Vivoryon Therapeutics N.V. Shares Highlights from Virtual R&D Event with Key Opinion Leaders

- *Multiple KOLs highlight varoglutamstat pathology, clinical development and clinical applicability of key endpoints in VIVIAD study*
- *VIVIAD progressing as planned with final results expected Q1/2024*

Halle (Saale) / Munich, Germany, October 17, 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 key takeaways from its virtual R&D Event with Key Opinion Leaders (KOLs), focusing on the Company's lead program, varoglutamstat, and VIVIAD, a state-of-the-art Phase 2b study being conducted in Europe and designed to evaluate its safety, tolerability, and efficacy in 259 (final number of randomized participants) subjects with mild cognitive impairment (MCI) and mild Alzheimer's disease (AD).

The event, which was moderated by Philip Scheltens, M.D., Ph.D., EQT Life Sciences Dementia Fund, featured presentations from Stephan Schilling, Ph.D., Fraunhofer Institute for Cell Therapy and Immunology, John Harrison, Ph.D., Scottish Brain Sciences, Sietske Sikkes, Ph.D., Alzheimer Center at Amsterdam UMC, Willem de Haan, M.D., Ph.D., Alzheimer Center at Amsterdam UMC, and Vivoryon Chief Executive Officer (CEO), Frank Weber, M.D.

"We are pleased to have hosted so many renowned KOLs as we discussed multiple important facets of varoglutamstat's clinical development, its pathology and the clinical utility of primary and secondary endpoints of the VIVIAD study. We have taken a meticulous and well thought out approach to the VIVIAD trial design and believe that the primary endpoint, Cogstate NTB (neurological test battery), represents the top standard in assessing cognition," said Frank Weber, M.D., CEO of Vivoryon. "While significant advancements have been made for AD patients, we believe that varoglutamstat has the potential to address vast unmet need by providing patients with an easy to administer, oral small molecule. We look forward to the final readout of VIVIAD in the first quarter of next year."

Highlights from Dr. Schilling's presentation include:

- Pyroglutamate-modified Abeta (N3pE-Abeta) is a trigger of toxicity in AD and there is a strong rationale for targeting N3pE-Abeta to create a tailored AD therapy.
- Experimental data show that N3pE-Abeta has very different physio-chemical properties compared to other Abeta variants, including its potential to form highly toxic oligomers and fibrils together with non-modified Abeta variants.

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- Strong pre-clinical evidence supports the hypothesis that reducing N3pE-Abeta formation by inhibiting the enzyme QPCT, has the potential to change the course of progression of AD.

Highlights from Dr. Harrison's presentation include:

- AD is a disorder of cognition, not just memory and MCI and early AD are characterized by a variety of cognitive deficits.
- The Cogstate NTB, which is used to assess the effect of varoglutamstat on cognition in the primary and secondary endpoints in the VIVIAD study, is a sensitive and well-established scale in the field of AD research. It has the advantage of investigating a broad range of cognitive domains acknowledged to be clinically meaningful measures of function.
- A preliminary blinded data analysis (cut-off May 2023) conducted for the Data Safety Monitoring Board (DSMB) showed that the trajectory of the Cogstate Brief Battery (CBB, which includes Identification, Detection, One Back, and One Card Learning of the NTB) in VIVIAD displayed a ~28% change from baseline (n= >250 patients) compared to the end of treatment (week 96 or early discontinuation of treatment; n=36 patients at data cut-off).
- Within this preliminary blinded analysis, the four individual test components of the CBB (Identification, Detection, One Back, One Card Learning) displayed declines that varied in trajectories, supporting the concept that patients with early AD have variable progression rates for individual memory functions. While these preliminary data support the selection of the Cogstate NTB as primary and key secondary endpoints in VIVIAD to assess the effect of varoglutamstat on cognition, it is important to note that no assessment of the efficacy of varoglutamstat can be derived from this preliminary and blinded dataset.

Highlights from Dr. Sikkes' presentation include:

- The Amsterdam IADL Questionnaire (A-IADL-Q) is applied in the VIVIAD study as a key secondary endpoint to assess the effect of varoglutamstat on the instrumental activities of daily living.
- The scale has been specifically developed and validated for patients with AD and incorporates the input of caregivers and clinicians, supporting its clinical meaningfulness.
- The A-IADL-Q is validated across several cultures, including the U.S. as well as the Western European countries in which the VIVIAD study is conducted.
- The A-IADL-Q contains relevant activities that matter to patients, caregivers and health care professionals.
- The high psychometric quality, i.e. reliability and validity, support its use as an outcome measure in treatment evaluation studies and for use in clinical practice.

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Highlights from Dr. de Haan's presentation include:

- EEG is a relatively direct, large-scale tool to capture neuronal and synaptic function. Normalization of EEG parameters (theta power, connectivity) is presumed to be beneficial for brain function in AD.
- The SAPHIR Phase 2a study of varoglutamstat has shown an improvement of theta power and connectivity.
- Based on the results in the SAPHIR study in early AD patients, theta power has been selected as a key secondary endpoint in the VIVIAD study. Other oscillatory, connectivity and network analysis will be conducted as exploratory analysis in the VIVIAD trial.

Highlights from Dr. Weber's presentation include:

- An overview of varoglutamstat's clinical development was provided, including a thorough discussion of study design and expectations for the first quarter 2024 data readout.
- In 2022, the DSMB decided that the VIVIAD study should be continued with the 600mg twice daily dose based on an analysis of safety and tolerability of 90 patients randomized 1:1:1 between placebo, 300mg and 600mg varoglutamstat twice daily and followed for at least 24 weeks post randomization.
- Vivoryon expects the final VIVIAD dataset to include an evaluation of patients following the 12-week titration period, which is the same for every patient randomized to the active arm. The 600mg twice daily dose is applied in approximately 75% of the treatment weeks of all patients and the 300mg twice daily dose is applied in approximately 25% of the treatment weeks.
- The study protocol defines a duration of treatment of 48 weeks minimum and 96 weeks maximum per patient dependent on when the patient was randomized into the study.
- A preliminary analysis of the blinded data shows that the expected average treatment duration in the VIVIAD study is more than 80 weeks with more than 60% of patients treated for 84 and 96 weeks, approximately 30% for 60 and 72 weeks, and less than 10% for 48 weeks.
- All data presented to-date are blinded and preliminary with the study still ongoing.

A Webcast of the virtual R&D Event will be available via the "Presentations & Webcasts" page in the Investor Relations section on the Company's website at www.vivoryon.com.

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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

Varoglutamstat Disclaimer for R&D Event

Varoglutamstat is not an approved medicine, the product is under development for the treatment of early AD. All data presented on the VIVIAD study to date are blinded and preliminary, the study is still ongoing with final readout expected in the first quarter of 2024. The data from the VIVIAD study presented to date shall not and cannot be interpreted in respect to whether varoglutamstat is safe or effective. The data from the VIVIAD study presented to date shall not and cannot be interpreted with respect to the final results and the outcome of the VIVIAD study.

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 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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