Vivoryon Therapeutics N.V. Reports Positive Outcome from Independent Data Safety Monitoring Board with Unanimous Decision for VIVA-MIND U.S. Study of Varoglutamstat in Alzheimer's Disease to Proceed at Highest Investigated Dose

- *Interim analysis completed, with 600mg twice daily dosing unanimously selected by independent DSMB as final dose for remainder of Phases 2a and 2b of VIVA-MIND study in U.S.*
- *Decision follows 2022 DSMB determination for VIVIAD Phase 2 EU study to proceed at 600mg twice daily based on safety and tolerability of 90 patients followed for at least 24 weeks post randomization*

Halle (Saale) / Munich, Germany, October 23, 2023 – Vivoryon Therapeutics N.V. (Euronext Amsterdam: VVY; NL00150002Q7) (**Vivoryon**), a clinical stage company focused on the discovery and development of small molecule medicines to modulate the activity and stability of pathologically altered proteins, today announced that the study's independent data safety monitoring board (DSMB) unanimously recommend that the VIVA-MIND study of varoglutamstat should proceed with a dose of 600mg twice daily (BID) through the remainder of Phases 2a and 2b.

VIVA-MIND (NCT03919162) is an ongoing Phase 2 study for varoglutamstat conducted in the U.S., complementary to Vivoryon's VIVIAD Phase 2b study being conducted in Europe. VIVA-MIND seeks to enroll 180 patients with early Alzheimer's disease (AD) into the Phase 2a adaptive dose finding portion and enroll a further 234 patients in the Phase 2b portion of the study. In July 2023, the Company announced that the first cohort of the study was fully randomized as planned and is now recruiting participants into the second cohort with 21 sites open across the U.S. The primary endpoint of the study is evaluating Clinical Dementia Rating scale Sum of Boxes (CDR-SB) over a 72-week treatment period.

"We are thrilled to report this new important and validating element of our rigorously and meticulously designed program for varoglutamstat. While all prior DSMB decisions have been favorable, we believe that this marks a critical next step on our path towards consciously determining the optimal dosing regimen for varoglutamstat. From the initial stages of determining the maximum tolerated dose in our completed SAPHIR Phase 2a study, through the extremely encouraging interim analyses of tolerability in our European VIVIAD Phase 2b study, we keep making key steps towards optimizing safety. At the same time, we are striving to ensure we can maintain high levels of target occupancy to maximize our probability of success in improving not only memory, but many other important elements of cognition in those suffering from mild cognitive impairment and early AD," said Frank Weber, M.D., CEO

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of Vivoryon. “We have designed two complimentary studies intended to support the efficient advancement of varoglutamstat towards regulatory approval. At our recent R&D Event, multiple perspectives from renowned Key Opinion Leaders further elucidated the solid base of understanding for the potential of varoglutamstat to treat early AD patients, in particular the endpoints in VIVIAD and VIVA-MIND, which we are confident will provide a deep understanding of varoglutamstat’s effect on relevant cognitive outcome parameters and patient function in separate sensitive and validated scales. Taken together, we believe that our unique approach has the potential to dramatically improve the lives of millions of people whose daily lives are impacted by AD.“

“I am very pleased to have received the unanimous recommendation of the independent DSMB of the VIVA-MIND trial to continue the highest investigated dose arm of 600mg BID for the remainder of the study. Importantly, the trial has now passed the milestone of an interim evaluation of a predetermined safety boundary of specified adverse events,” commented Dr. Howard Feldman, Professor of Neurosciences, Co-Director of The Alzheimer's Disease Cooperative Study (ADCS) at the University of California San Diego School of Medicine, and the VIVA-MIND Principal Investigator. “As varoglutamstat progresses further through its Phase 2a/b design, we will continue to gather further safety and tolerability data, of this oral treatment and its profile which may differentiate from anti-amyloid-antibodies which are delivered by infusion.“

The DSMB’s dose decision recommending that the highest dose of varoglutamstat of 600mg BID be selected for the remainder of the trial follows its September 18, 2023 quarterly safety review of adverse events, and labs, and its October 19, 2023 analysis of treatment-emergent adverse events of special interest (AESI) pertaining to skin and subcutaneous tissue disorders and hepatobiliary disorders, as well as target occupancy and plasma pharmacokinetic (PK) data.

In July 2023, Vivoryon announced that it commenced preparations for an open-label extension (OLE) study to provide a long-term treatment option to patients after completion of treatment under the VIVIAD or VIVA-MIND protocol. The launch of the OLE study is contingent on the outcome of VIVIAD. Vivoryon remains on track to report the final data readout from the VIVIAD study in the first quarter of 2024.

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About VIVA-MIND

VIVA-MIND is a complementary Phase 2 study being conducted in the U.S., coordinated by the Alzheimer's Disease Cooperative Study (ADCS) at the University of California San Diego (UCSD) School of Medicine and supported by the National Institute on Aging (NIA), part of the National Institutes of Health (NIH) with a $15 million grant (NIA award number R01AG061146). The study seeks to enroll 180 patients into the Phase 2a adaptive dose-finding portion with the Phase 2b portion, enrolling an additional 234 patients treated at the selected dose for at least 72 weeks, with a total of 414 patients being treated on stable doses of

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varoglutamstat for 18 months. The VIVA-MIND design was adapted in 2022 to enable all 180 patients in the Phase 2a portion to be treated for at least 72 weeks, allowing for the opportunity to progress seamlessly to a potential Phase 3 study. The flexible study design is aimed at increasing the probability of success by broadening option space for adjustments in clinical development based on learnings from VIVIAD and other developments in the field. The primary endpoint for this study is clinical dementia rating scale - sum of boxes (CDR-SB), an established approvable endpoint measuring a combination of cognitive abilities and activities of daily living. Secondary efficacy endpoints include quantitative EEG theta power, ADAS-Cog 13 and others. Exploratory endpoints include mini-mental state examination (MMSE), Montreal cognitive assessment (MoCA), quantitative EEG alpha power, relative QPCT activity in CSF and others.

About Vivoryon Therapeutics N.V.

Vivoryon is a clinical stage biotechnology company focused on developing innovative small molecule-based medicines. Driven by our passion for ground-breaking science and innovation, we strive to change the lives of patients in need suffering from severe diseases. We leverage our in-depth expertise in understanding post-translational modifications to develop medicines that modulate the activity and stability of proteins which are altered in disease settings. Beyond our lead program, varoglutamstat, which is in Phase 2 clinical development to treat Alzheimer's disease, we have established a solid pipeline of orally available small molecule inhibitors for various indications including cancer, inflammatory diseases and fibrosis. www.vivoryon.com

Vivoryon Forward Looking Statements

This press release includes forward-looking statements, including, without limitation, those regarding the business strategy, management plans and objectives for future operations of the Vivoryon Therapeutics N.V. (the "Company"), estimates and projections with respect to the market for the Company's products and forecasts and statements as to when the Company's products may be available. Words such as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "predict," "should" and "will" and similar expressions as they relate to the Company are intended to identify such forward-looking statements. These forward-looking statements are not guarantees of future performance; rather they are based on the Management's current expectations and assumptions about future events and trends, the economy and other future conditions. The forward-looking statements involve a number of known and unknown risks and uncertainties. These risks and uncertainties and other factors could materially adversely affect the outcome and financial effects of the plans and events described herein. Actual results, performance or events may differ materially from those expressed or implied in such forward-looking statements and from expectations. As a result, no undue reliance should be placed on such forward-looking statements. This press release does not contain risk factors. Certain risk factors that may affect the Company's future financial results are discussed in the published annual financial statements of the Company. This press release, including any forward-looking statements, speaks only as of the date of this press

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release. The Company does not assume any obligation to update any information or forward-looking statements contained herein, save for any information required to be disclosed by law.

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