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PureTech Founded Entity Vedanta Biosciences Publishes Phase 1a/1b Results for Lead Program VE303 in Cell Host & Microbe and Highlights Planned Presentations of Phase 2 VE303 Results

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PureTech Founded Entity Vedanta Biosciences Publishes Phase 1a/1b Results for Lead Program VE303 in *Cell Host & Microbe* **and Highlights Planned Presentations of Phase 2 VE303 Results**

Full Phase 1 data analysis of VE303, a defined bacterial consortium candidate for C. difficile *infection, published in* Cell Host & Microbe

Positive topline Phase 2 results for VE303 announced in 2021; Phase 3 preparations underway

Acceptance of three abstracts for podium presentations at Digestive Disease Week 2022

PureTech Health plc (Nasdaq: PRTC, LSE: PRTC) ("PureTech" or the "Company"), a clinical-stage biotherapeutics company noted that its Founded Entity, Vedanta Biosciences ("Vedanta"), today announced the publication in the journal *Cell Host & Microbe* of the results from a Phase 1a/1b study evaluating the safety, tolerability, and colonization dynamics of VE303 in healthy adults. VE303 is a potential first-in-class defined bacterial consortium candidate for the prevention of recurrent *Clostridium difficile* infection (CDI). Vedanta will also share three research updates across its VE303 and VE202 (for inflammatory bowel disease) programs in podium presentations at Digestive Disease Week in May 2022.

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.

The *Cell Host & Microbe* paper, "Colonization of the Live Biotherapeutic Product VE303 and Modulation of the Microbiota and Metabolites in Healthy Volunteers," details the results of a first-in-human Phase 1a/1b dose-escalation study of VE303 in healthy adults. VE303 was observed to be generally well-tolerated at all doses tested and to colonize optimally if dosed over multiple days after vancomycin pretreatment. The work illuminates some fundamental features of the colonization dynamics of a live biotherapeutic product (LBP) that may be generalizable. Specifically, it shows that the proportion of LBP strains that colonize, as well as the abundance and durability of colonization, can be significantly improved by the use of a higher dose, longer duration of dosing, and pretreatment with a short course of antibiotics to create an ecological niche for engraftment. VE303 colonization was associated with earlier and increased concentrations of secondary bile acids and short-chain fatty acids, and promoted the establishment of a microbiota community known to resist enteric pathogen colonization.

Vedanta will present three abstracts at Digestive Disease Week (DDW) 2022, held virtually and in person in San Diego, California, from May 21-24, 2022. Two of the abstracts are focused on VE303 Phase 2 topline results in CDI and one abstract is focused on VE202, a defined bacterial consortium candidate being developed as an oral treatment for inflammatory bowel disease.

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

Vedanta Biosciences Publishes Phase 1a/1b Results for Lead Program VE303 in *Cell Host & Microbe* **and Highlights Planned Presentations of Phase 2 VE303 Results**

Full Phase 1 data analysis of VE303, a defined bacterial consortium candidate for C. difficile *infection, published in* Cell Host & Microbe

Positive topline Phase 2 results for VE303 announced in 2021; Phase 3 preparations underway

Acceptance of three abstracts for podium presentations at Digestive Disease Week 2022

CAMBRIDGE, MA, April 13, 2022 - Vedanta Biosciences, a leading clinical-stage company developing a potential new category of oral therapies based on defined bacterial consortia, today announced the publication in the journal *Cell Host & Microbe* of the results from a Phase 1a/1b study evaluating the safety, tolerability, and colonization dynamics of VE303 in healthy adults. VE303 is a potential first-in-class defined bacterial consortium candidate for the prevention of recurrent *Clostridium difficile* infection (CDI). The company will also share three research updates across its VE303 and VE202 (for inflammatory bowel disease) programs in podium presentations at Digestive Disease Week in May 2022.

"In this publication of our Phase 1 results, we show that we were able to precisely quantify the colonization dynamics of microbiome-directed agents based on defined bacterial consortia, such as VE303, and identify key factors that drive better colonization," said Bernat Olle, Ph.D., Co-Founder and Chief Executive Officer of Vedanta Biosciences. Colonization dynamics are analogous to traditional drug pharmacokinetics and refer to the growth and persistence over time of bacterial strain populations in the human gut.

"This allows us to quantitatively describe the relationship between drug exposure and effect, which may enable optimized treatment regimens and rational analysis of clinical data. This predictability is missing from older approaches that rely on human donors, as the dose and identity of bacterial species vary widely with each fecal donation," continued Dr. Olle. "In our subsequent Phase 2 study of VE303 in CDI, we showed that better colonization correlates with greater likelihood of sustained clinical cure. Together, we believe these results offer a more rational path forward for clinical development of microbiome-directed medicines."

Phase 1a/1b study results

The *Cell Host & Microbe* paper, "Colonization of the Live Biotherapeutic Product VE303 and Modulation of the Microbiota and Metabolites in Healthy Volunteers," details the results of a first-in-human Phase 1a/1b dose-escalation study of VE303 in healthy adults. VE303 was observed to be generally well-tolerated at all doses tested and to colonize optimally if dosed over multiple days after vancomycin pretreatment. The work illuminates some fundamental features of the colonization dynamics of a live biotherapeutic product (LBP) that may be generalizable. Specifically, it shows that the proportion of LBP strains that colonize, as well as the abundance and durability of colonization, can be significantly improved by the use of a higher dose, longer duration of dosing, and pretreatment with a short course of antibiotics to create an ecological niche for engraftment. VE303 colonization was associated with earlier and increased concentrations of secondary bile acids and short-chain fatty acids, and promoted the establishment of a microbiota community known to resist enteric pathogen colonization.

Digestive Disease Week 2022 abstract acceptances

Vedanta will present three abstracts at Digestive Disease Week (DDW) 2022, held virtually and in person in San Diego, California, from May 21-24, 2022. Two of the abstracts are focused on VE303 Phase 2 topline results in CDI and one abstract is focused on VE202, a defined bacterial consortium candidate being developed as an oral treatment for inflammatory bowel disease.

Details of the presentations are as follows:

Abstract 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 of the phase 2 CONSORTIUM study
Presenter: Thomas Louie, M.D.
Session Type: Research Forum
Session Title: Mechanisms and Efficacy of Microbial Therapeutics in Infectious and

Functional GI Diseases
Session Date and Time: May 21, 2022, from 10:00 a.m. to 11:30 a.m. PDT
Presentation Time: 11:00 a.m. PDT

Abstract Title: Durable colonization of the rationally designed live biotherapeutic products VE202 and VE818 in healthy volunteers
Presenter: Emily Crossette, Ph.D.
Session Type: Research Forum
Session Title: The Role of the Microbiome in IBD
Session Date and Time: May 22, 2022, from 2:00 p.m. to 3:30 p.m. PDT
Presentation Time: 3:15 p.m. PDT

Abstract 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: Rajita Menon, Ph.D.
Session Type: Research Forum
Session Title: Diagnostic and Therapeutic implications of Gut Microbiome in Diarrheal Disorders including *C. difficile* Infection
Session Date and Time: May 24, 2022, from 8:00 a.m. to 9:30 a.m. PDT
Presentation Time: 8:15 a.m. PDT

About VE303
VE303 is a 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 grant from the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) in 2017 and a contract of up to $76.9 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 VE202
VE202 is a first-in-class, orally administered, 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, oncology, liver disease, and food allergy. 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 to be the world's biggest library 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 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 Vedanta's modern understanding of the cross-talk between the microbiome and the immune system.

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 25 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 Half Year 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 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.

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, 2020 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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