Vivoryon Therapeutics N.V. Presents Topline Phase 2 Data from VIVA-MIND Strongly Supporting Varoglutamstat's Potential to Improve Kidney Function

- *VIVA-MIND Phase 2 data confirm results of varoglutamstat's benefit on eGFR in VIVIAD; Company now has two independent double-blind placebo-controlled Phase 2 studies demonstrating a clinically meaningful treatment effect on kidney function*
- *Topline analysis of kidney function data in VIVA-MIND shows a statistically significant and clinically meaningful improvement of eGFR; average improvement of >4mL/min/1.73m^2 with varoglutamstat versus placebo across all visits (weeks 4–72) and all patients (p=0.004*)*
- *VIVA-MIND, a Phase 2 study in early Alzheimer's disease (AD), was discontinued early and did not meet its primary and key secondary endpoints in early AD, in line with the previously reported results from VIVIAD*
- *Varoglutamstat continues to demonstrate a favorable safety and tolerability profile in VIVA-MIND with no new safety signals detected and a total of over 400 participants treated with varoglutamstat in Phase 1 and Phase 2 studies to date*
- *Further detail on the topline results from VIVA-MIND to be shared in the Company's Q3 financial results webcast to be held on December 10, 2024, at 3:00 pm CET*

Halle (Saale) / Munich, Germany, December 9, 2024 – 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 positive Phase 2 topline data from its U.S. VIVA-MIND study of varoglutamstat (PQ912), an investigational oral glutaminyl cyclase (QPCT/L) inhibitor, in early AD. Analysis of kidney function data revealed a statistically significant improvement of >4mL/min/1.73m^2 in the estimated glomerular filtration rate (eGFR) in patients treated with varoglutamstat 600mg BID versus placebo across all visits and all patients (weighted average weeks 4-72; p=0.004*; total treated n=109; varoglutamstat n=52, placebo n=57). Analysis of eGFR was prospectively defined as a safety parameter in VIVA-MIND. These data reinforce the previously reported beneficial effect of varoglutamstat on eGFR in the completed Phase 2b VIVIAD study and support the Company's development strategy to advance into a Phase 2 study in diabetic kidney disease (DKD)[1].

"In clinical development it is highly relevant to replicate results in two independent high-quality studies. The topline VIVA-MIND data showed a consistent, statistically significant and clinically meaningful improvement of kidney function, as measured by eGFR, in patients treated with varoglutamstat versus placebo and clearly corroborate previously reported results from VIVIAD," said Frank Weber, M.D., CEO of Vivoryon.

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Analysis of VIVA-MIND data in AD showed no clinically meaningful and no statistically significant differences between varoglutamstat 600mg BID and placebo for the primary endpoint of CDR-SB, and key secondary endpoints including CFC2, ADAS-Cog 13, in patients treated with varoglutamstat compared to placebo, in line with the previously reported results in AD from VIVIAD.

Frank Weber continued, "As for the results in AD, these confirm the data seen in VIVIAD and are therefore not unexpected. While we would have wished for a different outcome of this study, we would like to thank all patients, their families and caregivers, the Alzheimer's Disease Cooperative Study (ADCS) at the University of California San Diego School of Medicine and clinical study investigators as well as the U.S. National Institutes of Health – enabling the VIVA-MIND study through a grant – for their commitment to the study and the varoglutamstat program."

VIVA-MIND met its safety endpoints with varoglutamstat being generally well tolerated with no new safety signals observed at the 600mg BID dose.

All topline VIVA-MIND results are preliminary and may be subject to change based on additional analysis and quality checks, however, the overall interpretation of the results is not expected to change significantly.

The Company will provide further detail on the topline VIVA-MIND data on December 10, 2024, in its Q3 financial results webcast.

Q3 Financial Results Conference Call and Webcast
Vivoryon will host a conference call and webcast on December 10, 2024, at 3:00 pm CET (9:00 am ET). A Q&A session will follow the presentation of the third quarter 2024 results and operational progress updates.
A live webcast and slides will be made available at: https://www.vivoryon.com/news-and-events/presentations-webcasts/

To join the conference call via phone, participants may pre-register and will receive dedicated dial-in details to easily and quickly access the call via the following website: https://register.vevent.com/register/BIf0be17873ad0409b83edd4eedbe3b7ac

It is suggested participants dial into the conference call 15 minutes prior to the scheduled start time to avoid any delays in attendance.

Approximately one day after the call, a slide-synchronized audio replay of the conference will be available on: https://www.vivoryon.com/news-and-events/presentations-webcasts/

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Definitions and notes: [1]The timing and execution of the planned Phase 2 study is subject to additional funding / partnership. CDR-SB: Clinical Dementia Rating Sum of Boxes; CFC2: Cognitive-Functional Composite 2, ADAS-Cog-13: Alzheimer's Disease Assessment Scale cognitive subscale.
* Corrected from the previously reported p<0.001

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About VIVA-MIND

VIVA-MIND is a Phase 2 study that was 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 originally sought to enroll 180 patients into the Phase 2a adaptive dose-finding portion and an additional 234 patients into the Phase 2b portion, with a total of 414 patients being treated on stable doses of varoglutamstat for 18 months. Based on the negative outcome reported from Vivoryon's VIVIAD study, which had also investigated the dose of 600mg varoglutamstat BID in a similar patient population in early AD, VIVA-MIND was discontinued early to enable accelerated data analysis and inform the overall varoglutamstat development strategy. Due to this change, the VIVA-MIND study only recruited a smaller number of patients (112 randomized and 109 treated) into Phase 2a and did not move into Phase 2b.

Varoglutamstat in Kidney Disease

Varoglutamstat (PQ912) is a proprietary, potent and selective inhibitor of human glutaminyl cyclases QPCT and QPCTL with therapeutic potential in indications including inflammatory and fibrotic diseases, neurodegenerative diseases, cancer and others. Initially advancing development aiming to treat Alzheimer's disease (AD), varoglutamstat has been investigated in a number of different clinical studies, all of which have consistently demonstrated a favorable safety and tolerability profile both in healthy volunteers and patients with AD. Based on the known anti-inflammatory activity of varoglutamstat, the protocol for the Phase 2 VIVIAD study in AD, which was completed in the first half of 2024, included the investigation of kidney function and measurement of biomarkers of kidney inflammation and fibrosis to explore the role of QPCT/L inhibition on kidney function. Although patients in VIVIAD were selected for their AD status and not for their kidney function level, many of them had reduced kidney function due to age and/or comorbidities. Analysis showed a statistically significant benefit of varoglutamstat on a prospectively defined key kidney function endpoint (eGFR) and a significant reduction of the pro-inflammatory cytokine pE-CCL2. A substantially higher treatment benefit of varoglutamstat on eGFR was observed in a post-hoc diabetes subgroup, triggering plans to advance varoglutamstat into Phase 2 study in DKD, which is currently in planning.

About Vivoryon Therapeutics N.V.

Vivoryon is a clinical stage biotechnology company focused on developing innovative small molecule-based medicines. Driven by its passion for ground-breaking science and innovation,

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the Company strives to change the lives of patients in need suffering from severe diseases. The Company leverages its 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. The Company has established a pipeline of orally available small molecule inhibitors for various indications including Alzheimer's disease, inflammatory and fibrotic disorders, including of the kidney, and cancer. 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 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. The Company's results of operations, cash needs, financial condition, liquidity, prospects, future transactions, strategies 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 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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