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PureTech Founded Vedanta Biosciences Publishes Additional Phase 2 VE303 Results in Nature Medicine

VE303 was well tolerated and decreased the odds of rCDI through multiple mechanisms

Analyses identified predictors of VE303 colonization and protection from CDI recurrence

Topline data for the ongoing Phase 3 pivotal RESTORATiVE303 study are expected in 2026

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company dedicated to changing the lives of patients with devastating diseases, noted that its Founded Entity, Vedanta Biosciences, a late clinical-stage company developing defined bacterial consortia as oral therapies for gastrointestinal diseases, today announced the publication of additional results from the Phase 2 CONSORTIUM study for its lead candidate, VE303, which is being evaluated for prevention of recurrent *Clostridioides difficile* infection (rCDI). The new analyses were published this month in Nature Medicine and can be viewed online.

VE303 is a potential first-in-class Live Biotherapeutic Product for the prevention of rCDI, which consists of a defined consortium of eight bacterial strains. Clinical results from Vedanta's successful Phase 2 CONSORTIUM study, published in the Journal of the American Medical Association (JAMA), demonstrated that the higher dose of VE303 studied was well tolerated and reduced the odds of CDI recurrence by more than 80% compared with placebo.

The new publication which is entitled "Multi-omic Profiling a Defined Bacterial Consortium for Treatment of Recurrent *Clostridioides difficile* Infection," reports additional results from CONSORTIUM. Profiling of microbiome composition, fecal metabolites, and host immune function indicated that VE303 works through multiple mechanisms to prevent rCDI by restoring a healthy gut microbial community, decreasing inflammation, and increasing levels of protective metabolites. In addition, the work identified predictors of high or low VE303 colonization and clinical response.

Taken together, these results demonstrate that VE303 works through multiple mechanisms to reduce CDI recurrence. Results from the CONSORTIUM study informed the design and dose selection for the global, pivotal Phase 3 study, RESTORATiVE303, that is currently underway to confirm the efficacy and safety profile of VE303 in the prevention of rCDI. Topline data for this study are expected in 2026.

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

Vedanta Biosciences Publishes Additional Phase 2 VE303 Results in Nature Medicine

VE303 was well tolerated and decreased the odds of rCDI through multiple mechanisms

Analyses identified predictors of VE303 colonization and protection from CDI recurrence

Topline data for the ongoing Phase 3 pivotal RESTORATiVE303 study are expected in 2026

CAMBRIDGE, Mass., January 23, 2025 -- Vedanta Biosciences, a late clinical-stage company developing defined bacterial consortia as oral therapies for gastrointestinal diseases, today announced the publication of additional results from the Phase 2 CONSORTIUM study for its lead candidate, VE303, which is being evaluated for prevention of recurrent *Clostridioides difficile* infection (rCDI). The new analyses were published this

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VE303 is a potential first-in-class Live Biotherapeutic Product for the prevention of rCDI, which consists of a defined consortium of eight bacterial strains. Clinical results from Vedanta's successful Phase 2 CONSORTIUM study, published in the Journal of the American Medical Association (JAMA), demonstrated that the higher dose of VE303 studied was well tolerated and reduced the odds of CDI recurrence by more than 80% compared with placebo. VE303 organisms rapidly and robustly colonize the gut in a dose-dependent manner. Colonization predicted greater recurrence-free probability, establishing a direct connection between exposure and clinical response.

The publication which is entitled "Multi-omic Profiling a Defined Bacterial Consortium for Treatment of Recurrent *Clostridioides difficile* Infection," reports additional results from CONSORTIUM. Profiling of microbiome composition, fecal metabolites, and host immune function indicated that VE303 works through multiple mechanisms to prevent rCDI by restoring a healthy gut microbial community, decreasing inflammation, and increasing levels of protective metabolites. In addition, the work identified predictors of high or low VE303 colonization and clinical response.

"This clinical research offers new insights into the mechanisms of action of VE303, providing a rationale for the drug's protective effects in rCDI," said Bernat Olle, Ph.D., Chief Executive Officer of Vedanta Biosciences. "Due to VE303's precisely known, defined composition, we can study its mechanisms of action and PK-PD relationships in a rigorous way, taking a step towards understanding why some patients respond better than others to a microbiome restoration intervention. We believe this line of work helps fill a knowledge gap in the field, since characterization of the mechanisms of action of first-generation fecal microbiota products has been very limited."

Highlights of the publication include:

- Abundance of specific VE303 strains, and of VE303 strains overall, was predictive of remaining recurrence-free.
- The strains that colonized well differed across individuals, suggesting that efficacy is derived from strains working together as a consortium.
- VE303 colonization and clinical benefit correlated with increased levels of short-chain fatty acids and key secondary bile acids, both of which have beneficial effects in conferring resistance to CDI.
- Faster recovery of a more diverse microbiome, which was seen in the high dose recipients of VE303, was associated with non-recurrence.
- The elimination rate of the antibiotic used for the CDI episode was a predictor of VE303 colonization. Given that clearance of residual antibiotic from stool varies significantly among individuals and can take a week or longer, treating with VE303 for 14 consecutive days following completion of standard-of-care antibiotics enabled VE303 strains to be inoculated when the intestinal environment was most permissive to colonization.
- VE303 use led to lower levels of pro-inflammatory and potentially pathogenic Gram-negative species, including Klebsiella and Citrobacter, that are linked to CDI recurrence and AMR bacterial infections.

Taken together, these results demonstrate that VE303 works through multiple mechanisms to reduce CDI recurrence. Results from the CONSORTIUM study informed the design and dose selection for the global, pivotal Phase 3 study, RESTORATiVE303, that is currently underway to confirm the efficacy and safety profile of VE303 in the prevention of rCDI. Topline data for this study are expected in 2026.

This project has been supported in whole or in part with federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority (BARDA), under contract number 75A50120C00177.

About VE303

VE303 is a potential first-in-class Live Biotherapeutic Product for the prevention of recurrent *Clostridioides difficile* infection (rCDI). VE303 is an orally administered, defined bacterial consortium therapeutic candidate which 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 direct sourcing of donor fecal material of inconsistent composition. Vedanta published positive results in JAMA in April 2023 from the Phase 2 CONSORTIUM trial, in which VE303 met its

published positive results in JAMA in April 2023 from the Phase 2 CONSORTIUM trial, in which VE303 met its primary endpoint of preventing *C. difficile* infection recurrence at eight weeks. Vedanta is currently enrolling patients into a Phase 3 RESTORATiVE303 registrational study of VE303 for the prevention of recurrent *C. difficile* infection. Vedanta Biosciences received a 5.4 million research grant from the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) in 2017 and a contract of up to 81.9 million from Biomedical Advanced Research and Development Authority (BARDA) in 2020 to support clinical studies of VE303. VE303 was granted Orphan Drug Designation in 2017 by the U.S. Food and Drug Administration (FDA) for the prevention of recurrent CDI.

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 three that have been approved by the U.S. Food and Drug Administration. 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 Vedanta's development plans for its pipeline of therapeutics of defined bacterial consortia as oral therapies for gastrointestinal diseases, including VE303, the timing of topline results for ongoing clinical trials, potential benefits to patients, and Vedanta's 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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