# PureTech Affiliate Vedanta Biosciences Announces Initiation of First-in-Patient Study of Immuno-Oncology Candidate VE800 In Combination with Bristol-Myers Squibb's Opdivo® (Nivolumab)

December 10, 2019

*First clinical study of a rationally-defined bacterial consortium (VE800) for the treatment of cancer*

*Vedanta forms Immuno-Oncology Scientific Advisory Board of industry experts to support the clinical development of VE800*

PureTech Health plc (LSE: PRTC) ("PureTech"), a clinical stage biotechnology company dedicated to discovering, developing and commercialising highly-differentiated medicines for devastating diseases, is pleased to announce that its affiliate, Vedanta Biosciences, has initiated a first-in-patient clinical study of its immuno-oncology candidate, VE800, in patients with select types of advanced or metastatic cancer.

This open-label, non-randomised study will evaluate the safety, tolerability and clinical activity of VE800 in combination with Bristol-Myers Squibb's programmed death-1 (PD-1) immune checkpoint inhibitor Opdivo® (nivolumab). Vedanta will target enrolment of over 100 patients in the United States diagnosed with advanced or metastatic melanoma, gastric/gastroesophageal junction adenocarcinoma or microsatellite-stable colorectal cancer.

Bharatt Chowrira, JD, PhD, president and chief of business and strategy at PureTech, said: "This study marks the beginning of Vedanta's fourth clinical programme and its first in clinical immuno-oncology. In preclinical work, VE800 was observed to enhance the ability of T cells to infiltrate tumours, promoting suppression of tumour growth and suggesting enhanced survival. This is why we believe it has the potential to substantially improve outcomes for patients with advanced or metastatic cancers. We are pleased with the progress of Vedanta's diversified clinical stage pipeline and their leadership in the development of live biotherapeutic products based on the human microbiome."

Vedanta also announced the formation of an Immuno-Oncology Scientific Advisory Board, comprised of experts in immunology, immuno-oncology and the microbiome, which will support the planned clinical development of VE800.

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

**Vedanta Biosciences Announces Initiation of First-in-Patient Study of Immuno-Oncology Candidate VE800 In Combination with Bristol-Myers Squibb's Opdivo® (Nivolumab)**

*First clinical study of a rationally-defined bacterial consortium (VE800) for the treatment of cancer*

*Company forms Immuno-Oncology Scientific Advisory Board of industry experts to support the clinical development of VE800*

**CAMBRIDGE, Mass., Dec. 10, 2019** —Vedanta Biosciences, Inc. (Vedanta Biosciences, Vedanta or the Company), a clinical-stage biopharmaceutical company developing a new category of therapies for immune-mediated diseases based on defined bacterial consortia, today announced the initiation of a first-in-patient clinical study of VE800 in combination with Bristol-Myers Squibb's programmed death-1 (PD-1) immune checkpoint inhibitor Opdivo® (nivolumab) in patients with select types of advanced or metastatic cancer. Vedanta also announced the formation of its Immuno-Oncology Scientific Advisory Board (SAB), which is comprised of experts in immunology, immuno-oncology and the microbiome, to support the planned clinical development of VE800.

The study, which is being conducted at clinical centres in the United States, will evaluate the safety and tolerability and clinical activity of VE800 in combination with Opdivo®, as measured by the confirmed overall response rate, in addition to other parameters. The open-label, non-randomised study will target enrolment of over 100 patients diagnosed with advanced or metastatic melanoma, gastric/gastroesophageal junction adenocarcinoma, or microsatellite-stable colorectal cancer. Eligible patients will receive daily VE800 dosing in combination with Opdivo®. Topline results are anticipated in 2021.

"Despite unprecedented global investment in checkpoint inhibitors, there is still a major need for differentiated approaches to further enhance and expand responses in cancer," said Bernat Olle, PhD, co-founder and chief executive officer of Vedanta Biosciences. "The role the gut microbiota plays in influencing responses to immunotherapies has been ignored by previous approaches, so we are excited about the potential of microbiome modulation to open up an entirely new approach to cancer therapy."

VE800 is made up of 11 commensal bacterial strains that act in concert to activate cytotoxic CD8+ T cells, which are the vanguard of the immune system's response to tumours and thus a key driver of effective immunotherapies. In preclinical studies, VE800 has been shown to enhance the ability of these T cells to infiltrate tumours, thereby promoting suppression of tumour growth and potentially enhancing survival. Preclinical data also suggest that VE800 may enhance the effects of checkpoint inhibitors.

Foundational work demonstrating VE800's novel anti-tumour activity and cooperatively potentiated responses to checkpoint inhibitor therapies and various immune challenges was published in Nature by Vedanta and its scientific co-founder Kenya Honda, MD, PhD, of Keio University School of Medicine. The research also showed that mice colonised with VE800 demonstrated enhanced therapeutic efficacy in a range of tumour models when VE800 was administered in conjunction with PD-1 or CTLA4 immune checkpoint inhibitors.

"The ability of bacterial consortia to mediate immune activity, including potential anti-cancer activity, is an exciting area for investigation in indications with some of the highest unmet medical need," said Hassane M. Zarour, MD, co-leader of the Cancer Immunology and Immunotherapy Program of the Hillman Cancer Center, University of Pittsburgh, and a member of Vedanta's newly formed Immuno-Oncology SAB. "We see enormous potential for this class of drugs to improve cancer patients' outcomes."

Vedanta's newly announced Immuno-Oncology SAB will work closely with the Company's scientific co-founders and leadership to further support the

clinical development of VE800. The SAB includes:

- **Antoni Ribas, MD, PhD** is a leading translational and clinical researcher in immuno-oncology with a focus on malignant melanoma. He is a professor of medicine, surgery and molecular and medical pharmacology at the University of California Los Angeles (UCLA), director of the tumor immunology program at the Jonsson Comprehensive Cancer Center, director of the Parker Institute for Cancer Immunotherapy Center at UCLA, chair of the Melanoma Committee at SWOG and president-elect 2019-2020 of the American Association for Cancer Research (AACR).
- **Josep Tabernero, MD, PhD** is a researcher focused on gastrointestinal cancers and cancer genetics. At Vall D'Hebron Institute of Oncology (VHIO), he is director of clinical research, co-director of the research unit for molecular therapy of cancer, head of the gastrointestinal and endocrine tumors group, and head of the medical oncology department of Vall d'Hebron University Hospital. He is also president of the European Society for Medical Oncology (ESMO).
- **Hassane Zarour, MD** is a researcher with expertise in melanoma and skin lesions, immunotherapy and cancer vaccines. At the University of Pittsburgh Medical Center, he is a professor of medicine, immunology and dermatology, co-leader of the melanoma program and the James W. and Frances G. McGlothlin chair in melanoma immunotherapy research.
- **Diwakar Davar, MBBS, MSc** is a leader in microbiome science and using the microbiome to treat melanoma. He is an assistant professor of medicine at the University of Pittsburgh Medical Center.
- **Bertrand Routy, MD, PhD** is recognised as one of the first researchers to demonstrate the negative impact of antibiotics and the microbiome on the efficacy of checkpoint inhibitor therapy. He is an assistant professor of hematology-oncology and director of the laboratory of immunotherapy / oncomicrobiome at the Centre hospitalier de l'Université de Montréal (CHUM).
- **Dan Littman, MD, PhD** is a scientific co-founder of Vedanta and a leader in T cell biology, including differentiation and lineage specification. He is the Helen L. and Martin S. Kimmel professor of molecular immunology and pathology and professor in the department of microbiology at the Skirball Institute of Biomolecular Medicine at New York University Langone School of Medicine.
- **Sasha Rudensky, PhD** is a scientific co-founder of Vedanta and a leader in molecular mechanisms of CD4 T cell differentiation, particularly regulatory T cells. He is chair of the immunology program at Sloan Kettering Institute (SKI) and director of the Ludwig Center at Memorial Sloan Kettering (MSK). About VE800 VE800 is Vedanta Biosciences' proprietary, orally administered immuno-oncology product candidate. It is produced from pure, non-pathogenic clonal bacterial cell banks, which yield a standardised drug product in powdered form. VE800 consists of a rationally-defined bacterial consortium of 11 commensal strains that, acting in concert, activate cytotoxic CD8+ T cells, a type of white blood cell that is the predominant effector in cancer immunotherapy. In preclinical studies, VE800 has been shown to enhance the ability of these T cells to infiltrate tumours, thereby promoting suppression of tumour growth and enhancing survival. Preclinical data also suggest that VE800 may enhance the effects of checkpoint inhibitors. Vedanta is evaluating VE800 as a potential treatment for patients with advanced or metastatic cancers.

**About Vedanta Biosciences**

Vedanta Biosciences is a clinical-stage microbiome leader developing a new category of therapies for immune-mediated diseases based on rationally-defined consortia of human microbiome-derived non-pathogenic bacteria. Vedanta's proprietary capabilities include what is believed to be the largest collection of human-gut associated bacteria, assays and bioinformatics techniques for consortia design and optimisation, vast 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 (2013, 2019), Cell, and Nature Immunology. Vedanta Biosciences has harnessed these biological insights and its capabilities to generate a pipeline of investigational live biotherapeutic products (LBPs) in infectious disease, autoimmune disease, allergy, and immuno-oncology. This pipeline includes four clinical-stage product candidates currently being evaluated for the treatment of recurrent C. difficile infection, inflammatory bowel disease (in collaboration with Janssen Biotech, Inc.), food allergy and advanced or metastatic cancers (in combination with Bristol-Myers Squibb's checkpoint inhibitor Opdivo ®), respectively.

Vedanta's IP portfolio contains over 30 issued patents with coverage through at least 2031. Vedanta Biosciences was founded by PureTech Health (LSE: PRTC). 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.

**About PureTech Health**

PureTech is a clinical stage biotechnology company dedicated to discovering, developing and commercialising highly differentiated medicines for devastating diseases, including intractable cancers, lymphatic and gastrointestinal diseases, central nervous system disorders, and inflammatory and immunological diseases, among others. The Company has created a broad and deep pipeline through the expertise of its experienced research and development team and its extensive network of scientists, clinicians and industry leaders. This pipeline, which is being advanced both internally and through PureTech's affiliates, is comprised of 24 product candidates and one product that has been cleared by the US Food and Drug Administration (FDA). All of the underlying programmes and platforms that resulted in this pipeline of product candidates were initially identified or discovered and then advanced by the PureTech team through key validation points based on the Company's unique insights into the biology of the brain, immune, and gut, or BIG, systems and the interface between those systems, referred to as the BIG Axis.

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.

*Opdivo*® is a registered trademark of Bristol-Myers Squibb Company.