VE303 strains colonized in a majority of volunteers).
4. VE303 accelerated microbiota recovery after vancomycin administration in a dose-dependent manner compared to recovery without VE303, demonstrating proof of mechanism.

"We believe these Phase 1a/1b results represent a significant milestone for the microbiome field. VE303's favorable safety profile, and - most notably - its ability to rapidly, abundantly, and durably colonize a heterogenous population of healthy adults provides a scientific rationale for use of defined bacterial consortium drugs and moves the field beyond the use of undefined fecal transplants," said Bernat Olle, Ph.D., Co-founder and Chief Executive Officer of Vedanta Biosciences. "The robust relationship between dose exposure and response we have observed informs a rational dose selection for VE303 Phase 2 studies and supports its potential as a first-in-class therapy for prevention of recurrent Clostridium difficile infection."

Unlike single strain approaches to microbiome modulation, Vedanta Biosciences is developing consortia of bacterial strains designed to effect robust and durable therapeutic changes in a patient's gut microbiota. Unlike fecal transplants or administration of fecal fractions, Vedanta Biosciences' consortia are defined compositions of bacteria manufactured from pure, clonal cell banks, bypassing the need to rely on direct sourcing of fecal donor material of inconsistent composition. VE303 is the first product candidate, to the Company's knowledge, consisting of a rationally-defined bacterial consortium in lyophilized powder form to be clinically investigated.

About the Study

The Phase 1a/1b study was an open-label, single-center, single- and multiple- dose-escalation study assessing the safety and tolerability of VE303 in healthy adult volunteers. Twenty-three volunteers were enrolled to receive VE303 after vancomycin administration, three cohorts received single ascending doses of VE303 that ranged from 1.6x109 to 8x109 CFU, and two cohorts received total cumulative doses of VE303 ranging from 4x1010 to 1.1x1011 CFU over five or 14 days. The study also included a control cohort of five volunteers who received only vancomycin. Metagenomic sequencing of fecal samples collected longitudinally over 12 weeks was used to assess VE303's pharmacokinetics (speed, durability, abundance, and robustness of bacterial strain colonization) and the pharmacodynamics of VE303's impact on post-antibiotic gut microbiota restoration.

About VE303

VE303 is an orally-administered investigational live biotherapeutic product (LBP). It is produced from pure, clonal bacterial cell banks, which yield a standardized drug product in powdered form and bypasses the need to rely on direct sourcing of fecal donor material of inconsistent composition. VE303 consists of a defined consortium of live bacteria designed to restore colonization resistance against gut pathogens, including C. difficile. In 2017, Vedanta Biosciences received a $5.4 million research grant from CARB-X (Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator) to support clinical studies of VE303. VE303 was granted Orphan Drug Designation in 2017 by the United States Food and Drug Administration (FDA) for the prevention of recurrent C. difficile infection (rCDI).

About Vedanta Biosciences

Vedanta Biosciences is a clinical-stage company developing a new category of therapies for immune-mediated diseases based on rationally defined consortia of human microbiome-derived bacteria. Vedanta Biosciences is a leader in the microbiome field with capabilities and deep expertise to discover, develop, and manufacture LBPs. These include what is believed to be the largest collection of human microbiome-associated bacterial strains, a suite of proprietary assays to select pharmacologically potent strains, vast proprietary datasets from human interventional studies, and facilities for cGMP-compliant manufacturing of rationally-defined bacterial consortia in powder form. Vedanta Biosciences' pioneering work, in collaboration with its scientific co-founders, has led to the identification of human commensal bacteria that induce a range of immune responses – including induction of regulatory T cells, CD8+ T cells, and Th17 cells, among others. These advances have been published in leading peer-reviewed journals, including Science(multiple), Nature (multiple), Cell, and Nature Immunology. Vedanta Biosciences has harnessed these biological insights and its capabilities to generate a pipeline of programs in infectious disease, autoimmune disease, allergy, and immuno-oncology.

Vedanta Biosciences was founded by PureTech Health (PRTC.L). Its scientific co-founders are world-renowned experts in immunology and microbiology who have pioneered the fields of innate immunity, Th17 and regulatory T cell biology, and include Dr. Ruslan Medzhitov (Yale and Howard Hughes Medical Institute (HHMI)), Dr. Brett Finlay (University of British Columbia and HHMI), Dr. Kenya Honda (inventor of Vedanta Biosciences' lead product candidate; Keio University and RIKEN), Dr. Dan Littman (New York University and HHMI), Dr. Alexander Rudensky (Sloan Kettering and HHMI), and Dr. Jeremiah Faith (Mount Sinai School of Medicine).

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