PureTech's Vedanta Biosciences Announces Initiation of a Phase 2 Study for Lead Product Candidate, VE303

December 17, 2018

First drug consisting of a rationally-defined bacterial consortium to advance to Phase 2 study

Previously announced Phase 1a/1b study demonstrated rapid, durable, dose-dependent colonisation and accelerated gut microbiota restoration after antibiotics

PureTech Health plc (LSE: PRTC) ("PureTech Health"), an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) Axis, is pleased to note that Vedanta Biosciences today announced the initiation of a Phase 2 study of VE303, the Company's lead, orally-administered, live biotherapeutic product (LBP) candidate for recurrent *Clostridium difficile* infection (rCDI). Vedanta Biosciences' pipeline comprises two clinical-stage programmes, including the recently announced Phase 1 study of VE202 with Janssen Biotech, Inc. for inflammatory bowel disease (IBD), and the Company expects to initiate two additional studies in 2019.

Bharatt Chowrira, JD, PhD, President and Chief of Business and Strategy at PureTech Health, said: "We are pleased with the progress Vedanta Biosciences has made across its pipeline of microbiome-derived live biotherapeutic product candidates, and we look forward to the initiation of two additional clinical trials in the coming months."

The full text announcement from Vedanta Biosciences is as follows:

Vedanta Biosciences Initiates Phase 2 Study for Lead Rationally-Defined Bacterial Consortium Product Candidate, VE303

First drug consisting of a rationally-defined bacterial consortium to advance to Phase 2 study

Previously announced Phase 1a/1b study demonstrated rapid, durable, dose-dependent colonisation and accelerated gut microbiota restoration after antibiotics

Cambridge, Mass., Dec. 17, 2018 - 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 it has initiated a Phase 2 study of its lead, orally-administered live biotherapeutic product (LBP) candidate, VE303, for recurrent *Clostridium difficile* infection (rCDI). Vedanta Biosciences' pipeline of microbiome-derived product candidates also includes the recently announced Phase 1 study of VE202 with Janssen Biotech, Inc. for inflammatory bowel disease (IBD), and the company expects to initiate a Phase 1/2 study of VE416 in food allergy in Q1 2019 in addition to a Phase 1/2 study of VE800 and *Opdivo* (nivolumab) in advanced or metastatic cancers in mid-2019.

The Phase 2, multi-centre, randomised, double-blind, placebo-controlled CONSORTIUM study is designed to evaluate the safety and efficacy of two doses of VE303 compared to placebo in patients with rCDI. The study is expected to enroll up to 146 patients with a recent diagnosis of rCDI, confirmed using a *Clostridium difficile* toxin assay, and who have completed a course of antibiotics but remain at risk for recurrence. The primary endpoint will be prevention of infection recurrence at eight weeks.

"The results of the VE303 Phase 1a/1b are very promising, and I look forward to the continued progression of this – and Vedanta's other product candidates – through the clinic," said Ciaran P Kelly, MD, Professor of Medicine, Harvard Medical School. "Vedanta's approach yields product candidates with a defined and uniform composition, potentially mitigating the safety and variability challenges associated with approaches based on faecal transplants or faecal fractions."

Dose selection for this study was based on the results of a recently concluded Phase 1a/1b study of VE303 in healthy volunteers. That study found that all doses of VE303 were safe and well-tolerated and that treatment with VE303 resulted in rapid, durable, and dose-dependent colonisation of VE303 strains. The Phase 1 study also found that VE303 treatment accelerated the restoration of gut microbiota after a course of antibiotics.

"This is the first Phase 2 study, to our knowledge, of a rationally-defined bacterial consortium candidate in any indication, so it represents a major milestone for Vedanta Biosciences and the field," said Bernat Olle, PhD, Co-founder and Chief Executive Officer of Vedanta Biosciences. "Our Phase 1a/1b study helped de-risk key questions for our modality, in particular whether robust, durable colonisation – superior to what has been reported for probiotics in the past – can be obtained with a defined consortium and whether the right consortium can rapidly restore the gut microbiota after antibiotics."

Unlike single strain or microbiome-derived metabolite 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. In contrast to faecal transplants or administration of faecal fractions, Vedanta Biosciences' consortia are defined compositions of bacteria manufactured from pure, clonal cell banks, bypassing the need to rely on direct sourcing of faecal donor material of inconsistent composition.

About VE303

VE303 is an orally-administered investigational live biotherapeutic product (LBP). It is produced from pure, clonal bacterial cell banks, which yield a standardised drug product in powdered form and bypasses the need to rely on direct sourcing of faecal donor material of inconsistent composition. VE303 consists of a defined consortium of live bacteria designed to restore colonisation 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 live bacteria drugs. 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 programmes in autoimmune disease, allergy, infectious disease, 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 Ruslan Medzhitov, PhD, (Yale and Howard Hughes Medical Institute (HHMI)), Brett Finlay, PhD, (University of British Columbia and HHMI), Kenya Honda, PhD, (inventor of Vedanta Biosciences' lead product candidate; Keio University and RIKEN), Dan Littman, PhD, (New York University and HHMI), Alexander Rudensky, PhD, (Sloan Kettering and HHMI), and Jeremiah Faith, PhD, (Mount Sinai School of Medicine).

About PureTech Health

PureTech Health (LSE: PRTC) is an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) Axis. The Company has developed deep insights into the connection between the individual components of these systems and the resulting role in many chronic diseases, which have proven resistant to established therapeutic approaches. By harnessing this emerging field of human biology, PureTech Health is developing new categories of medicines with the potential to have great impact on people with serious diseases.

PureTech Health is advancing a rich pipeline of innovative therapies across two divisions: the Affiliates division and the Internal division. Its Affiliates division includes two product candidates that have been filed with the US Food and Drug Administration (FDA) for review and several other novel clinical and pre-clinical programmes. These affiliates are developing ground-breaking platforms and therapeutic candidates in collaboration with some of the world’s leading experts.

PureTech’s Internal division is advancing a pipeline fuelled by recent discoveries in lymphatics and immune cell trafficking to modulate disease in a tissue-specific manner. These programmes leverage the transport and biodistribution of various immune system components for the targeted treatment of diseases with major unmet needs, including cancers, autoimmune diseases, and neuroimmune disorders.

For more information, visit www.puretechhealth.com or connect with us on Twitter @puretechh.

Forward Looking Statement

This press release contains statements that are or may be forward-looking statements, including statements that relate to the company's future prospects, developments and strategies. The forward-looking statements are based on current expectations and are subject to known and unknown risks and uncertainties that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, those risks and uncertainties described in the risk factors included in the regulatory filings for PureTech Health plc. These forward-looking statements are based on assumptions regarding the present and future business strategies of the company and the environment in which it will operate in the future. Each forward-looking statement speaks only as at the date of this press release. Except as required by law and regulatory requirements, neither the company nor any other party intends to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.