Vor Biopharma Announces Publication of Proof-of-Concept Study of its Lead Program 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 28, 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 leukemia (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, M.D., D.Phil, 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 tumor-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 leukemia 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 leukemias (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 aims to transform the lives of cancer patients by pioneering engineered hematopoietic stem cell (eHSC) therapies. Vor’s eHSCs are designed to generate healthy, fully functional cells with specific advantageous modifications, protecting healthy cells from the toxic effects of antigen-targeted therapies, while leaving tumor cells vulnerable.

Vor’s platform could potentially be used to change the treatment paradigm of both hematopoietic stem cell transplants and antigen-targeted therapies, such as antibody drug

conjugates, bispecific antibodies and CAR-T cell treatments. A proof-of-concept study for Vor's lead program has been published in *Proceedings of the National Academy of Sciences*.

Vor is based in Cambridge, Mass. and has a broad intellectual property base, including inlicenses from Columbia University, where foundational work was conducted by inventor and Vor Scientific Board Chair Siddhartha Mukherjee, MD, DPhil. Vor was founded by Dr. Mukherjee and PureTech Health and is supported by leading investors including 5AM Ventures and RA Capital Management, Johnson & Johnson Innovation — JJDC, Inc. (JJDC), Novartis Institutes for BioMedical Research and Osage University Partners.

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