Vivoryon Therapeutics N.V. Reports Q1 2024 Financial Results and New Data Reinforcing Strategic Focus in Kidney Disease

- *Additional kidney function analyses strongly support Vivoryon's shift in strategic focus to inflammatory and fibrotic diseases, and are a further step towards securing Company's future*

- *Varoglutamstat`s beneficial effect of improving kidney function, as demonstrated by an increase of estimated glomerular filtration rate (eGFR), confirmed by various sensitivity and subgroup analyses*

- *A significant and dose dependent reduction of the pyroglutamated version of CCL2 (pE-CCL2) in serum demonstrates effectiveness of varoglutamstat in inhibiting systemic intracellular QPCT/L and strongly supports an anti-inflammatory effect*

- *Alzheimer's disease: No consistent effect on cognition could be shown in a subgroup of VIVIAD participants with higher drug exposure; VIVA-MIND topline results available end 2024 to inform next steps in AD*

Halle (Saale) / Munich, Germany, May 23, 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 first quarter of 2024, ending March 31, 2024, and provides a corporate update.

"Vivoryon has now achieved proof of concept for varoglutamstat and validated the mechanism of action of QPCT/L inhibition. While the results in early AD were not what we had hoped for, we are excited about the promising effect of varoglutamstat on the pre-specified endpoint of kidney function given the established role of pro-inflammatory cytokines and peptides in driving the progression of kidney disease. In the past weeks, our team, which remains highly dedicated to driving our strategic shift and transformation, has continued to delve into the data on kidney function and we are pleased to see consistent results. We have observed robust and meaningful improvements in eGFR in patients treated with varoglutamstat compared to placebo across a range of different methods assessing eGFR. Effect sizes in favor of varoglutamstat were confirmed in patients with risk factors for CKD including diabetes and hypertension and were observed consistently across the range of eGFR baseline impairment levels in the study. We are now working on crystallizing our strategy and positioning in the kidney disease market and establishing potential clinical development plans for varoglutamstat in both large indications, such as CKD, and in certain rare diseases that impact kidney function," said Frank Weber, MD, CEO of Vivoryon.

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Q1 2024 and Post-Period Updates

Strategic shift towards a focus on inflammatory and fibrotic diseases:

- Following the announcement on March 4, 2024, that the VIVIAD Phase 2b study did not achieve its primary and key secondary endpoints in early AD and the subsequent results showing a significant positive effect of varoglutamstat on kidney function, Vivoryon announced on April 24, 2024, a strategic shift towards a focus on inflammatory and fibrotic diseases. Key priorities now include: exploring varoglutamstat's potential in inflammatory and fibrotic disorders, including of the kidney; concluding VIVIAD Phase 2b clinical study program and in-depth analysis; discontinuing VIVA-MIND clinical Phase 2 study with varoglutamstat in the U.S. in early AD in the second half of 2024; leveraging the data from VIVA-MIND to inform next steps in AD; and continuing to actively pursue potential business development and financing opportunities.

Varoglutamstat – kidney disease:

- QPCT/L inhibition has shown robust evidence of benefits in animal models of inflammatory and fibrotic disorders such as glomerulonephritis and non-alcoholic steatohepatitis (NASH). The VIVIAD protocol prospectively specified measurement of kidney function by estimated glomerular filtration rate (eGFR), a primary endpoint in many development programs of kidney disorders, and additional biomarkers, in order to further investigate this potential activity.
- Varoglutamstat 600mg BID increased eGFR over the treatment period up to 96 weeks in patients with early AD, indicating a potential benefit of varoglutamstat on kidney function.
- Further sensitivity and subgroup analysis has shown this effect is observed across the range of eGFR levels at baseline in the study, and when assessed using a set of diverse and validated methods for calculating kidney function.
- Additionally, the Company has explored the effect of varoglutamstat on levels of pyroglu-CCL2 (pE-CCL2), a pro-inflammatory cytokine. Persistent, low grade inflammation is considered a hallmark feature of chronic kidney disease (CKD). Results showed a significant and dose-dependent reduction in pE-CCL2 in the serum of VIVIAD patients following treatment with varoglutamstat. This demonstrates the effectiveness of varoglutamstat in inhibiting systemic intracellular QPCT/L and strongly supports an anti-inflammatory effect.
- Vivoryon is evaluating a clinical development path, as well as business development and financing opportunities, to further explore the potential of varoglutamstat and QPCT/L

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inhibitors in kidney disease in both large indications, such as CKD, and in certain rare diseases that impact kidney function, such as Alport Syndrome.

Primary analysis of change of estimated glomerular filtration rate (eGFR, slope analysis including all measurement timepoints during treatment):

	Annualized change of eGFR*	P-Value	Annualized Change of eGFR*	P-Value
Formula (creatinine)	MDRD		CKD-EPI 2021	
Placebo	-1.51		-0.75	
Varoglutamstat	+1.92		+1.44	
Treatment Effect (Δ)	3.43	p=0.0002	2.19	p=0.0015

* mL/min/1.73m^2/year

Sensitivity analysis of estimated glomerular filtration (eGFR) rate using Cystatin C and Creatinine (remeasured on Atellica® platform) CKD-EPI 2021 formula at baseline, week 24 and week 48:

	Cystatin C		Cystatin C and Creatinine		Creatinine	
	Week 24	Week 48	Week 24	Week 48	Week 24	Week 48
Placebo (eGFR mL/min)	73.88	71.39	84.15	82.07	89.74	88.74
Varoglutamstat (eGFR mL/min)	78.15	80.88	88.91	91.21	93.33	93.98
Treatment Effect* (Δ)	4.27	9.49	4.76	9.14	3.59	5.24
P-Value	0.0186	<0.0001	0.0041	<0.0001	0.0019	0.0003

* Baseline Adjusted LSMean Estimates

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Varoglutamstat – early Alzheimer's disease (AD):

- In recent weeks Vivoryon has continued its in-depth analysis of the VIVIAD data, following the March 4, 2024, and April 24, 2024, disclosures. While these analyses remain ongoing, findings to date continue to confirm there is no consistent effect of varoglutamstat up to 600mg BID on cognition and function, including in high exposure patients. Data from VIVA-MIND, anticipated by the end of 2024, is expected to contribute to the overall dataset informing varoglutamstat's development strategy in AD.

Early-Stage Pipeline

- Vivoryon's main focus is on its clinical-stage activities, however it will continue to explore pre-clinical QPCT/L inhibitors for use in inflammatory and fibrotic disorders and other indications such as oncology and CNS as well as pre-clinical meprin inhibitors, in particular for fibrotic disorders, and QPCT/L inhibitors with good blood brain barrier penetration. The Company's antibody program, PBD-C06, will remain active as a candidate for further potential partnering opportunities.

Corporate Development Updates

- In March 2024, Kugan Sathiyanandarajah and Professor Dr. Morten Asser Karsdal stepped down from Vivoryon's Board of Directors. They had been appointed as Non-Executive Directors in June 2023.
- In March 2024, Anne Doering, CFA, assumed the role of Chief Financial Officer (CFO) of Vivoryon, following her previous position as Chief Strategy & Investor Relations Officer.
- In May 2024, Vivoryon announced it will hold its 2024 Annual General Meeting on Friday, June 21, 2024, at 1:00 p.m. (CEST) in Amsterdam, the Netherlands. The full agenda and all relevant documents are available on the Company's website (https://www.vivoryon.com/2024-annual-general-meeting/).

Financial Results for the First Quarter of 2024

Revenues were zero in the three months ended March 31, 2024, as well as in the three months ended March 31, 2023.

Research and development expenses increased by EUR 4.3 million to EUR 7.4 million in the three months ended March 31, 2024, compared to EUR 3.1 million in the three months ended March 31, 2023. This increase was largely attributable to the increase in clinical development costs from the VIVIAD and VIVA-MIND studies.

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General and administrative expenses were EUR 2.1 million in the three months ended March 31, 2024, compared to EUR 1.9 million in the three months ended March 31, 2023. The increase of EUR 0.2 million was largely attributable to higher expenses for share-based payments as well as legal and consulting fees.

Net loss for the three months ended March 31, 2024, was EUR 9.3 million, compared to EUR 5.1 million for the three months ended March 31, 2023.

The Company held EUR 22.0 million in **cash and cash equivalents** as of March 31, 2024, compared to EUR 28.6 million, which includes cash and cash equivalents and financial assets, as of December 31, 2023.

Outlook & Financial Guidance

As published on April 24, 2024, the Company expects, on the basis of its most recent financial and business plan, that its existing cash and cash equivalents will be sufficient to fund its operating plans, excluding any additional financings, into the second quarter of 2025.

This cash runway guidance reflects the shift in focus of research and development resources towards inflammatory and fibrotic disorders, such as of the kidney, and an overall reduction in cash utilization including the ramp down of spending on VIVIAD as it approaches its conclusion, the discontinuation of VIVA-MIND, the discontinuation of VIVALONG preparation activities given the developments of VIVIAD and VIVA-MIND, as well as the streamlining of manufacturing costs and programs for API development.

The viability of the Company beyond the second quarter of 2025 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.

Conference Call and Webcast
Vivoryon will host a conference call and webcast today, May 23, 2024, at 3:00 pm CEST (9:00 am EDT). A Q&A session will follow the presentation of the first quarter results.
A live webcast and slides will be made available at: www.vivoryon.com/investors-news/news-and-events/presentations-webcasts/

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/BI9aadfa99e014435493eca917a11150f1

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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: www.vivoryon.com/investors-news/news-and-events/presentations-webcasts/

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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 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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