PureTech Health Affiliate Vor Biopharma Publishes Proof-of-Concept Study of its Lead Programme in the Scientific Journal Proceedings of the National Academy of Sciences

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Preclinical study supports Vor's approach for overcoming important toxicities encountered by targeted immunotherapies for blood cancers

Paper co-authored by Vor co-founder Dr Siddhartha Mukherjee

PureTech Health plc (LSE:PRTC) ("PureTech Health"), an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) axis, is pleased to note that its affiliate Vor Biopharma ("Vor") today announced the publication of an important paper in the scientific journal *Proceedings of the National Academy of Medicines* supporting Vor's novel approach to treating cancer via engineered hematopoietic stem cells (HSCs).

Vor's approach is designed to address a serious limitation of most targeted immunotherapies: the targets they bind are present on both healthy cells and cancer cells. In the case of haematological cancers, this poor discrimination can result in devastating collateral damage to healthy immune cells and severe toxicities. Vor's lead programme, VOR33, is a novel HSC therapy consisting of donor-derived HSCs that are engineered to lack the cell surface protein CD33. When removed from the cell surface, VOR33 cells do not appear to have any measurable changes to their biological function but are shown to be highly resistant to attack from CD33-targeted immunotherapies. When infused into a patient, the engineered stem cells are designed to mature and differentiate into a full spectrum of healthy immune and blood cells that would be untouched by the cancer treatment. As the preclinical research published today suggests, this approach has the potential to minimize immunotherapy toxicities and maximize the potency of anti-CD33 therapies.

Bharatt Chowrira, JD, PhD, president and chief of business and strategy at PureTech Health, said: "Vor's novel approach is designed to reboot the patient's immune system with an infusion of healthy blood stem cells that are protected from the toxic effects of targeted immunotherapies. This approach has the potential to minimize the toxicities associated with immunotherapies and greatly expand the reach of this class of medicines, well beyond what is currently possible. We are excited and encouraged by these results and look forward to Vor's progress in advancing its lead candidate VOR33 and other therapies built around engineered HSCs."

The full text announcement from Vor Biopharma is as follows:

Vor Biopharma Announces Publication of Proof-of-Concept Study of its Lead Programme in the Scientific Journal *Proceedings of the National Academy of Sciences*

Preclinical study supports Vor's approach for empowering targeted immunotherapies through hematopoietic stem cell editing

Paper co-authored by Vor co-founder Dr Siddhartha Mukherjee

BOSTON, May 29, 2019 —Vor Biopharma, an immuno-oncology company pioneering engineered hematopoietic stem cell (HSC) therapies for hematologic malignancies, today announced a publication in the scientific journal *Proceedings of the National Academy of Sciences (PNAS)* titled "Gene-Edited Stem Cells Enable CD33-Directed Immune Therapy for Myeloid Malignancies." The research describes the successful editing of HSCs that are engineered to be selectively deficient in the myeloid lineage antigen CD33. These CD33-deficient HSCs were shown to successfully engraft into the bone marrow of their host. Furthermore, there was evidence these cells could functionally repopulate the hematopoietic system. When subjected to aggressive doses and regimens of CD33-targeted immuonotherapies in a murine model of acute myeloid leukaemia (AML), Vor-engineered HSCs were protected from depletion by the immunotherapy while cancer cells were selectively targeted.

These newly published results are the basis for Vor's lead product candidate, VOR33, and outline Vor's unique therapeutic approach. The paper was co-authored by Vor co-founder Siddhartha Mukherjee, MD, DPhil, of Columbia University Irving Medical Center, and his team.

Vor's approach is designed to enable broadly targeting lineage antigens, which are attractive targets but face serious limitations, since they are expressed on both healthy cells and cancerous cells. Currently, targeting lineage antigens for treating hematologic malignancies depletes the healthy blood cells of the targeted lineage, causing severe toxicities. These toxicities have prevented the successful development or broader use of several otherwise promising drugs. In patients, Vor-engineered HSCs are expected to mature and differentiate into healthy blood cells that do not display a particular lineage antigen, therefore making that lineage antigen tumour-specific and safe to target.

The preclinical research published today suggests that VOR33 cells will produce healthy blood cells that will not display the lineage antigen CD33, and therefore will not be depleted by CD33-targeted therapies. The publication further indicates that this approach minimizes on-target toxicities and maximizes the potency of lineage-targeted immunotherapies, including antibody-drug conjugates, bispecific antibodies, and chimeric antigen receptor (CAR) T cells.

"We are hoping to protect the patient's immune system from damage during targeted immunotherapy treatment. This approach has the potential to transform the use of immunotherapies in hematologic diseases by enabling the use of highly potent drugs, improving dosing, and fundamentally changing the treatment paradigm. The novelty of the strategy is that rather than focus only on the cancer, we are making the host – the patient – resistant to the therapy, so that the cancer remains vulnerable. This strategy has never been attempted in cancer," said Dr Mukherjee. "This preclinical study demonstrates that Vor's technology can clear leukaemia and repopulate healthy hematopoietic cell populations through the use of engineered HSCs combined with a CAR-T or an antibody-drug conjugate (ADC) or a range of other targeted immunotherapy approaches. Remarkably, we saw

that it was also possible to use a CAR-T and an ADC in combination without untoward myelosuppression. This research gives us great hope as we advance toward the clinic with VOR33 and look to expand our novel approach into other cancers."

In February 2019, Vor announced the completion of a $42 million Series A financing round led by 5AM Ventures and RA Capital to advance its lead candidate for the treatment of AML towards the clinic, and to further build its pipeline to treat hematologic malignancies. In November 2018, Vor announced that the United States Patent and Trademark Office issued U.S. Patent No. 10,137,155, which covers compositions and methods related to using modified HSCs to enable targeted immunotherapies. This patent, the first of its kind and foundational for the field, established Vor as the pioneer in developing modified HSC therapies to enable targeted immunotherapy. Subsequent to this patent's initial filing, additional laboratories successfully replicated key aspects underlying the technology.

About VOR33

Vor's lead product candidate, VOR33, is designed to produce healthy blood cells that lack CD33, potentially protecting them from the toxic effects of CD33-targeted immunotherapies. CD33 is a myeloid lineage antigen that is present in the majority of acute myeloid leukaemias (AML) but is also expressed abundantly on normal myeloid cells. Depletion of normal myeloid progenitor cells during treatment for AML limits the dosage and duration of CD33-targeted therapies. By empowering CD33-targeted therapy, VOR33 has the potential to overcome current limitations.

About Vor Biopharma

Vor Biopharma is taking a fundamentally novel approach to treat cancer by developing engineered hematopoietic stem cells (HSCs). Vor's engineered HSCs are designed to generate healthy, functional blood cells that lack the binding site of lineage antigen-targeted therapies. Removal of the binding site protects these HSCs from depletion by lineage antigen-targeted immunotherapies.

Vor's platform is broad and could potentially be used to vastly improve the therapeutic window of several lineage antigen-targeted therapies, such as antibody drug conjugates (ADCs), bispecific antibodies, and chimeric antigen receptor T cells (CAR-Ts). This technology platform is covered by broad intellectual property exclusively licensed from Columbia University, as well as Vor-owned intellectual property. Co-founded by PureTech Health (LSE: PRTC) and Siddhartha Mukherjee, MD, DPhil, Vor is working with some of the world's leading oncologists and immunologists to develop a pipeline of potentially life-altering immunotherapies that extend beyond what is possible with current treatment.

About PureTech Health

PureTech Health (LSE: PRTC) is an advanced biopharmaceutical company developing BIG medicines for dysfunctions of the Brain-Immune-Gut axis. The Company has gained deep insights into the connection between these systems and the resulting role in diseases that have proven resistant to established therapeutic approaches. By harnessing this emerging field of human biology, PureTech Health is developing new categories of medicines with the potential to have great impact on people with serious diseases.

PureTech Health is advancing a rich pipeline of innovative therapies with an unbiased, non-binary, and capital efficient R&D model across its affiliates and its internal labs. PureTech's affiliates include seven clinical-stage platforms, including one product that has been cleared by the US Food and Drug Administration (FDA) and a second product candidate that has been filed with the FDA for review, and several other novel preclinical programmes. The PureTech Health pipeline includes ground-breaking platforms and therapeutic candidates that were developed in collaboration with some of the world's leading experts.

PureTech's internal research and development is centred on tissue-selective immunomodulation for the treatment of oncology, autoimmune, and CNS-related disorders, with a near-term focus on targeting newly-discovered, foundational immunosuppressive mechanisms in oncology and novel approaches that harness the lymphatic infrastructure.

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.