PureTech's Microbiome Programme Advances into a Phase 1a/1b Clinical Trial

December 7, 2017

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PureTech Health plc (LSE: PRTC), an advanced, clinical-stage biopharmaceutical company, is pleased to note that Vedanta Biosciences, an affiliate of PureTech Health, today announced the initiation of a Phase 1a/1b clinical trial of VE303, the Company's lead, orally-administered, human microbiome-derived product candidate.

VE303 is the first known investigational drug consisting of rationally-defined bacterial consortium in powder form to enter the clinic. It is comprised of a group of bacteria selected based on their ability to shield against life-threatening infections, including recurrent C. *difficile* infection (rCDI). The Phase 1a/1b clinical trial is expected to be completed in the first half of 2018, and, pending those results, Vedanta plans to initiate a Phase 2 trial in 2018 for the treatment of rCDI.

Joe Bolen, PhD, Chief Scientific Officer of PureTech Health said: "We believe VE303 is the only rationally-defined bacterial consortium in powder form to advance into the clinic in any indication. This is a key milestone for the microbiome field as this new category of medicine requires a reproducible, predictable, and scalable composition to realise its full potential."

Vedanta also announced today that the United States Food and Drug Administration (FDA) have granted VE303 Orphan Drug Designation. Orphan Drug Designation is a status given to drugs and biologics that are intended for the safe and effective treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the US. rCDI is one of the most urgent bacterial threats and accounts for 15,000 deaths each year in the US alone. Existing interventions include antibiotics, which have an undesirable side effect of damaging the gut microbiome and leaving patients vulnerable to re-infection and building resistance to antibiotics. Microbiome-based therapies offer an alternative to antibiotics that could address both of these problems at once, and in November of this year, Vedanta Biosciences was selected for a $5.4 million research grant from CARB-X (Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator) to support clinical testing of VE303.

The full text of the announcement from Vedanta Biosciences is as follows:

Vedanta Biosciences Announces Initiation of Phase 1a/1b Trial for New Drug Class of Rationally-Defined Bacterial Consortium Derived from the Human Microbiome

VE303 is first known rationally-defined bacterial consortium in powder form to enter the clinic and has received Orphan Drug Designation from the US FDA for C. difficile *indication*

CAMBRIDGE, Massachusetts, December 7, 2017 —Vedanta Biosciences, an affiliate of PureTech Health (LSE: PRTC) developing a new category of therapies for immune-mediated and infectious diseases based on rationally defined consortium of human microbiome-derived bacteria, today announced the initiation of a Phase 1a/1b, first-in-human, clinical trial of VE303, the Company's lead, orally-administered microbiome therapeutic product candidate for recurrent Clostridium *difficile* infection (rCDI). VE303 is the first known investigational drug consisting of a rationally-defined bacterial consortium in powder form to enter the clinic. Vedanta also today announced that VE303 has been granted Orphan Drug Designation by the United States Food and Drug Administration (FDA).

"The initiation of this study marks an important milestone for both Vedanta Biosciences and the microbiome field, as we've been able to advance a new class of drugs to the clinic," said Bernat Olle, PhD, Chief Executive Officer of Vedanta Biosciences. "First-generation approaches in the microbiome field have relied on uncharacterised faecal material or spore fractions of faecal material, which are inherently inconsistent procedures. Products with a rationally-defined composition are the next logical step in the evolution of the microbiome field. We believe VE303 is the first rationally-defined bacterial consortium in powder form to advance into the clinic in any indication, and we plan to rapidly advance two additional programmes into clinical development in 2018."

VE303 is an orally-administered investigational microbiome therapeutic consisting of live bacteria designed to restore colonisation resistance against gut pathogens, including C. *difficile*, following recurrence. The Phase 1a/1b, dose-escalating study will assess the safety, tolerability, and colonisation of VE303 in healthy volunteers, and will enrol approximately 30 subjects. The primary outcome of the study is the evaluation of the safety and tolerability of VE303, and secondary outcomes include the kinetics of intestinal colonisation by the bacteria in VE303. The study is expected to be completed in the first half of 2018. Pending the results of this study, Vedanta plans to initiate a Phase 2 trial in rCDI in 2018.

VE303 has also been granted Orphan Drug Designation by the United States Food and Drug Administration (FDA). Orphan Drug Designation is a status given to drugs and biologics that are intended for the safe and effective treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the US. The Centers for Disease Control and Prevention (CDC) considers C. *difficile* infections one of the most urgent bacterial threats. *C. difficile* infections account for 15,000 deaths each year in the US alone. Existing interventions for C. *difficile* infections include antibiotics, which have the undesirable side effect of damaging the gut microbiome, leaving patients vulnerable to re-infection and building resistance to antibiotics. Microbiome-based therapies offer an alternative to antibiotics that could address both of these problems at once.

About VE303

VE303 is an orally-administered investigational microbiome therapeutic. It is produced from pure, clonal cell banks, which yield a standardised drug

product in powder form and bypass the need to rely on direct sourcing of faecal donor material of inconsistent composition. It consists of a defined consortium of live bacteria designed to restore colonisation resistance against gut pathogens, including C. *difficile*. VE303 was generated using Vedanta's proprietary discovery platform, which leverages what is believed to be the largest collection of human microbiome-associated bacterial strains, and is manufactured in-house at Vedanta's state-of-the-art, cGMP-compliant facilities.

In November 2017, the VE303 programme received a grant of up to $5.4 million from CARB-X (Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator), a global public-private partnership focused on funding the development of promising new antibacterial products and rapid diagnostics. This was CARB-X's first award announced for a microbiome project and also the first for a project targeting C. *difficile*.

About Vedanta Biosciences

Vedanta Biosciences is pioneering development of a new category of therapies for immune-mediated and infectious diseases based on rationally designed consortia of bacteria derived from the human microbiome. An affiliate of PureTech Health (PureTech Health plc, PRTC.L), Vedanta's founding team includes a group of world-renowned experts in immunology and microbiology. Vedanta Biosciences is a leader in the microbiome field with capabilities and deep expertise to discover, develop and manufacture drugs based on live bacterial consortia. The Company's facilities include integrated manufacturing operations providing cGMP-compliant manufacturing of rationally-designed bacterial consortia in powder form. Leveraging its proprietary technology platform and the expertise of its team of scientific co-founders, Vedanta Biosciences has isolated and maintains the largest collection of human microbiome-associated bacterial strains and has characterised, in collaborations with leading experts, how the immune system recognises and responds to these microbes. This pioneering work 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 – as well as the characterisation of novel molecular mechanisms of microbial-host communication. 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, its proprietary library of microbiome-derived bacterial strains, as well as data from clinical translational collaborations, to generate a pipeline of programmes addressing infectious diseases, autoimmune diseases, inflammation and immune-oncology indications.

Vedanta Biosciences' scientific co-founders have pioneered the fields of innate immunity, Th17 and regulatory T cell biology, and include Dr Ruslan Medzhitov (Professor of Immunobiology at Yale), Dr Alexander Rudensky (tri-institutional Professor at the Memorial Sloan-Kettering Institute, the Rockefeller University and Cornell University), Dr Dan Littman (Professor of Molecular Immunology at NYU), Dr Brett Finlay (Professor at the University of British Columbia) and Dr Kenya Honda (Professor, Keio University School of Medicine). Vedanta is backed by Seventure, Invesco Asset Management, and Rock Springs Capital and has collaborations with leading institutions including Janssen Biotech, Inc., NYU Langone Health and its Perlmutter Cancer Center, Stanford University School of Medicine, Leiden University Medical Center, University of Tokyo, Keio University, RIKEN, and the University of South Alabama Mitchell Cancer Institute.

About PureTech Health

PureTech Health (PureTech Health plc, PRTC.L) is an advanced, clinical-stage biopharmaceutical company developing novel medicines targeting serious diseases that result from dysfunctions in the nervous, immune, and gastrointestinal systems (brain-immune-gut or the "BIG" axis), which together represent the adaptive human systems. PureTech Health is at the forefront of understanding and addressing the biological processes and crosstalk associated with the BIG axis. By harnessing this emerging field of human biology, the Company is pioneering new categories of medicine with the potential to have great impact on people with serious diseases. PureTech Health is advancing a rich pipeline of innovative therapies that includes two pivotal stage programmes, multiple human proof-of-concept studies and a number of early clinical and pre-clinical programmes. PureTech's rich research and development pipeline has been advanced in collaboration with some of the world's leading scientific experts, who along with PureTech's team of biopharma pioneers, entrepreneurs and seasoned Board, identify, invent, and clinically de-risk new medicines. With this experienced team pursuing cutting edge science, PureTech Health is building the biopharma company of the future focused on improving and extending the lives of people with serious disease. 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 PureTech'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. 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 PureTech Health nor any other party intends to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.