PureTech's Vedanta Biosciences Announces Initiation of Phase 1 Clinical Study with Janssen of Microbiome-Derived Product Candidate for Inflammatory Bowel Disease

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First clinical study of a rationally-defined bacterial consortium for an immune-mediated disease

Milestone triggers $12 million in payments to Vedanta Biosciences from Janssen

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 1 clinical study of VE202, the Company's orally-administered, live biotherapeutic product (LBP) candidate for inflammatory bowel disease (IBD) that was licensed to Janssen Biotech, Inc. in 2015. In conjunction with the initiation of this study, Vedanta Biosciences will receive $12 million from Janssen in milestone payments as part of the ongoing collaboration, which has development and commercialisation milestone payments of up to a total of $339 million in addition to royalty payments.

Bharatt Chowrira, JD, PhD, President and Chief of Business and Strategy at PureTech Health, said: "This is an important milestone as it represents what we believe to be the first clinical study of a rationally-defined bacterial consortium for an immune-mediated disease. We look forward to the continued partnership with Janssen as we advance VE202 through the clinic for IBD, and we are pleased with the overall progression of Vedanta's pipeline, which now includes two clinic-stage live biotherapeutic product candidates."

The full text announcement from Vedanta Biosciences is as follows:

Vedanta Biosciences Announces Initiation of Phase 1 Clinical Study with Janssen of Microbiome-Derived Product Candidate for Inflammatory Bowel Disease

First clinical study of a rationally-defined bacterial consortium for an immune-mediated disease

Milestone triggers $12 million in payments from Janssen

CAMBRIDGE, Mass., Nov. 27, 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 the initiation of a Phase 1 clinical study in healthy volunteers of VE202, the Company's orally-administered, live biotherapeutic product (LBP) candidate for inflammatory bowel disease (IBD). The study is being conducted by Janssen Research & Development, LLC. In conjunction with the initiation of this study, Vedanta Biosciences will receive $12 million from Janssen in milestone payments as part of an ongoing collaboration that has development and commercialisation milestone payments of up to a total of $339 million in addition to royalty payments.

"There is significant evidence highlighting the role of the microbiome in the pathogenesis of IBD. Current treatments effectively block mediators of inflammation, but they do not address the underlying alterations in the gut microbiota that may be driving the inflammation in the first place, leaving a need for safe approaches that address this aspect of the disease," said Bernat Olle, PhD, Co-founder and Chief Executive Officer of Vedanta Biosciences. "To our knowledge, VE202 is the first drug candidate based on a rationally-defined bacterial consortium to enter the clinic for an autoimmune disease. We are pleased to collaborate with Janssen's team, which has produced several important drugs for people living with IBD."

VE202 is based on the work of Vedanta Biosciences co-founder Kenya Honda, PhD, of Keio University, who in 2011 published in *Science* foundational research demonstrating that members of the gut microbiota could impact the number and activity of regulatory T cells in the gut mucosa. In two further publications in *Nature,* in collaboration with Vedanta Biosciences, Honda's group identified cellular mechanisms driving these and other immune-microbiota interactions and demonstrated their potential utility in disease models. Informed by this work, Vedanta Biosciences advanced VE202, a drug candidate consisting of a rationally-defined consortium of regulatory T cell – inducing bacteria.

"Randomised clinical trials of faecal microbiota transplants (FMT) have provided strong evidence for the microbiome's involvement in inflammatory bowel diseases albeit with varying clinical success depending on the donor used and the frequency of instillations. The inconsistent composition of faecal donor material and the need for chronic administration make FMT a challenging modality for treating IBD," said Balfour Sartor, MD, Midget Distinguished Professor of Medicine, Microbiology & Immunology and Co-Director of the UNC Multidisciplinary IBD Center at the University of North Carolina at Chapel Hill. "I believe that a better, more consistent therapeutic approach is to use a well-characterised, rationally-defined, and orally-delivered LBP using bacterial species normally found in the intestine of healthy subjects. I am encouraged by the work Vedanta Biosciences is conducting, and I look forward to the results of this latest clinical study."

Vedanta Biosciences controls an extensive foundational patent estate in the United States, Europe and Japan broadly covering pharmaceutical compositions including *Clostridium* bacterial strains and methods of use for therapeutic products, including both consortia of bacterial strains and spore-forming fractions based on beneficial bacteria. The intellectual property estate covers several of Vedanta Biosciences' therapeutic candidates in development. The company has also been issued patents specifically around the composition and use of VE202 in IBD.

About Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is estimated to affect over one million people in the United States, with as many as 70,000 new cases of the disease diagnosed each year. IBD is believed to result from interactions between genetic factors and environmental triggers, such as commensal bacteria with

pathogenic potential. It is associated with chronic inflammation in the gastrointestinal (GI) tract, impairing the ability of affected GI organs to function properly. Symptoms can vary but include diarrhoea, abdominal pain, cramping, rectal bleeding, and fatigue. Currently available medications alleviate inflammation and reduce symptoms, but do not provide a cure or prevent long-term complications.

About VE202

Janssen Biotech, Inc. licensed VE202 from Vedanta Biosciences in 2015. VE202 is an orally-administered investigational live biotherapeutic product (LBP). 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. VE202 consists of a defined consortium of live bacteria designed to modulate the activity of regulatory T cells and thereby potentially treat inflammatory bowel disease (IBD).

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 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 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.