Vivoryon Therapeutics N.V. Reports H1 2024 Progress Marked by Compelling Kidney Function Data and Execution of Strategy to Advance Varoglutamstat in Kidney Disease

- *Primary focus is developing varoglutamstat, a Phase 2 investigational medicine with potential to improve kidney function in patients with kidney disease*
- *Statistically significant benefit of varoglutamstat on prospectively defined key kidney function endpoint (eGFR[1]) and significant reduction of pro-inflammatory cytokine pE-CCL2 observed in VIVIAD Phase 2b AD study*
- *Substantially higher treatment benefit of varoglutamstat on eGFR observed in post-hoc diabetes subgroup[2] triggering plans to advance varoglutamstat into Phase 2 study in DKD[3]*
- *Gained further insight into AD results through clear evidence of differences between kidney and AD outcomes from PK/PD analysis and new target occupancy information*
- *Management to host a conference call today at 3:00pm CEST (9:00am EDT)*
- *Vivoryon to host a virtual Kidney Disease KOL (Key Opinion Leaders) webcast on Monday, September 30 at 3:00 pm CEST (9:00 am EDT) to elaborate on varoglutamstat's potential in kidney disease with an emphasis on DKD*

Halle (Saale) / Munich, Germany, September 12, 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 six-month period ended June 30, 2024, and provides a corporate update. The report is available on the Company's website https://www.vivoryon.com/financial-information/.

"The VIVIAD Phase 2b study showed outstanding results in improving kidney function and we made strong progress during the first half of 2024 in forging a new development strategy for varoglutamstat in diabetic kidney disease (DKD)," said Frank Weber, MD, CEO of Vivoryon. "In parallel, we advanced pharmacokinetic and biomarker analyses which demonstrate a strong

[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 is subject to additional funding / partnership.

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dose response of varoglutamstat on kidney function improvement. Furthermore, as we continue the evolution of our understanding of the Alzheimer's disease (AD) VIVIAD results, we have generated the first evidence that varoglutamstat activity is required in the cells of the brain – not only in the cerebrospinal fluid - to stop the pathological process of pE-Abeta production." He concluded, "The VIVIAD data demonstrate varoglutamstat has an excellent safety and tolerability profile, provide strong support for our understanding of the potential of QPCTL inhibitors in inflammatory and fibrotic diseases and lay the foundation for our strategic shift towards kidney disease based on the outstanding effect we observed on eGFR."

H1 2024 and Post-Period Updates

Strategic shift towards a focus on inflammatory and fibrotic diseases

A significant positive effect of varoglutamstat on kidney function observed in the VIVIAD Phase 2b study in AD underpins the strategic shift to inflammatory and fibrotic diseases. In April 2024, Vivoryon announced this strategic shift following the announcement in March 2024 that the VIVIAD Phase 2b study did not achieve its primary and key secondary endpoints in early AD.

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.

Key priorities now include:

- Preparing for a proposed Phase 2 clinical study for varoglutamstat in diabetic kidney disease (subject to additional funding and/or partnership);
- Concluding VIVIAD Phase 2b clinical study program and in-depth analysis;
- Analyzing the data of the VIVA-MIND Phase 2 clinical study with varoglutamstat in the U.S. in early AD by year end 2024;
- Continuing to actively pursue potential business development and financing opportunities.

Varoglutamstat Mechanism of Action

- Post-translational modification occurs both physiologically and in disease settings and it is a crucial process to functionalize proteins. Many different post-translational modifications are catalyzed by enzymes that have become known drug targets, e.g. kinases, proteases, or methylases.
- Pyroglutamate (pE) formation, a specific post-translational modification catalyzed by the glutaminyl cyclase enzymes QPCT and QPCTL, has emerged as a central element in different diseases including neurodegenerative, inflammatory and fibrotic diseases as well as cancer.

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- Varoglutamstat is a highly potent oral small molecule inhibitor of human QPCT and QPCTL, designed to prevent inflammatory and fibrotic processes by blocking pyroglutamate formation on key disease drivers.
- QPCTL inhibition has demonstrated robust evidence of efficacy in animal models of inflammatory and fibrotic disorders such as glomerulonephritis and non-alcoholic steatohepatitis (NASH).

Varoglutamstat – VIVIAD kidney function results (total study population)

- 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. The treatment effect in the overall VIVIAD study population was 3.4mL/min/1.73m2/year (p<0.001; varoglutamstat n=141 / placebo n=117).
- 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 QPCTL and strongly supports an anti-inflammatory effect.

Significant effects of varoglutamstat in diabetes subgroup[2]

- Analysis of eGFR in a subgroup of patients with diabetes[2] in the VIVIAD Phase 2b study reveals a substantially higher treatment effect[4] 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 were observed in the diabetes subgroup in varoglutamstat treated patients including a reduction in liver transaminases, mild weight loss, and a reduction in diastolic blood pressure.
- 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.

[4]Treatment effect – the between-group difference in eGFR slope between varoglutamstat and placebo.

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- 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 (DKD)[3]

- 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. 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.
- Vivoryon is evaluating business development and financing opportunities, to further explore the potential of varoglutamstat and QPCT/L inhibitors in kidney disease in both large indications, such as DKD, and in certain rare diseases that impact kidney function, such as Fabry disease and Alport Syndrome.

Varoglutamstat – early Alzheimer's disease (AD)

- Vivoryon has continued its in-depth analysis of the VIVIAD data. 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. Results from pharmacokinetic, pharmacodynamic and biomarker data, including an assay for measuring pE-Abeta forms, suggests that intracellular QPCT may play a greater role in driving clinical outcomes in AD. 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.

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.
- Vivoryon held its 2024 Annual General Meeting (AGM) on Friday, June 21, 2024, at 1:00 p.m. (CEST) in Amsterdam, the Netherlands. The shareholders approved all items on the agenda of the meeting. The full agenda and all relevant documents are available on the Company's website (https://www.vivoryon.com/2024-annual-general-

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meeting/). Agenda items of particular note include the reappointment of Dr. Michael Schaeffer, Chief Business Officer, as executive director as well as the amendment to the Company's articles of association with regard to, among other changes, the decrease of the nominal value of the shares in the capital of the Company to EUR 0.01 from EUR 1.00, which was implemented on September 5, 2024.

Financial Results for the First Half of 2024

Revenues were zero in the six months ended June 30, 2024, as well as in the six months ended June 30, 2023.

Research and development expenses increased by EUR 4.0 million to EUR 10.3 million in the six months ended June 30, 2024, compared to EUR 6.3 million in the six months ended June 30, 2023. This increase was largely attributable to the increase in clinical development costs from the VIVIAD and VIVA-MIND studies as well as early investments into kidney related research.

General and administrative expenses were EUR 3.5 million in the six months ended June 30, 2024, compared to EUR 4.4 million in the six months ended June 30, 2023. The decrease of EUR 0.9 million was largely attributable to higher non-executive board compensation in 2023.

Net loss for the six months ended June 30, 2024, was EUR 13.6 million, compared to EUR 10.7 million for the six months ended June 30, 2023.

The Company held EUR 15.3 million in **cash and cash equivalents** as of June 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 six months of 2024 reflects the intensive investment period in VIVIAD and VIVA-MIND, both of which are expected to meaningfully ramp down in the second half 2024 as both studies approach their conclusion.

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

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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, September 12, 2024, at 3:00 pm CEST (9:00 am EDT). A Q&A session will follow the presentation of the first half 2024 results. A live webcast and slides will be made available at: https://www.vivoryon.com/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/BIb82f5f65fffe4d5faaade135258da32a

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/

Virtual Kidney Disease Key Opinion Leaders Event on September 30, 2024
Vivoryon will host a virtual Kidney Disease KOL (Key Opinion Leaders) conference call and webcast on Monday, September 30, 2024, 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.

Featured speakers:

- **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.

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- **Kevin Carroll, PhD** - CEO, KJC Statistics. Acting as statistical analysis expert, providing and calculating statistical read-outs and advising on clinical study statistical aspects.

Conference call details
Date: September 30, 2024
Time: 3:00 pm CEST / 9:00 am EDT

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

Please register to join the conference call via the following website:
https://edge.media-server.com/mmc/p/b8g57xvh/

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Vivoryon Therapeutics N.V. Financial Statements
Unaudited Statement of Operations and Comprehensive Loss for the Six Months Ended June 30, 2024 and 2023

in kEUR, except for share data	For the six months ended June 30, 2024 (unaudited)	2023 (unaudited)
Research and development expenses	(10,308)	(6,259)
General and administrative expenses	(3,501)	(4,433)
Operating loss	**(13,809)**	**(10,692)**
Finance income	303	258
Finance expenses	(53)	(327)
Finance result	**250**	**(69)**
Result before income taxes	**(13,559)**	**(10,761)**
Income taxes	—	45
Net loss for the period	**(13,559)**	**(10,716)**
Items not to be reclassified subsequently to profit or loss		
Remeasurement of the net defined benefit pension liability	39	(9)
Total other comprehensive profit / (loss)	**39**	**(9)**
Comprehensive loss	**(13,520)**	**(10,725)**
Loss per share in EUR (basic and diluted)	(0.52)	(0.44)

The accompanying notes are an integral part of these condensed interim financial statements.

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Vivoryon Therapeutics N.V.
Unaudited Condensed Statements of Financial Position as of June 30, 2024 and December 31, 2023 (audited)

in kEUR	June 30, 2024 (unaudited)	December 31, 2023 (audited)
ASSETS		
Non-current assets		
Property, plant and equipment	31	40
Intangible assets	904	941
Right-of-use assets	9	36
Total non-current assets	**944**	**1,017**
Current assets		
Financial assets	74	10,165
Other current assets and prepayments	701	1,085
Cash and cash equivalents	15,272	18,562
Total current assets	**16,047**	**29,812**
TOTAL ASSETS	**16,991**	**30,829**
Equity		
Share capital	26,067	26,067
Share premium	135,671	135,671
Other capital reserves	14,817	13,599
Accumulated other comprehensive loss	(217)	(256)
Accumulated deficit	(162,358)	(148,799)
Total equity	**13,980**	**26,282**
Non-current liabilities		
Pension liability	1,287	1,353
Provisions long-term	12	12
Total non-current liabilities	**1,299**	**1,365**
Current liabilities		
Trade payables	1,465	2,894
Lease liabilities	10	38
Other liabilities	237	250
Total current liabilities	**1,712**	**3,182**
Total Liabilities	**3,011**	**4,547**
TOTAL EQUITY AND LIABILITIES	**16,991**	**30,829**

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Vivoryon Therapeutics N.V.
Unaudited Condensed Statements of Changes in Shareholders' Equity for the six months ended June 30, 2024 and 2023

in kEUR	Share capital	Share premium	Other capital reserves	Accumulated other compre-hensive loss	Accumulated deficit	Total equity
January 1, 2024	**26,067**	**135,671**	**13,599**	**(256)**	**(148,799)**	**26,282**
Net loss for the period	–	–	–	–	(13,559)	(13,559)
Remeasurement of the net defined benefit pension liability	–	–	–	39	–	39
Comprehensive loss	**–**	**–**	**–**	39	**(13,559)**	**(13,520)**
Proceeds from the issuance of common shares	–	–	–	–	–	–
Transaction costs of equity transactions	–	–	–	–	–	–
Share-based payments	–	–	1,218	–	–	1,218
Exercise of share options	–	–	–	–	–	–
June 30, 2024	**26,067**	**135,671**	**14,817**	**(217)**	**(162,358)**	**13,980**
January 1, 2023	**24,105**	**113,382**	**9,656**	**(180)**	**(120,457)**	**26,506**
Net loss for the period	–	–	–	–	(10,716)	(10,716)
Remeasurement of the net defined benefit pension liability	–	–	–	(9)	–	(9)
Comprehensive loss	**–**	**–**	**–**	**(9)**	**(10,716)**	**(10,725)**
Proceeds from the issuance of common shares	1,786	23,214	–	–	–	25,000
Transactions costs of equity transactions	–	(2,095)	–	–	–	(2,095)
Exercise of share options	–	–	2,305	–	–	2,305
Share-based payments	71	472	–	–	–	542
June 30, 2023	**25,962**	**134,973**	**11,961**	**(189)**	**(131,173)**	**41,534**

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Vivoryon Therapeutics N.V.
Unaudited Condensed Statements of Cash Flows for the six months ended June 30, 2024 and 2023

in kEUR	For the six months ended June 30, 2024 (unaudited)	2023 (unaudited)
Operating activities		
Net loss for the period	(13,559)	(10,716)
Adjustments for:		
Finance result	(250)	69
Depreciation and amortization	73	79
Share based payments	1,218	2,305
Foreign currency gain (loss) from other items than cash	(25)	(59)
Deferred income tax	—	(45)
Other non-cash adjustments	19	(33)
Changing in:		
Financial assets	(4)	(8,938)
Other current assets and prepayments	383	(2,036)
Pension liabilities	(66)	(13)
Trade payables	(1,429)	(1,252)
Other liabilities	(13)	306
Interest received	353	51
Interest paid	—	(1)
Cash flows used in operating activities	**(13,300)**	**(20,283)**
Investing activities		
Purchase of plant and equipment	—	(9)
Proceeds from sale of financial assets	10,000	—
Cash flows used in investing activities	**10,000**	**(9)**
Financing activities		
Proceeds from the issuance of common shares	—	25,000
Capital raising costs	—	(2,095)
Proceeds from exercise of share options	—	542
Payment of lease liabilities	(28)	(47)
Cash flows provided by financing activities	**(28)**	**23,400**
Net increase in cash and cash equivalents	**(3,328)**	**3,109**
Cash and cash equivalents at the beginning of period	18,562	26,555
Effect of exchange rate fluctuation on cash held	38	(82)
Cash and cash equivalents at end of period	**15,272**	**29,582**

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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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