PureTech's Vedanta Biosciences Announces Successful Phase 1a/1b Demonstrating Safety, Tolerability, and Proof of Mechanism for Lead Product Candidate, VE303

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

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

PureTech Health plc (LSE: PRTC) ("PureTech Health"), an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) Axis, today announced that Vedanta Biosciences reported 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. A Phase 2 study in this therapeutic indication is expected to begin before the end of the year.

The results showed that VE303 was safe and well-tolerated at all doses. The study also demonstrated rapid, abundant, and durable intestinal colonisation of the VE303 strains, demonstrating proof of mechanism for this product candidate consisting of a defined consortium of human microbiome-derived bacteria.

Joseph Bolen, PhD, Chief Scientific Officer at PureTech Health, said: "We know that a community of microbes – versus a single strain – is required to re-establish a healthy microbiome since these bacteria work in concert with each other to promote the growth of beneficial bacteria and reduce the levels of pathogenic bacteria. This is the foundation for Vedanta's consortia-based approach, which is now supported by these results and the fact that we were able to track the robust and durable colonisation of each bacterial strain comprising VE303. This rational development of proprietary microbiome-based drugs is the hallmark of Vedanta's pipeline, which is expected to include three additional clinical-stage product candidates in IBD (in partnership with Janssen), food allergy, and cancer immunotherapy within the next nine months."

The full text announcement from Vedanta Biosciences is as follows:

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

Cambridge, Massachusetts, October 4, 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 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 colonisation 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 10^{11} 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 colonisation of VE303 strains that lasted for at least 12 weeks was detected at all doses.
3. Repeated dosing led to increased robustness of strain colonisation (i.e., a majority of VE303 strains colonised 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 favourable safety profile, and - most notably - its ability to rapidly, abundantly, and durably colonise 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 faecal transplants," said Bernat Olle, PhD, 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 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. VE303 is the first product candidate, to the Company's knowledge, consisting of a rationally-defined bacterial consortium in lyophilised powder form to be clinically investigated.

About the Study

The Phase 1a/1b study was an open-label, single-centre, 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 $1.6x10^9$ to $8x10^9$ CFU, and two cohorts received total cumulative doses of VE303 ranging from $4x10^{10}$ to $1.1x10^{11}$ CFU over five or 14 days. The study also included a control cohort of five volunteers who received only vancomycin. Metagenomic sequencing of faecal samples collected longitudinally over 12 weeks was used to assess VE303's pharmacokinetics (speed, durability, abundance, and robustness of bacterial strain colonisation) 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 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 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 programmes 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).

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.