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Issuer Free Writing Prospectus dated February 3, 2021
Relating to Preliminary Prospectus issued February 3, 2021
Registration No. 333-252175

This free writing prospectus relates to the initial public offering of shares of common stock of Vor Biopharma Inc. (the "Company"). On February 3, 2021, the Company filed with the U.S. Securities and Exchange Commission (the "SEC") Amendment No. 2 to its Registration Statement on Form S-1 (Registration No. 333-252175) relating to its initial public offering ("Amendment No. 2"). Amendment No. 2 updates and supplements certain information set forth in Amendment No. 1 to the Company's Registration Statement on Form S-1 filed with the SEC on February 1, 2021 ("Amendment No. 1"). Amendment No. 2 can be accessed through the following link:
https://www.sec.gov/Archives/edgar/data/1817229/000119312521026728/d942530ds1a.htm.

This free writing prospectus should be read together with Amendment No. 2 to the Registration Statement, including the preliminary prospectus contained therein, especially the "Risk Factors" section and the financial statements and related notes, before deciding to invest in these securities. Unless the context otherwise requires, the terms "we," "us" and "our" in this free writing prospectus refer to Vor Biopharma Inc.

Set forth below are the updates and supplements contained in Amendment No. 2 relative to Amendment No. 1.

Risk Factors (page 21)

We are substantially dependent on the success of our two most advanced product candidates, VOR33 and VCAR33. If we are unable to complete development of, obtain approval for and commercialize VOR33 or VCAR33 in a timely manner, our business will be harmed.

Our future success is dependent on our ability to timely advance and complete clinical trials, obtain marketing approval for and successfully commercialize our product candidates VOR33 and VCAR33. We are investing significant efforts and financial resources in the research and development of these product candidates. Our IND application for VOR33 in combination with Mylotarg in patients with AML was submitted to the FDA in December 2020 and took effect in January 2021, and we expect to initiate a Phase 1/2a clinical trial of VOR33 in the first half of 2021. VCAR33 is also undergoing a multi-site, investigator-initiated Phase 1/2 clinical trial in relapsed AML patients as a monotherapy in a bridge-to-transplant setting. The VCAR33 trial is currently sponsored and overseen by the National Marrow Donor Program (NMDP), however, we expect to either assume sponsorship and oversight of the trial prior to its completion or enter into an agreement with the NMDP providing us with the right to cross-reference the trial results in future IND applications that we may submit to the FDA. VOR33 and VCAR33 will each require additional clinical development, evaluation of clinical, preclinical and manufacturing activities, marketing approval from government regulators, substantial investment and significant marketing efforts before we can generate any revenues from product sales. We are not permitted to market or promote VOR33, VCAR33 or any other product candidate, before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of VOR33 and VCAR33 will depend on several factors, including the following:

- the acceptance by the FDA of our IND application to allow us to proceed with a clinical trial of VOR33 in combination with Mylotarg for the treatment of patients with AML who are at high risk for relapse;
- the acceptance of individual investigational review boards (IRBs) and scientific review committees at each clinical trial site as to the adequacy of the preclinical data package to support clinical development of VOR33 and their overall general agreement with the use of VOR33 in the intended patient population in the intended manner;
- the willingness of clinical investigators to place patients in the clinical trials, and the willingness of patients to enroll in a clinical trial studying a first-in-human cell therapy;
- the successful and timely completion of our planned Phase 1/2a clinical trial of VOR33 and the ongoing Phase 1/2 clinical trial of VCAR33;
- our ability to incorporate the results of the ongoing Phase 1/2 clinical trial of VCAR33 for the treatment of AML into future regulatory filings, either as a result of the timely transfer to us by the NMDP of the related IND or obtaining cross-reference rights to those trial results;
- the initiation and successful patient enrollment and completion of additional clinical trials of VOR33 and VCAR33 on a timely basis;
- maintaining and establishing relationships with contract research organizations (CROs) and clinical sites for the clinical development of VOR33 and VCAR33 both in the United States and internationally;
- the frequency and severity of adverse events in the clinical trials;
- the results of clinical trials conducted by third parties in hematopoietic stem cell transplant (HSCT) if such trials result in changes to the standard of care for HSCT or otherwise cause us to change our clinical trial protocols; for example, the National Heart, Lung, and Blood Institute (NHLBI), in collaboration with the Blood and Marrow Transplant Clinical Trials Network and the National Cancer Institute, is sponsoring a Phase 3 clinical trial of the use in HSCT of CD34 selected T cell depleted HSCs (CD34 HSCs), which are the same types of cells used in manufacturing VOR33, in patients with acute leukemia or myelodysplasia, and if the data from this trial suggests that these cells are inferior to the standard of care, our planned Phase 1/2a clinical trial of VOR33 could be significantly delayed;
- the efficacy, safety and tolerability profiles that are satisfactory to the FDA, EMA or any comparable foreign regulatory authority for marketing approval;
- the timely receipt of marketing approvals for VOR33 and VCAR33 from applicable regulatory authorities;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- the maintenance of existing or the establishment of new supply arrangements with third-party suppliers and manufacturers for clinical development of VOR33 and VCAR33;
- the maintenance of existing, or the establishment of new, scaled production arrangements with third-party manufacturers to obtain finished products that are appropriate for commercial sale of VOR33 and VCAR33, if either is approved;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- the protection of our rights in our intellectual property portfolio;

- the successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors;
- our ability to obtain coverage and adequate reimbursement from third-party payors for our products and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement; and
- our ability to compete with other treatments.

With respect to the NHLBI trial above, on February 2, 2021, we became aware of an abstract summarizing preliminary results of the trial, which are scheduled to be presented orally at a scientific conference on February 12, 2021. According to the abstract, the NHLBI trial did not observe a statistically significant difference between the CD34 HSC grafts and the bone marrow grafts that served as a comparison with respect to the primary endpoint of graft versus host disease (GVHD) (moderate/severe) relapse-free survival at 12 months. There was a statistically significantly lower incidence of chronic GVHD in the CD34 HSC arm of the trial. There was also a statistically significantly higher incidence of treatment related mortality (TRM) in the CD34 HSC arm, contributing to poorer overall survival compared to the bone marrow arms. Additional details about TRM in the trial were not disclosed in the abstract. Due to our current lack of additional information regarding the TRM observed in the trial, including the cause or causes, we are unable to evaluate the significance of these trial results for our own manufacturing process or clinical development plan for VOR33. If and as we learn more about the results of the NHLBI trial, we may decide that the manufacturing process or clinical trial protocol for VOR33 merit changes in response to this new information. Any amendments to our clinical trial protocol to accommodate these changes would introduce delays into our current clinical development timeline, including delays in initiating our first-in-human clinical trial of VOR33. Additional results from this third party trial may also result in enrollment delays.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize VOR33 and/or VCAR33, which would materially harm our business. If we do not receive marketing approvals for VOR33 and VCAR33 we may not be able to continue our operations.

Commencing clinical trials in the United States for VOR33 is subject to acceptance by the FDA of our IND for this program and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests, the start of our first clinical trial for VOR33 may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect.

Business (page 130)

One of the components of our current manufacturing protocol for VOR33 is the use of CD34-selected T cell-depleted HSCs (CD34 HSCs) as grafts in the HSCT process. The National Heart, Lung, and Blood Institute (NHLBI), in collaboration with the Blood and Marrow Transplant Clinical Trials Network and the National Cancer Institute, is currently sponsoring a Phase 3 clinical trial in patients with acute leukemia or myelodysplasia evaluating the use of CD34 HSC grafts in HSCT in comparison to bone marrow grafts. The trial included 104 patients in the CD34 HSC arm (of whom only 89 received per protocol therapy) and 232 patients in the bone marrow graft arms. The primary endpoint of the trial was chronic graft versus host disease (GVHD) (moderate/severe) relapse-free survival at 12 months, with secondary endpoints of overall survival, GVHD, relapse-free survival, relapse and transplant-related mortality (TRM), which is a general categorization of deaths related to the transplant that do not result from relapse. On February 2, 2021, we became aware of an abstract summarizing preliminary results of the NHLBI's trial, which are scheduled to be presented orally at a scientific conference on February 12, 2021. According to the abstract, the NHLBI trial did not observe a statistically significant difference between the CD34 HSC grafts and the bone marrow grafts with respect to the primary endpoint. There was a statistically significantly lower incidence of chronic GVHD in the CD34 HSC arm of the trial, indicating that grafts lacking in T cells were less likely to be associated with these negative immune reactions in transplant recipients. There was also a statistically significantly higher incidence of TRM in the CD34 HSC arm, contributing to poorer overall survival compared to the other arms. Additional details about TRM in the trial were not disclosed in the abstract. TRM can result from a number of different causes and TRM results in the trial could have been confounded by a variety of factors, including the use of different donor sources, conditioning regimens and the original treated disease, as well as non-compliance within each arm with respect to donor collection. Due to our current lack of additional information regarding the TRM observed in the trial, including the cause or causes, we are unable to evaluate the significance of these trial results for our own clinical development plan for VOR33. If and as we learn more about the results of the NHLBI trial, we may decide that the clinical trial protocol or manufacturing process for VOR33 merit changes in response to this new information. Any amendments to our manufacturing process or clinical trial protocol to accommodate these changes would introduce delays into our current clinical development timeline, including delays in initiating our first-in-human clinical trial of VOR33. Additional results from this third party trial may also result in enrollment delays. We do not believe the results of the NHLBI trial undermine the fundamental scientific premise of VOR33 nor do we believe these results adversely impact the overall viability of the VOR33 program.