Vivoryon Therapeutics N.V. Announces New Data Showing Unique Treatment Effects of Varoglutamstat on Kidney Function in Patients with Diabetes and Outlines Proposed Clinical Development Plan in Diabetic Kidney Disease

- *New data confirm beneficial treatment effect of varoglutamstat on kidney function*
- *Treatment effect[1] in diabetes subgroup[2] of >8mL/min/1.73m2/year in estimated glomerular filtration rate (eGFR); reinforces previously reported treatment effect of 3.4mL/min/1.73m2/year (p<0.001) in the overall VIVIAD Phase 2b study population*
- *Excellent tolerability profile with no meaningful difference in adverse events between overall population and diabetes subgroup*
- *Additional health benefits including promising effects on weight loss, diastolic blood pressure and liver enzymes observed in diabetes subgroup*
- *New proposed Phase 2 clinical development plan for varoglutamstat in diabetic kidney disease announced*
- *Analyst/Investor call & webcast today, July 18, 2024, at 3:00 pm CEST / 9:00 am EDT*

Halle (Saale) / Munich, Germany, July 18, 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 that it will provide updates on its progress towards developing its lead asset varoglutamstat, an investigational QPCT/L inhibitor, in kidney disease during an R&D update call and webcast. The update includes new kidney function analysis in a diabetes subgroup from the VIVIAD Phase 2b study of varoglutamstat in Alzheimer's disease, as well as the Company's proposed development plan for varoglutamstat in its initial target indication, diabetic kidney disease (DKD).

"The extremely promising data we are presenting today in a diabetes subgroup build on the strong body of evidence in the overall VIVIAD study population, where we observed a robust beneficial effect of varoglutamstat on kidney function," said Frank Weber, MD, CEO of Vivoryon. "Specifically, new analysis reveals a significant and unique treatment effect in patients with diabetes which is coupled with additional potential health benefits on weight and blood pressure, and an excellent safety profile. Given these compelling results, we plan to

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advance varoglutamstat into a Phase 2 clinical study in patients with diabetic kidney disease, specifically in more advanced patients with a high risk of end stage kidney disease where there continues to be a significant unmet need for new therapies to stabilize and protect kidney function."

R&D Update: Key Highlights

Significant Effect of Varoglutamstat in Diabetes Subgroup[2]

- New analysis of eGFR, a measure of kidney function, in a subgroup of patients with diabetes[1] in the VIVIAD Phase 2b study reveals a substantially higher treatment effect[3] of >8mL/min/1.73m2/year (p=0.02; varoglutamstat n=20 / placebo n=12) compared to the overall VIVIAD study population where the treatment effect was 3.4mL/min/1.73m2/year (p<0.001; varoglutamstat n=141 / placebo n=117).
- Promising additional effects observed in the diabetes subgroup in varoglutamstat treated patients included
    - a reduction in liver transaminases (AST/ALT[4] reduction of 6 units average)
    - a mild weight loss (- 4kg)
    - a reduction in diastolic blood pressure (- 6 mmHg)
    - All results reported were observed at 48 weeks of treatment versus baseline. Similar observations were not made in the placebo group nor in the overall VIVIAD study population.
- Data revealed that the positive effect on kidney function in the diabetes subgroup appears to be independent of any change in glycemic control (HbA1C remained steady over the period for the varoglutamstat group).
- A reduction of the plasma concentration of the inflammatory and fibrosis inducing pE-CCL2 (p=0.004) was observed in the varoglutamstat arm, indicating a strong anti-inflammatory effect.
- Varoglutamstat was well-tolerated at the dose tested (up to 600mg twice daily) and there were no meaningful differences in adverse events observed in renal and metabolic system organ classes versus placebo or the total population.

Proposed Clinical Development Plan in Diabetic Kidney Disease[5]

- Despite advances in the standard of care for DKD, there remains a significant unmet need for new therapies to stabilize kidney function and prevent disease progression.
- Vivoryon plans to start a Phase 2 study in DKD that is intended to include patients with disease stages more advanced than those observed in the VIVIAD Phase 2 study, enabling an expansion of the overall target patient population. The Company envisages a placebo-controlled study of up to approximately 120 subjects with stage 3b/4 DKD

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and >100mg/g albuminuria/proteinuria. These subjects would be randomized 1:1 to varoglutamstat 600mg twice daily or placebo, on top of standard of care medications. Key endpoints are planned to include eGFR slope analysis, measures of albuminuria (UA(p)CR), inflammation and fibrosis-related biomarkers, as well as safety.

Collaborating with Key Experts to Advance Development Strategy

The Company is collaborating with medical advisors and industry leaders to further shape its shift towards inflammatory/fibrotic disease, including:

- Tobias B. Huber, MD - Chair of the Center of Internal Medicine and Director of the III. Department of Medicine - University Medical Center Hamburg-Eppendorf (UKE), Germany. Acting as Medical Advisor for clinical study design. Research collaboration with Vivoryon focusing on pre-clinical and mechanistic activities relating to varoglutamstat and the role of QPCT/L on kidney function.
- Florian Jehle - CEO of Vifor-FMC Renal Pharma. Acting as Industry Expert Advisor to Vivoryon in the kidney field including strategic business and commercial advice.
- Kevin Carroll, PhD - CEO, KJC Statistics. Acting as statistical analysis expert, providing and calculating statistical read-outs and advising on clinical study statistical aspects.

Detailed data and the Company's plans will be presented during the R&D update call, with the presentation available on the Vivoryon website during and after the event.

Definitions and notes: 1. Treatment effect – the between-group difference in eGFR slope between varoglutamstat and placebo. 2. 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. 3. 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%. 4. AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase. 5. The timing and execution of the planned Phase 2 study is subject to additional funding / partnership.

R&D Update conference call and webcast details

Date: July 18, 2024
Time: 3:00 pm CEST / 9:00 am EDT. The call is expected to last approximately 60 minutes, including Q&A, and will be available via phone and webcast.

A live webcast and slides will be made available at: https://www.vivoryon.com/news-and-events/presentations-webcasts/

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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/BI3f611b5b7efe42389221ad3f4906aca8

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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About Varoglutamstat
Varoglutamstat (PQ912) is a proprietary, potent, nanomolar, oral 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 most recent efficacy data in patients with early AD, which suggest no consistent effect of varoglutamstat at the doses tested, and highly encouraging efficacy data suggesting an improvement in kidney function in this elderly population, the Company is currently focusing on developing varoglutamstat in kidney disease. Varoglutamstat has not yet been approved by any regulatory authority and the safety and efficacy have not yet been established.

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," "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

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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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