Vivoryon Therapeutics N.V. Provides Update on VIVIAD Phase 2b Study of Varoglutamstat in Early Alzheimer's Disease

- *VIVIAD Phase 2b study did not meet its primary and key secondary endpoints*
- *Varoglutamstat was generally well tolerated with low discontinuation rates due to adverse events and no evidence of symptomatic ARIAs in the clinical setting*
- *VIVIAD is a comprehensive, diligently designed and high-quality study; baseline demographics in the study were highly representative of early AD patient population*
- *Company is conducting an in-depth analysis of the results, including analyses of additional pre-specified and exploratory endpoints*
- *Further update expected to be provided no later than with publication of Company's full year 2023 financial results*

Halle (Saale) / Munich, Germany, March 4, 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 topline results from its Phase 2b European VIVIAD study of varoglutamstat (PQ912), an investigational oral glutaminyl cyclase (QPCT) inhibitor in development for the treatment of early Alzheimer's disease (AD). The VIVIAD study did not meet its primary endpoint and did not show a statistically significant difference in change over time on cognition, as measured by a combined score (Z-score) of the Detection test, the Identification test and the 'One Back' test (attention and working memory domains) of the Cogstate neuropsychological test battery (NTB), called "Cogstate 3-item scale". Additionally, the study did not meet key secondary endpoints measuring cognition (Cogstate Brief Battery, CBB, and complete Cogstate NTB), Instrumental Activities of Daily Living Questionnaire (A-IADL-Q) and electroencephalogram (EEG) global theta power. Varoglutamstat was generally well tolerated and showed rates similar to placebo of serious and severe treatment emergent adverse events (TEAEs), low discontinuation rates due to adverse events and no evidence of symptomatic ARIAs (amyloid-related imaging abnormalities) in the clinical setting.

The Company is conducting an in-depth analysis of the results, including analyses of additional pre-specified exploratory endpoints (e.g. WAIS-IV coding test, executive function and episodic memory domains, Winterlight Labs speech assessment, cerebrospinal fluid (CSF) biomarkers and additional EEG analysis) and distinct patient cohorts as defined in the statistical analysis plan, including ApoE4 status, tau level, dose level and pre-treatment.

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"We are profoundly disappointed by the outcome of the VIVIAD Phase 2b study of varoglutamstat in the early AD patient population given the huge unmet need for new safe and effective oral therapies," said Frank Weber, M.D., CEO of Vivoryon. "I would like to express our gratitude to the patients, their families and caregivers, as well as the investigators for participating in the VIVIAD study, and to our incredible team at Vivoryon for their tireless efforts. While these results are not what we had hoped for, VIVIAD is a comprehensive, diligently designed and high-quality study and we are doing all we can to fully analyze the dataset as quickly as possible to gain insights into key findings that might influence varoglutamstat clinical development and help advance the science and understanding of this devastating disease."

A further update is expected to be provided no later than with the publication of the Company's full year 2023 financial results which are expected in mid to late April 2024.

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About Varoglutamstat

Varoglutamstat (PQ912) is a differentiated oral small-molecule targeting the toxic Abeta species N3pE which is being developed as disease-modifying therapy and is designed to target AD pathology upstream of Abeta-antibody focused approaches. Varoglutamstat blocks the enzyme glutaminyl cyclase (QPCT) and its isoenzyme QPCTL. QPCT catalyzes the formation of N3pE amyloid, a particularly neurotoxic variant of Abeta peptides, which is only found in patients with AD and not present in the brains of healthy individuals. N3pE amyloid in the brain acts as a seeding element for Abeta aggregation, thus providing a starting point for plaque formation. It has been described to correlate with the cognitive ability of patients with AD. Beyond Abeta pathology, varoglutamstat has also been shown to impact synaptic impairment. Through a second mode of action, the inhibition of full CCL2 maturation via QPCTL, varoglutamstat modulates pro-inflammatory signaling and tau pathology, thereby simultaneously addressing multiple hallmarks of AD. Vivoryon has received Fast Track designation for varoglutamstat in early AD by the U.S. Food and Drug Administration (FDA). It is being investigated in two Phase 2 clinical studies, one in Europe (VIVIAD, NCT04498650) and one in the U.S. (VIVA-MIND, NCT03919162). Varoglutamstat has not yet been approved by any regulatory authority and the safety and efficacy have not yet been established.

About VIVIAD

VIVIAD is a state-of-the-art Phase 2b study conducted in Europe and designed to evaluate the safety, tolerability, and efficacy of varoglutamstat in 259 participants with mild cognitive impairment (MCI) and mild AD (collectively referred to as "early AD"). The primary endpoint is the change over time on working memory and attention as measured by a combined score (Z-score) of the Detection test, the Identification test and the 'One Back' test (attention and working memory domains) of the Cogstate neuropsychological test battery (NTB), called "Cogstate 3-item scale". Key secondary efficacy endpoints include in hierarchical order:

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Cogstate Brief Battery (CBB, 4-item scale), the complete Cogstate NTB (8-item scale), the Amsterdam Instrumental Activities of Daily Living Questionnaire (A-IADL-Q), and electroencephalogram (EEG) global theta power.

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 as well as on evaluations made by the Company of estimates, projections and other statistical data made by independent third parties. 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 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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