Vivoryon Therapeutics N.V. Provides R&D-Update Further Strengthening Development Pipeline in Kidney Disease

- *A meta-analysis of VIVIAD and VIVA-MIND[1] data confirmed that treatment with varoglutamstat at 600mg twice daily significantly improved eGFR[2] kidney function in the overall study population*
- *The meta-analysis also confirmed a substantially larger effect size in study participants with diabetes[3] compared to those without diabetes*
- *Vivoryon further strengthened its patent portfolio for varoglutamstat in kidney disease, including patent filings on medical use, dosing and a new composition of matter patent on the active polymorph*
- *A novel, next-generation QPCT/L inhibitor candidate with compelling pharmacological activity was nominated for development in inflammatory and fibrotic diseases, including potentially in DKD/CKD and orphan diseases*

Halle (Saale) / Munich, Germany, January 14, 2025 - 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 provided an update on the Company's progress of varoglutamstat development in kidney disease and efforts to solidify its QPCT/L inhibitor pipeline in inflammatory and fibrotic diseases.

"Vivoryon has thoroughly analyzed kidney function data of the two independent Phase 2 studies VIVIAD and VIVA-MIND. The results were highly consistent between the two studies which were carried out in different regions (EU vs U.S.) and with different CROs and laboratories. In both studies, a significant improvement in kidney function measured by eGFR was demonstrated in the overall population and, also in both studies, patients with diabetes displayed a substantially larger effect size than patients without diabetes. These findings were confirmed by a recently completed meta-analysis," said Frank Weber, MD, CEO of Vivoryon. "We also enhanced the value of our development pipeline by adding three new patent filings to our patent portfolio, including a composition of matter patent of the active polymorph for varoglutamstat, as well as by identifying and nominating a novel and potent QPCT/L inhibitor for development in inflammatory and fibrotic diseases. Vivoryon is developing a highly innovative, focused portfolio of QPTC/L inhibitors grounded in the proof that QPCT/L inhibition leads to reduction in the activity of potent pro-inflammatory and fibrotic peptides."

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VIVIAD and VIVA-MIND: Meta-analysis All Patients

- A total of 286 patients were randomized into the 600mg twice daily (BID) varoglutamstat and placebo groups in VIVIAD and VIVA-MIND studies, with 112 allocated to 600mg BID varoglutamstat and 174 to placebo.
- Meta-analysis of VIVIAD and VIVA-MIND data confirmed that treatment with varoglutamstat at 600mg BID significantly improved kidney function as measured by eGFR (estimated glomerular filtration rate) in the overall population.
- The difference of change from baseline in eGFR between varoglutamstat and placebo became significant starting after 24 weeks of treatment and the treatment effect was maintained throughout the study duration up to 2 years (96 weeks).

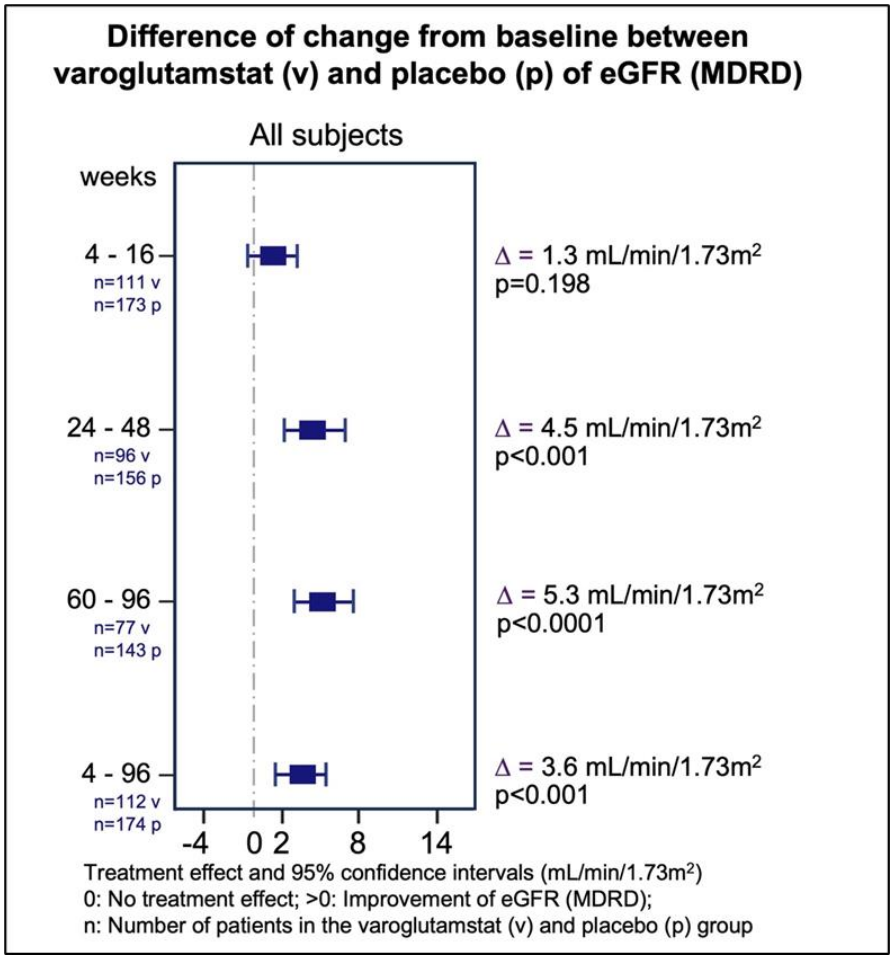

Figure 1

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VIVIAD and VIVA-MIND Meta-analysis: Stratification in Patients with Diabetes and without Diabetes

- A total of 39 patients with diabetes were randomized into the 600mg BID varoglutamstat (n=19) and placebo (n=20) groups in total (VIVIAD n=23, VIVA-MIND n=16).
- The corresponding numbers for study participants without diabetes were 93 patients randomized to varoglutamstat 600mg BID and 154 patients randomized to placebo (total n=247).
- The effect size is substantially larger in patients with diabetes compared to patients without diabetes, starting 24 weeks after initiation of treatment and sustained until the end of treatment.
- The results were consistent between VIVIAD and VIVA-MIND.
- A positive and statistically significant treatment effect was also observed in patients without diabetes.

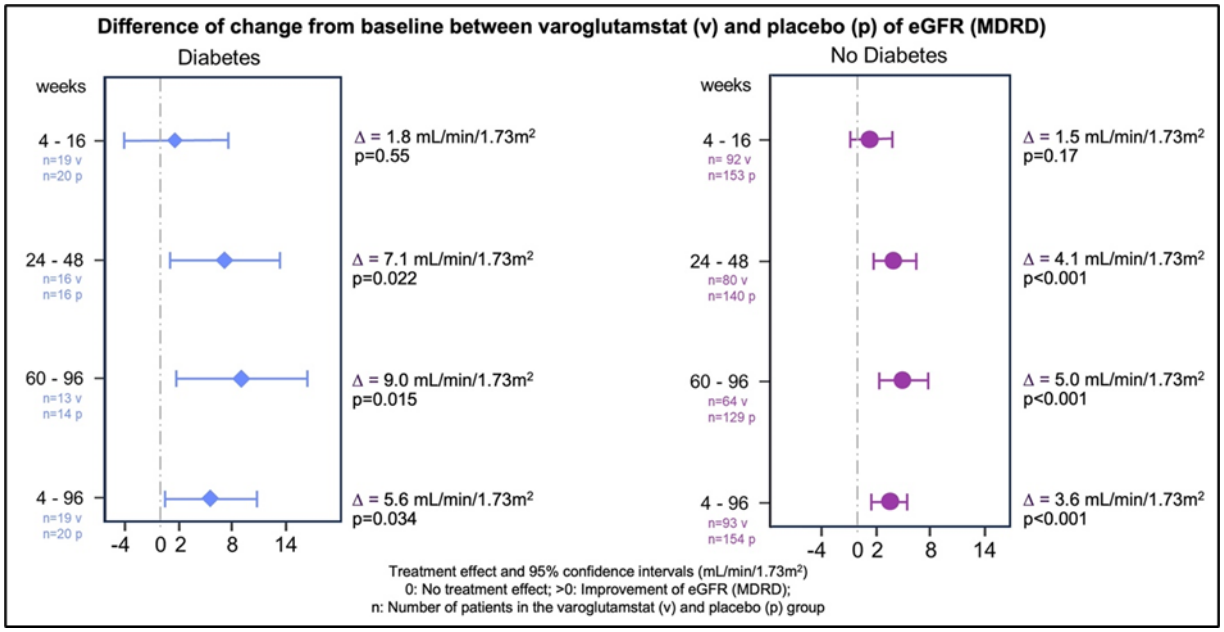

Figure 2

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Key Strategic Priority for 2025: Focus on Planned Study in Diabetic Kidney Disease (DKD)

Vivoryon's key strategic priority for 2025 is to advance varoglutamstat in kidney disease and confirm the previously reported compelling data from two independent Phase 2 studies, VIVIAD and VIVA-MIND, by conducting a Phase 2b clinical study in patients with advanced diabetic kidney disease (DKD). The proposed study is expected to include up to 120 subjects with stage 3b/4 DKD, randomized 1:1 to varoglutamstat 600mg orally twice daily or placebo, on top of standard of care medications. Intended endpoints include eGFR slope analysis, measures of albuminuria (UA(p)CR), inflammation and fibrosis-related biomarkers, as well as safety. Exploring the potential of varoglutamstat in rare kidney diseases, depending on additional non-clinical data, the Company intends to initiate a small proof of concept study of varoglutamstat in orphan kidney disorders. Initiation of all future studies is subject to additional funding and/or partnership, which Vivoryon will continue to actively explore.

Strengthened Varoglutamstat Patent Portfolio in Kidney Disease

Vivoryon has a strong patent portfolio for QPTC/L inhibition. As of December 31, 2024, Vivoryon's patent portfolio consisted of 20 owned patent families, which comprise approximately 402 national patent applications and issued patents. In 2024, the Company further strengthened the patent portfolio with regard to its frontrunner molecule varoglutamstat (PQ912) and applications in kidney diseases. These activities included patent filings on (1) medical use in kidney diseases, (2) dosing and (3) a new composition of matter patent on the active polymorph form for PQ912, which, if granted, would extend the natural patent runtime for PQ912 to 2044. This patent was filed in mid-2023 and prioritized examination for this composition of matter patent has been initiated. The examination process and potential granting should be expected within 12 months.

Novel Candidate for Development in Inflammatory and Fibrotic Diseases

The Company has enlarged its portfolio by nominating a novel, next generation QPCT/L inhibitor showing compelling pharmacological activity. This candidate, VY2149, is a potential fast follower in DKD or could also be explored for other inflammatory and fibrotic diseases including orphan diseases and chronic kidney disease (CKD). VY2149 is expected to enter formal, late-stage preclinical development within this year, subject to additional funding and/or partnership, which Vivoryon will continue to actively explore.

Upcoming Investor Meetings

The Company will be hosting investor meetings January 14/15, 2025 around the J. P. Morgan conference in San Francisco, at which these updates will be shared. You can find a copy of the presentation that will be used in the investor meetings, including updated data from the

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VIVIAD/VIVA-MIND meta-analysis in the Investor section on the Company's website at https://www.vivoryon.com/news-and-events/presentations-webcasts/.

Definitions and notes:

[1] VIVIAD and VIVA-MIND Phase 2 studies in early Alzheimer's disease (AD) included prospectively defined measures of kidney function as safety and other exploratory endpoints, the primary and secondary endpoints in early AD were not met

[2] eGFR: estimated glomerular filtration rate, a validated measure of kidney function

[3] Defined as patients having at baseline either medical history of diabetes (type 1 or 2) and/or comedication with drugs used in diabetes and/or untreated with an HbA1c > 6.5%

Figures: MDRD method: modification of diet in renal disease method

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About Varoglutamstat

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 advanced development aiming to treat Alzheimer's disease (AD), varoglutamstat has been investigated in a number of different clinical studies. Based on the known anti-inflammatory and anti-fibrotic activity of varoglutamstat, the protocol for the Phase 2b VIVIAD study in early AD included the investigation of kidney function (measured using eGFR) and measurement of biomarkers of kidney inflammation and fibrosis to explore the role of QPCT/L inhibition on kidney function. eGFR was also analyzed as a prospectively defined safety parameter in the VIVA-MIND Phase 2 study in the U.S.

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, 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,"

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"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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