Vivoryon Therapeutics N.V. Presents Outstanding Phase 2b Results of Varoglutamstat on Kidney Function at ASN Kidney Week 2024

- *Selected for late-breaking oral presentation at ASN kidney week, the world's premier nephrology meeting*
- *Results presented show a statistically significant and clinically meaningful improvement of the prospectively defined kidney function parameter eGFR[1] by 3.4ml/min/year (p<0.001*) in the varoglutamstat arm compared to placebo*
- *Results in the subgroup of patients with diabetes[2] showed an 8.4ml/min/year difference in favor of varoglutamstat (p=0.02)*
- *The results were consistent in several sensitivity analyses including using the CKD-EPI 2021 formula for both creatinine and cystatin-C*
- *Varoglutamstat demonstrated an excellent safety and tolerability profile and there were no signs of increased proteinuria*
- *A new Phase 2 study is in planning to confirm the effect in patients DKD[3] stage 3b and 4*

Halle (Saale) / Munich, Germany, October 26, 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 announces highlights from late-breaking oral presentation held yesterday, October 25, 2024, at the American Society of Nephrology (ASN) Kidney Week 2024 in San Diego, California.

The presentation by the Company's CEO, Frank Weber, M.D. titled "Varoglutamstat Increases Glomerular Filtration in Elderly Patients without Signs of Proteinuria and Potentially Offers a New Approach to Treat Diabetic Kidney Disease (DKD)" featured Phase 2 clinical study data substantiating the opportunity to further develop varoglutamstat, Vivoryon's Phase 2 investigational medicine with the potential to improve kidney function, in people with kidney disease.

"We're privileged to have been accepted to share the exciting results of varoglutamstat on kidney function with so many scientific and medical experts in the kidney field. Varoglutamstat showed statistically significant and clinically meaningful improvements of eGFR versus placebo and a sustained improvement of eGFR above baseline, potentially indicating partial recovery of the kidney. We are grateful for many fruitful discussions and extremely encouraged by the positive reactions we received from the community," said Frank Weber, M.D., CEO of Vivoryon. "The efficacy and safety data presented at ASN represent a unique profile for an oral

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product for treating kidney disorders and guide the future development of varoglutamstat. Our primary focus is delivering a much-needed novel treatment option for patients suffering from DKD. Beyond this, we see potential for varoglutamstat across a broad range of kidney diseases including rare diseases affecting kidney function, such as Fabry disease and Alport syndrome."

Presentation Highlights

Background:

- Varoglutamstat is a specific and selective inhibitor of glutaminyl cyclases and confers a novel mechanism of action that attenuates inflammation and fibrosis through reduction of pyroglutamized versions of chemokines and pro-fibrotic peptides, thereby positively impacting kidney function.
- Assessment of progression of kidney dysfunction as measured by the eGFR slope[4] was included prospectively in VIVIAD (NCT04498650), Vivoryon's Phase 2b multicenter, randomized, double-blind, placebo-controlled, parallel group dose-finding study in 259 patients in Alzheimer's disease.
- The average age of participants in VIVIAD was >68 years, dosing was twice-daily with either 300mg or 600mg varoglutamstat, or placebo and treatment duration was 48-96 weeks; key kidney -related study features included a mean baseline eGFR of ~80mL/min/1.73m^2, eGFR, urine dipstick and vital signs measured every 12 weeks; the diabetes subgroup comprised ~12% of VIVIAD patients

Compelling efficacy and safety data in elderly people at risk for kidney disease:

- eGFR improved significantly for varoglutamstat compared to placebo and above baseline in both total population and diabetes subgroup, with the latter revealing a substantially higher treatment effect[5] of >8mL/min/1.73m^2/year (p=0.02; varoglutamstat n=20 / placebo n=12) compared to the overall VIVIAD study population (3.4mL/min/1.73m^2/year (p<0.001; varoglutamstat n=141 / placebo n=117))
- Results and effect size were consistent using a set of diverse and validated methods for eGFR assessment (2021 CKD-EPI cystatin C, 2021 CKD-EPI creatinine-cystatin C 2021 CKD-EPI creatinine, MDRD[6])
- Urine dipstick analysis showed no evidence of increased proteinuria in the treatment group compared to placebo, with the majority of study participants having no proteinuria through all time points measured in the study
- Robust safety data confirmed varoglutamstat's excellent safety profile consistent across two years study duration with no adverse kidney effects and no meaningful differences observed in renal and metabolic systems adverse events in both total population and diabetes subgroup

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Next steps:

- Placebo-controlled Phase 2 study in stage 3b/4 DKD patients on top of SoC in planning to confirm the results to date and investigate additional endpoints including albuminuria/proteinuria, inflammation and fibrosis-related biomarkers
- Pre-clinical investigation of additional rare/orphan kidney disorders (Alport syndrome, Fabry disease)

[1] Estimated glomerular filtration rate (eGFR), a validated measure of kidney function, was calculated as a slope analysis across two years taking all available data into account. [2] Diabetes subgroup 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%. [3] The timing and execution of the planned Phase 2 study in diabetic kidney disease is subject to additional funding / partnership. [4] Measuring the eGFR slope via random coefficients (RC) analysis was the primary efficacy endpoint in recent FDA approvals in CKD, as well as in many ongoing Phase 3 studies. [5] Treatment effect – the between-group difference in eGFR slope between varoglutamstat and placebo. [6] Estimated glomerular filtration rate based on creatinine and calculated using modification of diet in renal disease (MDRD) method.
** corrected from the previously reported p<0.0001*

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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, 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

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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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