PureTech Founded Entity Vedanta Biosciences Presents Data from Multiple Studies at Digestive Disease Week 2022 Annual Meeting

May 24, 2022

RNS Number : 5236M
PureTech Health PLC
24 May 2022

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Further CONSORTIUM study analysis shows that the VE303 high dose led to more robust colonization, which in turn correlated with prevention of recurrence

Safety and colonization analyses of VE202 and VE818 Phase 1 studies show they were well tolerated, colonized robustly after vancomycin pretreatment, and were associated with increased production of secondary bile acids that are known to induce immune tolerance

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company noted that its Founded Entity, Vedanta Biosciences, Inc. ("Vedanta"), today announced the details of three podium presentations of research informed by multiple clinical studies at Digestive Disease Week (DDW) 2022, being held both virtually and in person in San Diego, CA on May 21-24. The analyses cover several defined bacterial consortia candidates developed by Vedanta, and include assessments of safety, tolerability, efficacy, and the relationships between dosing regimen, consortium strain colonization, and restoration of a patient's resident microbial community. These analyses further deepen Vedanta's understanding of the clinical pharmacology and potential benefits of defined bacterial consortia, and help inform future clinical research. This body of data builds on published analyses from earlier clinical work that identified key factors that drive colonization of Vedanta's candidates.

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

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CAMBRIDGE, MA - Vedanta Biosciences, a clinical-stage biopharmaceutical company pioneering the development of oral therapies based on defined bacterial consortia, today announced the details of three podium presentations of research informed by multiple clinical studies at Digestive Disease Week (DDW) 2022, being held both virtually and in person in San Diego, CA on May 21-24. The analyses cover several defined bacterial consortia candidates developed by Vedanta, and include assessments of safety, tolerability, efficacy, and the relationships between dosing regimen, consortium strain colonization, and restoration of a patient's resident microbial community. These analyses further deepen Vedanta's understanding of the clinical pharmacology and potential benefits of defined bacterial consortia and help inform future clinical research. This body of data builds on published analyses from earlier clinical work that identified key factors that drive colonization of Vedanta's candidates.

"As leaders in the research and development of defined bacterial consortia-based therapies, we are continually pushing to deepen our ability to understand and shape clinical outcomes by quantifying the colonization dynamics of our rationally designed and rigorously manufactured product candidates. This effort is part of our work to overcome the limitations of older methods, such as fecal matter transplants and spore fractions, which are inherently variable, challenging to scale, and susceptible to pathogen transmission from donors," said Jeffrey Silber, M.D., Chief Medical Officer of Vedanta Biosciences. "These analyses from three different clinical programs provide substantial further elucidation of the factors that affect the behavior and clinical impact of defined bacterial consortia in patients. As we prepare for our first Phase 3 clinical trial, for VE303, we are drawing upon a comprehensive body of knowledge to shape our clinical strategy."

Colonization dynamics is analogous to traditional drug pharmacokinetics and refers to the growth and persistence over time of bacterial strain populations in the human gut.

Details of the Oral Presentations at DDW 2022:

Title: *An 8-strain, rationally defined bacterial consortium, VE303, reduces the risk of* Clostridioides difficile *infection (CDI) recurrence compared with placebo in adults at high risk for recurrence: Results for the Phase 2 CONSORTIUM study*

Presenter: Thomas Louie, M.D.

The design and topline results of this study were announced in October 2021, which formed the basis for this presentation. Overall, in the CONSORTIUM study, VE303 was well tolerated and highly active at preventing CDI recurrence in subjects at high risk of recurrence.

The VE303 high dose met the primary endpoint of a lower recurrence rate at eight weeks, when compared with placebo (13.8 percent versus 45.5 percent). This 31.7 percent reduction in absolute risk of recurrence reflected a greater than 80 percent reduction in the odds of a recurrence in the VE303 high-dose group compared with the placebo group (odds ratio 0.192; 90 percent confidence interval 0.048, 0.712; p=0.0077). Most patients in the study reported one or more adverse events, but the overall safety profiles were similar across the active and placebo groups, and most adverse events were of mild intensity. There were no treatment-related serious adverse events in any group.

Title: *Rapid and durable colonization of VE303 in* Clostridioides difficile *infection (CDI) patients is associated with clinical efficacy: Results of the Phase 2 CONSORTIUM study*

Presenter and time: Rajita Menon, Ph.D.

This analysis evaluated fecal samples from study participants in the Phase 2 CONSORTIUM study that were obtained during dosing and at weeks four and seven. Metagenomic sequencing was performed to identify associations between VE303 strain colonization, resident microbes, and clinical safety and efficacy endpoints.

Among the enrolled patients who were at high risk of CDI recurrence, the VE303 high dose led to more robust colonization of the eight consortium strains at Day 14 than the VE303 low dose, in terms of both strain detection (median, six versus three strains) and relative abundance (median, 5.2 percent versus 0.8 percent). Better VE303 strain colonization was associated with clinical activity and was greatest among those who received the VE303 high dose. Across all VE303 recipients, higher colonization at the end of dosing was associated with a lower probability of CDI recurrence. Higher bacterial species diversity and more rapid recovery of the normal resident microbial community were observed with use of VE303 high dose and were also associated with non-recurrence.

Title: *Durable colonization of the rationally designed live biotherapeutic products VE202 and VE818 in healthy volunteers.*

Presenter: Emily Crossette, Ph.D.

The Phase 1 studies of VE202 (a defined bacterial consortium candidate for inflammatory bowel disease) and VE818 (a defined bacterial consortium candidate for an undisclosed indication) were similarly designed double-blind, placebo-controlled studies in healthy adults, enrolling a total of 31 and 74 subjects, respectively. The studies assessed safety, tolerability, and colonization dynamics. Subjects received a low dose, high dose, or placebo for one or 14 days, with or without vancomycin antibiotic pretreatment, and were followed for six months after treatment. Strain colonization was quantified with metagenomics and quantitative polymerase chain reaction (qPCR). Additionally, levels of bacterial metabolites associated with immune tolerance were measured.

Both VE202 and VE818 were well tolerated. Vancomycin pretreatment was required to ensure robust strain colonization. Strain colonization was persistent in most subjects through the end-of-study visit. Additionally, dose duration was an important driver of long-term persistence of colonization. Colonization with VE202 and VE818 was associated with increased stool concentrations of secondary bile acids, which have several beneficial immunoregulatory functions, as early as the first week of treatment.

About VE303

VE303 is a first-in-class defined bacterial consortium therapeutic candidate designed for the prevention of recurrent *Clostridioides difficile* infection (rCDI). It consists of eight strains that were rationally selected using Vedanta's discovery engine. VE303 is produced from pure, clonal bacterial cell banks, which yield a standardized drug product in powdered form and bypasses the need to rely on direct sourcing from donor fecal material of inconsistent composition. Vedanta reported positive topline results in October 2021 from the Phase 2 CONSORTIUM trial, in which VE303 was associated with a 31.7% 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. Vedanta believes VE303 has the potential to become a first-in-class therapeutic based on a rationally defined bacterial consortium. Vedanta Biosciences received a $5.4 million research award from the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) in 2017 and a contract of up to $76.9 million from the Biomedical Advanced Research and Development Authority (contract number 75A50120C00177) within the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response 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 VE202

VE202 is a first-in-class defined bacterial consortium therapeutic candidate for the treatment of inflammatory bowel disease (IBD). It consists of 16 bacterial strains of the Clostridia class that were rationally selected. It is designed to induce immune tolerance in the gut, reverse the gut microbiota abnormalities that are common in patients with IBD, and strengthen the epithelial barrier. Results describing the biology and candidate selection of VE202 were previously described in multiple publications in *Science* and *Nature*. In a Phase 1 study conducted in healthy adults, VE202 colonized abundantly following a short course of antibiotic pretreatment, with most strains detected in stool samples from most study participants within 1 week and persisting through the final sample at Week 24. Multiple-day dosing led to significantly greater and more durable colonization than did single-day dosing. VE202 was also well tolerated, with most adverse events unrelated to study treatment, gastrointestinal in nature, and of mild or moderate intensity.

About Vedanta Biosciences

Vedanta Biosciences is leading the development of a potential new category of oral therapies based on defined consortia of bacteria isolated from the human microbiome and grown from pure clonal cell banks. The company's clinical-stage pipeline includes product candidates being evaluated for the treatment of high-risk *C. difficile* infection, inflammatory bowel diseases, food allergy, liver disease, and cancer. These investigational therapies are grounded in pioneering research - published in leading journals including Science, Nature, and Cell - to identify beneficial bacteria that live symbiotically within the healthy human gut, fight pathogens and induce a range of potent immune responses. *Vedanta Biosciences controls a foundational portfolio of more than 45 patents and has built what it believes is one of the largest libraries of bacteria derived from the human microbiome. Proprietary* capabilities include deep expertise in consortium design, vast datasets from human interventional studies, and CGMP-compliant manufacturing of oral Live Biotherapeutic Product (LBP) candidates containing pure, clonally-derived bacterial consortia in powdered form. Vedanta Biosciences was founded by PureTech Health (Nasdaq: PRTC, LSE: PRTC) and a global team of scientific co-founders who pioneered the modern understanding of the cross-talk between the microbiome and the immune system.

About Digestive Disease Week®

Digestive Disease Week® (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW is an in-person and virtual meeting from May 21-24, 2022. The meeting showcases more than 3,100 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. More information can be found at www.ddw.org.

Acknowledgement and Disclaimer:

Vedanta's VE303 program has been funded in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract No.75A5012C00177.

The VE303 research reported in this press release is supported in part by CARB-X. CARB-X's funding for this project is sponsored by the Cooperative Agreement Number IDSEP160030 from ASPR/BARDA and by an award from Wellcome. The content is solely the responsibility of the authors and does not necessarily represent the official views of CARB-X or any of its funders.

About PureTech Health

PureTech is a clinical-stage biotherapeutics company dedicated to discovering, developing and commercializing highly differentiated medicines for devastating diseases, including inflammatory, fibrotic and immunological conditions, intractable cancers, lymphatic and gastrointestinal diseases and neurological and neuropsychological disorders, 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 Founded Entities, is comprised of 27 therapeutics and therapeutic candidates, including two that have received both U.S. FDA clearance and European marketing authorization, as of the date of PureTech's most recently filed Annual Report and corresponding Form 6-K. 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 based on unique insights in immunology and drug development.

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

Cautionary Note Regarding Forward-Looking Statements

This press release contains 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 statements that relate to Vedanta's future prospects, development plans, 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, 2021 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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