Vivoryon Therapeutics N.V. Reports Q3 2024 Results and Highlights Progress on Varoglutamstat in Kidney Disease

- *Varoglutamstat Phase 2 program shows highly consistent, statistically significant and clinically meaningful improvement of kidney function (eGFR[1]) versus placebo in two independent randomized double-blind placebo-controlled studies*
- *VIVA-MIND topline analysis of kidney function data reported yesterday provides a second Phase 2 long-term dataset demonstrating varoglutamstat's potential to improve eGFR*
- *VIVIAD Phase 2b results of varoglutamstat on kidney function highlighted as late-breaking oral presentation at ASN Kidney Week 2024 in October*
- *Comprehensive data set provides a solid base to advance proposed clinical development plan for varoglutamstat in Diabetic Kidney Disease (DKD)*
- *Update to financial guidance, Company now expects cash and cash equivalents to be sufficient for funding operations into the third quarter of 2025[2]*
- *Management to host a conference call today at 3:00 pm CET (9:00 am ET)*

Halle (Saale) / Munich, Germany, December 10, 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 financial results for the nine-month period ended September 30, 2024, and provided a corporate update.

"During the third quarter of 2024 we have made strong progress on transforming Vivoryon into a clinical development leader for novel treatments of kidney disorders," said Frank Weber, MD, CEO of Vivoryon. "We have achieved considerable recognition for the VIVIAD study results during ASN Kidney Week 2024, and the outstanding results from the VIVA-MIND study published yesterday validate and confirm the beneficial effect of varoglutamstat on kidney function. Based on our data to date, the varoglutamstat program has shown a clear dose response with 600mg BID being superior to 300mg BID, a good safety profile suitable for a convenient dose escalation schedule, as well as an excellent correlation of the eGFR change with the MoA-relevant biomarker pE-CCL2. All results support the development of varoglutamstat as a convenient oral therapeutic in diabetic kidney disease. Varoglutamstat also has potential across a broad range of other kidney diseases, including rare diseases affecting kidney function such as Fabry disease and Alport syndrome."

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Q3 2024 and Post-Period Updates

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. 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.

Outstanding VIVIAD Phase 2b Results of Varoglutamstat on Kidney Function Presented at ASN Kidney Week 2024

- On October 25, 2024, Vivoryon held a late-breaking oral presentation at the American Society of Nephrology (ASN) Kidney Week 2024 in San Diego, California. The presentation by the Company's CEO, Frank Weber, MD 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 2b clinical study data from VIVIAD substantiating the opportunity to further develop varoglutamstat in people with kidney disease.
- Results presented showed a statistically significant and clinically meaningful improvement of the prospectively defined kidney function parameter eGFR by 3.4mL/min/1.73m^2/year ($p<0.001$; slope analysis) in the varoglutamstat arm compared to placebo.
- Results in the subgroup of patients with diabetes[3] showed an 8.2mL/min/1.73m^2/year difference in favor of varoglutamstat ($p=0.02$; slope analysis).
- 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.

VIVA-MIND Phase 2 Data[4] Confirm Results of Varoglutamstat's Benefit on eGFR in VIVIAD

- On December 9, 2024, the Company reported topline results from the VIVA-MIND Phase 2 study of varoglutamstat in early AD, corroborating earlier reports of varoglutamstat's beneficial effect on kidney function as measured by eGFR. VIVA-

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MIND was discontinued early, and did not meet its primary and key secondary endpoints in early AD, in line with the previously reported results from VIVIAD.
- Topline analysis of kidney function data showed a statistically significant and clinically meaningful improvement of eGFR; average improvement of >4mL/min/1.73m^2 with varoglutamstat versus placebo across all visits (weeks 4 – 72) and all patients (p=0.004[5]; mean weighted average).
- Varoglutamstat continues to demonstrate a favorable safety and tolerability profile in VIVA-MIND with no new safety signals detected with a total of over 400 participants treated with varoglutamstat in Phase 1 and Phase 2 studies to date.

Strategic Focus and Proposed Clinical Development Plan in DKD

Kidney function data from the Phase 2 VIVIAD and VIVA-MIND studies inform the proposed clinical development of varoglutamstat in kidney disease, including DKD. Key priorities include:

- Vivoryon plans to start a Phase 2 study in DKD that is intended to include patients with kidney disease at more advanced stages than those in the VIVIAD or VIVA-MIND Phase 2 studies. The Company envisages a placebo-controlled study of up to approximately 120 subjects with stage 3b/4 DKD. 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.
- The Phase 2 study is subject to additional funding and/or partnership, which the Company continues to actively explore.

Varoglutamstat in Early Alzheimer's Disease

- On March 4, 2024, Vivoryon announced that findings from an analysis of data from VIVIAD confirmed that there was no consistent effect of varoglutamstat up to 600mg BID on cognition and function, including in high exposure patients. Results from pharmacokinetic, pharmacodynamic and biomarker data, including an assay for measuring pE-Abeta forms, suggest that intracellular QPCT may play a greater role in driving clinical outcomes in AD.
- On December 9, 2024, the Company reported that a topline analysis of VIVA-MIND data[4] in AD showed no clinically meaningful and no statistically significant differences between varoglutamstat 600mg BID and placebo for the primary endpoint of CDR-SB, and key secondary endpoints including CFC2, ADAS-Cog 13, in patients treated with varoglutamstat compared to placebo, in line with the previously reported results in AD from VIVIAD.

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Corporate Development Updates

- On September 5, 2024, Vivoryon implemented the decrease in the nominal value of the shares in the capital of the Company to EUR 0.01 from EUR 1.00. The underlying amendment to the Company's articles of association was approved by the Annual General Meeting held on June 21, 2024.
- On September 30, 2024, Vivoryon hosted a virtual Kidney Disease KOL (Key Opinion Leaders) conference call and webcast featuring expert presentations by seasoned KOLs followed by a Q&A session on the standard of care and existing medical need, market development and commercial potential in kidney disorders, as well as evidence generation and statistical principles in kidney disease drug development, with special emphasis on diabetic kidney disease. A replay of the event is available here.

Financial Results for the Nine Months Ended September 30, 2024

Revenues were zero in the nine months ended September 30, 2024, as well as in the nine months ended September 30, 2023.

Research and development expenses increased by EUR 2.2 million to EUR 12.6 million in the nine months ended September 30, 2024, compared to EUR 10.4 million in the nine months ended September 30, 2023. This increase was largely attributable to the increase in clinical development costs from the VIVIAD and VIVA-MIND studies as well as investments in kidney related research and analysis.

General and administrative expenses were EUR 4.9 million in the nine months ended September 30, 2024, compared to EUR 6.8 million in the nine months ended September 30, 2023. The decrease of EUR 1.9 million was largely attributable to higher non-executive board compensation in 2023.

Net loss for the nine months ended September 30, 2024, was EUR 17.1 million, compared to EUR 17.1 million for the nine months ended September 30, 2023.

The Company held EUR 12.5 million in **cash and cash equivalents** as of September 30, 2024, compared to EUR 28.6 million, which includes cash and cash equivalents and term deposits within financial assets, as of December 31, 2023. Cash utilization for the first nine months of 2024 reflects the intensive investment period in VIVIAD and VIVA-MIND, especially in the first six months of the year, both of which are expected to continue to ramp down in the months ahead as both studies approach their conclusion.

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Outlook & Financial Guidance

The Company expects, based on its most recent financial and business plan, that its existing cash and cash equivalents will be sufficient to fund its operating plans into the third quarter of 2025, subject to the occurrence of unforeseen circumstances and without taking into account potential additional financing transactions, if any. This guidance is updated from the Company's prior guidance of cash runway into the second quarter of 2025, as published on April 24, 2024.

This cash runway guidance reflects an overall reduction in cash utilization, particularly the ramp down of spending on Alzheimer's disease clinical development as well as the Company's strategic reallocation of research and development resources towards inflammatory and fibrotic disorders, including preclinical studies focused on furthering the Company's updated strategy centered on kidney diseases, and a diligent effort to optimize operating expenses. Importantly, the launch and execution of the planned clinical Phase 2 study in DKD will require additional funding and/or partnership.

The viability of the Company's business beyond its current guidance is dependent on its ability to raise additional funds to finance its operations which also depends on the success of its research and development activities such as those focusing on exploring opportunities in kidney disease.

The Company expects to have continuing operating losses for the foreseeable future and the need to raise additional capital to finance its future operations. The Company has concluded that the ability to continue as a going concern in the financial year 2025, as stated in the Company's Annual Report 2023 published on April 24, 2024, depends on the ability to generate additional funding. Please refer to the Company's Annual Report 2023 for further information.

Conference Call and Webcast

Vivoryon will host a conference call and webcast today, December 10, 2024, at 3:00 pm CET (9:00 am ET). A Q&A session will follow the presentation of the third quarter 2024 results and operational progress updates.
A live webcast and slides will be made available at:
www.vivoryon.com/news-and-events/presentations-webcast

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/BIf0be17873ad0409b83edd4eedbe3b7ac

It is suggested participants dial into the conference call 15 minutes prior to the scheduled start time to avoid any delays in attendance.

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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/

Definitions and notes:

[1]*Estimated glomerular filtration rate (eGFR), a validated measure of kidney function, was calculated in VIVIAD as a slope analysis across two years taking all available data into account and as mean weighted average in VIVA-MIND.*

[2]*Further funding and/or partnerships required to support potential future clinical studies.*

[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]*All topline VIVA-MIND results are preliminary and may be subject to change based on additional analysis and quality checks, however, the overall interpretation of the results is not expected to change significantly.*

[5]*Corrected from the previously reported p<0.001.*

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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 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 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

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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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