PureTech Founded Entity Vedanta Biosciences Enrolls First Patient in Pivotal Phase 3 RESTORATiVE303 Study of VE303 for the Prevention of Recurrent C. difficile Infection

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VE303 is an orally administered, potential first-in-class live biotherapeutic product candidate being developed to prevent recurrence of Clostridioides difficile *infection* (CDI)

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company, noted today that its Founded Entity, Vedanta Biosciences, a clinical-stage company that is developing a potential new category of oral therapies based on defined bacterial consortia, announced that the first patient has been dosed in the global Phase 3 RESTORATiVE303 clinical study of VE303, which is an orally administered defined bacterial consortium candidate that is being developed for the prevention of recurrent *C. difficile* infection (rCDI). The RESTORATiVE303 trial is evaluating the efficacy and safety of VE303 in patients with rCDI and is intended to form the basis for a Biologics License Application to be filed with the U.S. Food and Drug Administration.

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

Vedanta Biosciences Enrolls First Patient in Pivotal Phase 3 RESTORATiVE303 Study of VE303 for the Prevention of Recurrent *C. difficile* Infection

VE303 is an orally administered, potential first-in-class live biotherapeutic product candidate being developed to prevent recurrence of Clostridioides difficile *infection* (CDI)

CAMBRIDGE, MA, May 21, 2024 - Vedanta Biosciences, a clinical-stage company that is developing a potential new category of oral therapies based on defined bacterial consortia, today announced that the first patient has been dosed in the global Phase 3 RESTORATiVE303 clinical study. VE303 is an orally administered defined bacterial consortium candidate that is being developed for the prevention of recurrent *C. difficile* infection (rCDI). The RESTORATiVE303 trial is evaluating the efficacy and safety of VE303 in patients with rCDI and is intended to form the basis for a Biologics License Application (BLA) to be filed with the U.S. Food and Drug Administration.

"Initiation of the RESTORATiVE303 study represents a key clinical milestone for the VE303 program. Building on the successes of earlier VE303 clinical studies, RESTORATiVE303 is the first pivotal Phase 3 study of a live biotherapeutic product for prevention of recurrent CDI, a potentially serious infection that affects up to 175,000 patients and results in approximately 20,000 deaths annually in the U.S.," said Jeffrey Silber, M.D., Chief Medical Officer of Vedanta Biosciences. "Based on the efficacy and safety data we have generated to date for this program, we believe that an oral, rationally designed, defined consortium candidate has the potential to offer patients with rCDI an attractive alternative to undefined, donor-derived fecal approaches."

In April 2023, Vedanta published results from the Phase 2 CONSORTIUM trial, in which treatment with VE303 was associated with a 30.5% adjusted absolute risk reduction in the rate of recurrence when compared with placebo, representing a greater than 80% reduction in the odds of a CDI recurrence.

"CDI may recur in 25% or more of those affected, sometimes repeatedly, despite initially successful antibiotic treatment. With each subsequent recurrence, CDI can have a severe and worsening effect on quality of life, leading to hospitalization and increased risk of death," said Paul Feuerstadt, M.D., FACG, AGAF, of Yale University School of Medicine, and a RESTORATiVE303 study investigator. "Precision approaches based on defined bacterial consortia represent the next generation of microbiome therapeutics for patients with CDI, and we welcome the opportunity to join the pivotal study for the first candidate based on this important new modality."

About the RESTORATiVE303 Study

RESTORATiVE303 is a randomized, double-blind, placebo-controlled Phase 3 clinical trial evaluating the safety and efficacy of VE303 in patients at high risk for recurrence of CDI after completing a course of antibiotics for a prior CDI episode. The trial is being conducted at approximately 200 sites in 22 countries, across four continents. The primary endpoint is the comparison of CDI recurrence rates at eight weeks in the VE303 and placebo groups. The Phase 3 study design and VE303 dosing regimen are based on the completed Phase 2 trial, in which VE303 met its primary endpoint for preventing CDI recurrence at eight weeks and was observed to be generally well-tolerated. For more information on RESTORATiVE303 (NCT06237452) please visit clinicaltrials.gov.

About VE303

VE303 is a potential first-in-class live biotherapeutic product (LBP) candidate consisting of a defined bacterial consortium designed for the prevention of recurrent *Clostridioides difficile* infection (rCDI). It consists of eight strains that were rationally selected using Vedanta's product engine. VE303 is produced from pure, clonal bacterial cell banks, which yield a standardized drug product in powdered form and bypass the need to rely on donor fecal material of inconsistent composition. Vedanta published study results in April 2023 from the Phase 2 CONSORTIUM trial, in which treatment with the VE303 high dose was associated with a 30.5% adjusted absolute risk reduction in the rate of recurrence when compared with placebo, representing a greater than 80% reduction in the odds of a CDI recurrence. VE303 was granted Orphan Drug Designation in 2017 and Fast Track Designation in 2023 by the U.S. Food and Drug Administration (FDA) for the prevention of recurrent CDI.

This project has been funded in part with federal funds from the U.S. Department of Health and Human Services (HHS); Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under contract number 75A5012C00177 for a contract value up to $104.2 million. This project has also received a $5.4 million research grant from the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) in 2017.

About Vedanta Biosciences

Vedanta Biosciences is a clinical-stage biopharmaceutical company developing medicines for the treatment of gastrointestinal diseases. The company's lead assets are potential first-in-class oral therapies - VE303, in a Phase 3 registrational trial for prevention of recurrent *C. difficile* infection, and VE202, in a Phase 2 trial for treatment of ulcerative colitis. Vedanta's pipeline has been built using the company's industry-leading product engine for the development of therapies based on defined consortia of bacteria grown from pure clonal cell banks. The product engine, supported by broad foundational intellectual property, includes one of the largest libraries of bacteria isolated from the human microbiome, vast clinical datasets, proprietary capabilities in consortium design, and end-to-end CGMP manufacturing capabilities at commercial launch scale.

About PureTech Health

PureTech is a clinical-stage biotherapeutics company dedicated to giving life to new classes of medicine to change the lives of patients with devastating diseases. The Company has created a broad and deep pipeline through its experienced research and development team and its extensive network of scientists, clinicians and industry leaders that is being advanced both internally and through its Founded Entities. PureTech's R&D engine has resulted in the development of 29 therapeutics and therapeutic candidates, including two that have received both U.S. FDA clearance

and European marketing authorization and a third (KarXT) that has been filed for FDA approval. A number of these programs are being advanced by PureTech or its Founded Entities in various indications and stages of clinical development, including registration enabling studies. All of the underlying programs and platforms that resulted in this pipeline of therapeutic candidates were initially identified or discovered and then advanced by the PureTech team through key validation points.

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

Cautionary Note Regarding Forward-Looking Statements

This press release contains statements that are or may be forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation those related to the VE303 development program, development plans and potential benefits to patients, and our future prospects, developments and strategies. The forward-looking statements are based on current expectations and are subject to known and unknown risks, uncertainties and other important factors that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, those risks, uncertainties and other important factors described under the caption "Risk Factors" in our Annual Report on Form 20-F for the year ended December 31, 2023 filed with the SEC and in our other regulatory filings. 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, we disclaim any obligation to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.

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