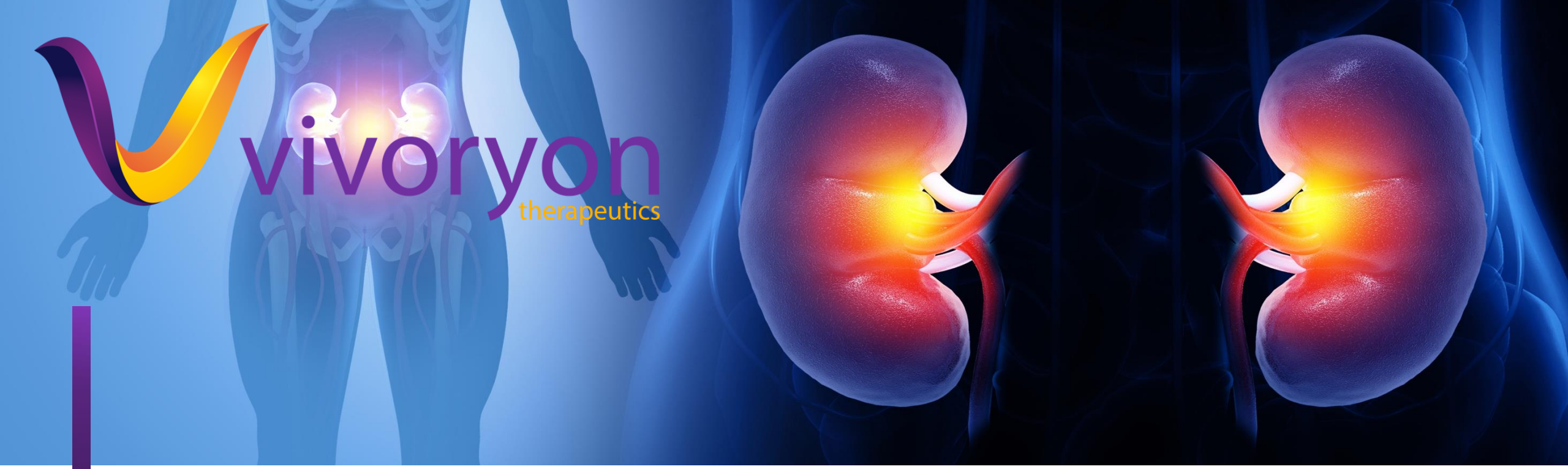

# Q3 2024: Financial Results & Operational Update

## Strong Progress Advancing Varoglutamstat in Kidney Disease

December 10, 2024

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# Q3 2024 Key Highlights and Post-period Updates

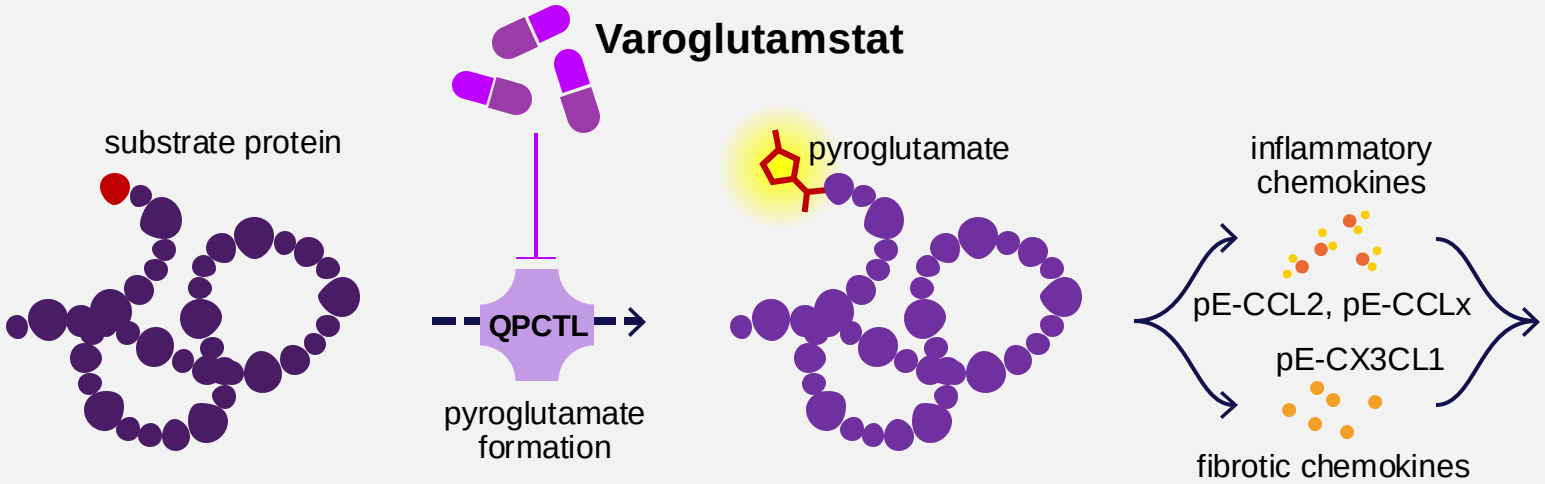
- Reported that VIVA-MIND shows highly significant improvement of eGFR versus placebo, confirming VIVIAD eGFR results
- Presented kidney outcome results from VIVIAD study in late breaking oral session at ASN Kidney Week, the world's premiere nephrology meeting
- Hosted virtual kidney disease KOL event on standard of care and new developments in kidney disease highlighting potential of varoglutamstat
- Continued progress in implementing strategic focus on DKD, driven by compelling kidney function data

*ASN: American Society of Nephrology*

# VAROGLUTAMSTAT
# MOA & CLINICAL DATA

# Groundbreaking discovery: Inhibition of QPCTL reduces kidney inflammation and fibrosis, and improves kidney function

**Pro-inflammatory and fibrotic peptides require pyroglutamate formation at N-terminal for full potency**




**QPCTL inhibition leads to reduction in potent pro-inflammatory and fibrotic peptides**

**Pyroglutamate formation (pE-formation) is exclusively catalyzed by QPCTL (iso-glutaminyl cyclase enzyme)**

| Inflammation | |
|---|---|
| pE-CCL2 | ↓ |
| IFNγ | ↓ |
| TNFα | ↓ |

| Fibrosis | |
|---|---|
| Collagen 3 | ↓ |
| α-SMA | ↓ |
| CX3CL1 | ↓ |

| Kidney function | |
|---|---|
| eGFR | ↑ |
| Urea | ↓ |
| Cystatin C | ↓ |



*Kehlen et.al. Biosci Rep, 2017; Cynis et.al. EMBO, 2011; Cynis et al, Int. J Exp Path, 2013; Kanemitsu et al., 2021; Vivoryon company data, 2024; pE-CCLx – other potential pE chemokines; Notes: Graphic is for illustrative purposes only.*

# VIVA-MIND U.S. study design in early AD

**1:1 randomization**
109 patients treated
for up to 72 weeks

**Q3 2023:**
DSMB confirmed continuation
on 600mg BID

**Q2 2024:**
Decision to discontinue
study early[1]

Placebo

Varoglutamstat
600mg BID

**Patients[2]:**

- Early Alzheimer's disease[3]
- MMSE 20 -30
- CDR-SB global score 0.5 or 1
- 50 – 89 years of age

**Objectives:**

- Assess the safety and tolerability of varoglutamstat
- Assess the efficacy of varoglutamstat with the primary endpoint of CDR-SB
- Assess the efficacy and pharmacodynamic effects of varoglutamstat at an interim stage gate analysis after 180 patients were treated for at least 24 weeks

**Kidney Function:**

- eGFR measurements were prospectively defined as a safety parameter

All 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



*[1] Due to the study being discontinued early, only 109 of 180 planned subjects were treated; [2] More information at clinicaltrials.gov ID NCT03919162; [3] Mild Cognitive Impairment (MCI) due to AD or Mild probable AD according to NIA-AA guidelines; BID: twice daily; MMSE: mini-mental state exam; CDR-SB: clinical dementia rating sum of boxes; eGFR: estimated glomerular filtration rate*

# VIVA-MIND Phase 2: Baseline characteristics and disposition

| | VIVA-MIND total population[1] | |
|---|---|---|
| Demographics & baseline characteristics | Varoglutamstat N (%) | Placebo N (%) |
| Number randomized | 53 | 59 |
| **Number of participants (mITT)** | **52** | **57** |
| **Sex - n (%)** | | |
| Female | 24 (46.2) | 30 (52.6) |
| Male | 28 (53.8) | 27 (47.4) |
| **Age (in years) - mean (SD)** | 72.9 (8.3) | 70.8 (7.4) |
| **Average treatment duration (weeks)[2] - mean (SD)** | 45.3 (24.1) | 46.1 (26.0) |
| **CDR-SB at baseline[3] - mean (SD)** | 3.35 (1.53) | 2.99 (1.70) |
| **eGFR (mL/min/1.73m2) at baseline[3] - mean (SD)** | 76.9 (16.3) | 78.1 (17.8) |
| Disposition[4] | Varoglutamstat (%) | Placebo (%) |
| Completed study (to week 72) | 24.5% | 33.9% |
| Discontinued | | |
| Termination by sponsor | 37.7% | 39.0% |
| Withdrawal by subject | 22.6% | 18.6% |
| All other | 15.2% | 8.5% |

*[1] Total of 112 subjects randomized; 109 received study medication (mITT); [2] Based on safety analysis population (N=53 varoglutamstat/N=56 placebo; one patient in placebo group received single dose of varoglutamstat in error); [3] Baseline defined as last non-missing value prior to first study treatment administration; [4] Based on number randomized*

# VIVA-MIND analysis reveals no consistent effect of varoglutamstat 600mg BID on pre-specified AD endpoints

## Pre-specified endpoints

- No clinically meaningful and no statistically significant differences between varoglutamstat 600mg BID and placebo for
  - CDR-SB
  - CFC2
  - ADAS-Cog 13
- Additional data including EEG, QPCT/L activity and other biomarkers in the CSF expected to become available in Q1 2025

## Status and context

- VIVA-MIND was designed as a stage-gated seamless Phase 2a/b study with a total of 414 patients to be randomized
- The VIVA-MIND study was discontinued early based on the negative outcome of the VIVIAD study investigating a similar AD population and dose of varoglutamstat, where no clinically meaningful efficacy signal was observed
- Consequently, only 109 of the planned 180 patients were treated in the VIVA-MIND Phase 2a portion and the study did not progress into Phase 2b



*CDR-SB: Clinical Dementia Rating Sum of Boxes; CFC2: Cognitive-Functional Composite 2; ADAS-Cog-13: Alzheimer's Disease Assessment Scale cognitive subscale; EEG: electroencephalogram; CSF: Cerebrospinal fluid*

# Varoglutamstat continues to demonstrate a favorable safety and tolerability profile with no new safety signals identified in VIVA-MIND

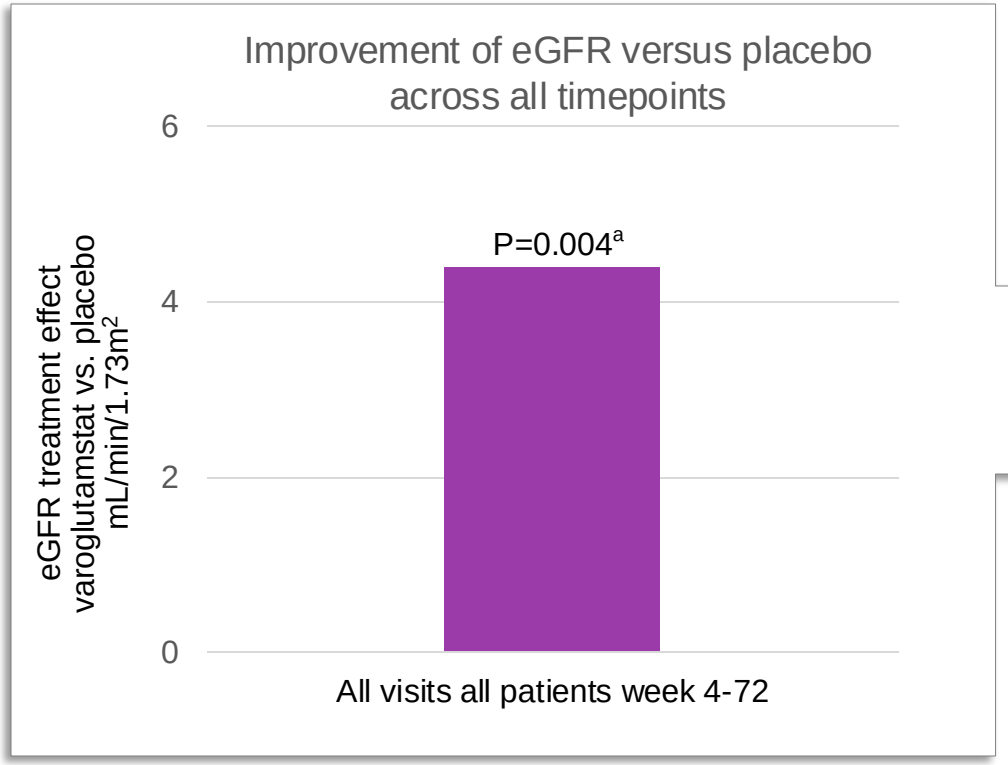
| Adverse event category (%) | Varoglutamstat (N=53)* | Placebo (N=56)* | Overall (N=109) |
|---|---|---|---|
| any TEAE | 84.9 | 78.6 | 81.7 |
| any related TEAE | 30.2 | 32.1 | 31.2 |
| TEAE by severity | | | |
| mild | 26.4 | 41.1 | 33.9 |
| moderate | 47.2 | 28.6 | 37.6 |
| severe | 11.3 | 8.9 | 10.1 |
| serious TEAE | 15.1 | 8.9 | 11.9 |
| related serious TEAE | 0 | 1.8 | 0.9 |
| TEAE leading to any study drug dose modification (excluding discontinuation) | 5.7 | 7.1 | 6.4 |
| TEAE leading to study drug discontinuation | 7.5 | 3.6 | 5.5 |
| TEAE leading to death[1] | 1.9 | 0 | 0.9 |

*[1] One patient died after a head injury from a fall and the patient had a patient's provision to not resuscitate. A second patient had surgery for gastrointestinal bleeding after stopping study medication and died from complications of the surgery several weeks later. The deaths were considered not / unlikely related to varoglutamstat – the DSMB recommended continuation of study without changes after occurrence of these events during the study.*

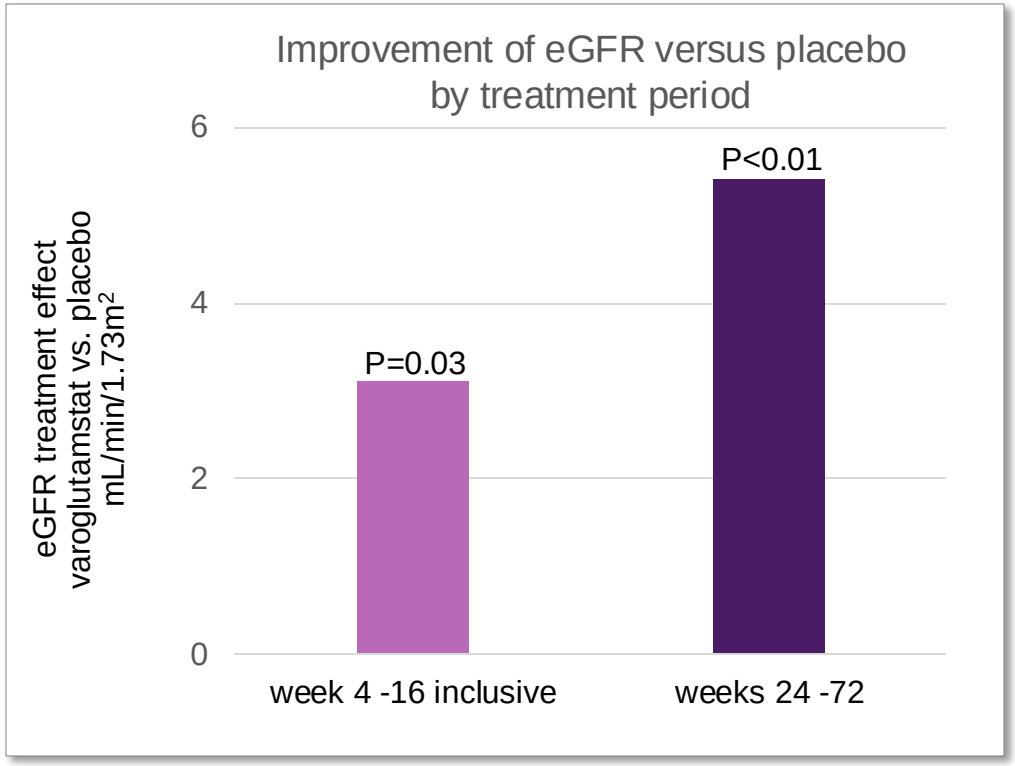


*TEAE: Treatment emergent adverse events occurring during the treatment period; table does not include events occurring after end of treatment (EOT); * TEAEs are for Safety Analysis population which included patients who received ≥1 dose of varoglutamstat 600mg; the varoglutamstat arm includes one placebo patient who was identified as receiving a single dose of varoglutamstat in error and this person has been allocated to the varoglutamstat arm for Safety Analysis accordingly*

# Statistically significant and clinically meaningful improvement vs. placebo in kidney function measured by eGFR (changes from baseline; total population; MDRD)




Average improvement across all visits and all patients > 4mL/min/1.73m$^2$



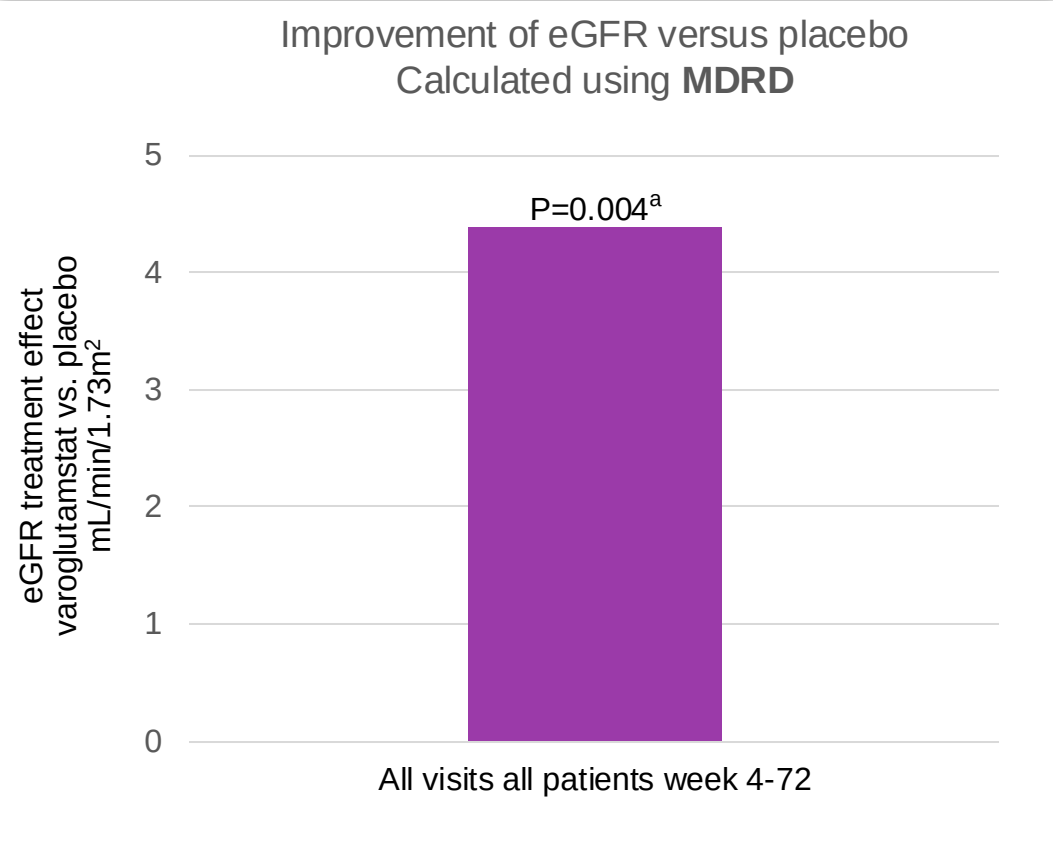

Effect size in the first 16 weeks of treatment approx. 3mL/min/1.73m$^2$ and between 24 and 72 weeks above 5mL/min/1.73m$^2$

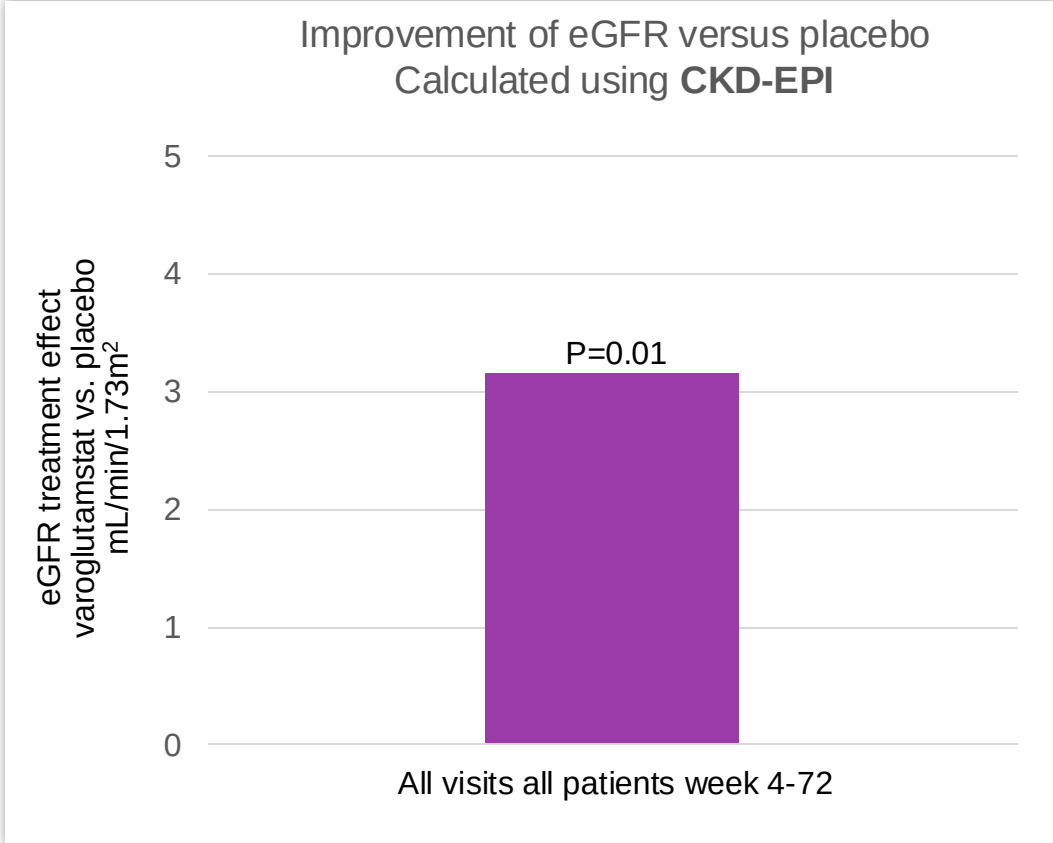
Placebo N=57, Varoglutamstat 600mg BID N=52

Calculations based on weighted average change from baseline

[a] *Corrected from the previously reported p<0.001*

# Sensitivity analysis: MDRD and CKD-EPI calculations show consistent and comparable statistically significant improvement vs. placebo on eGFR




Placebo N=57, Varoglutamstat 600mg BID N=52

Calculations based on weighted average change from baseline

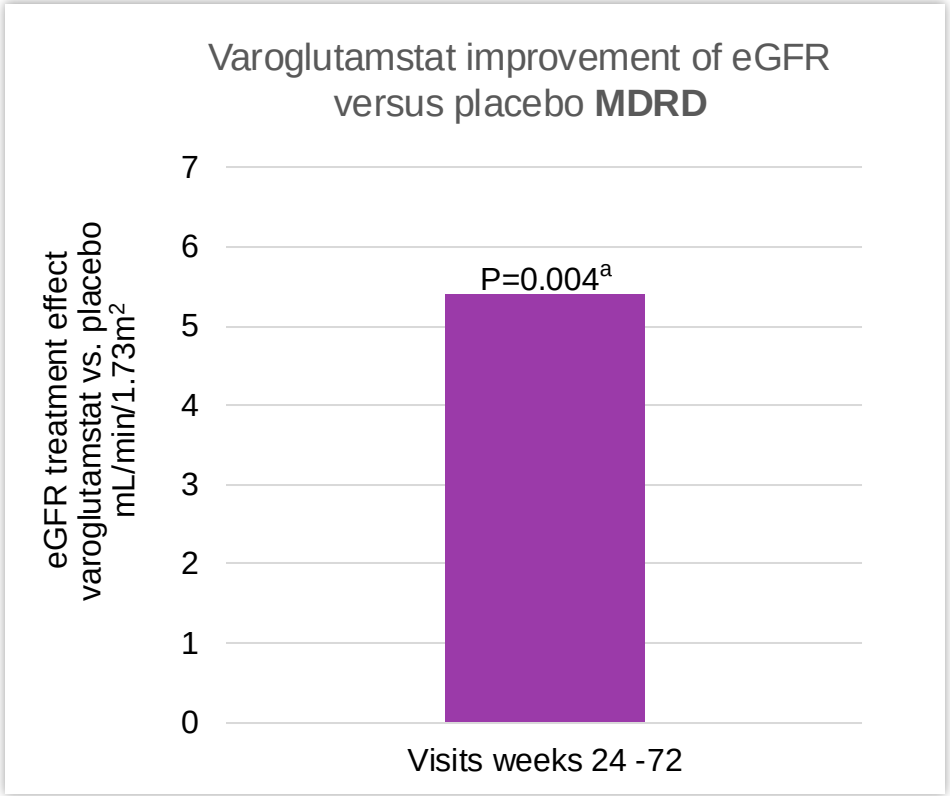
[a] *Corrected from the previously reported p<0.001*

# Similarities and differences between VIVA-MIND and VIVIAD studies

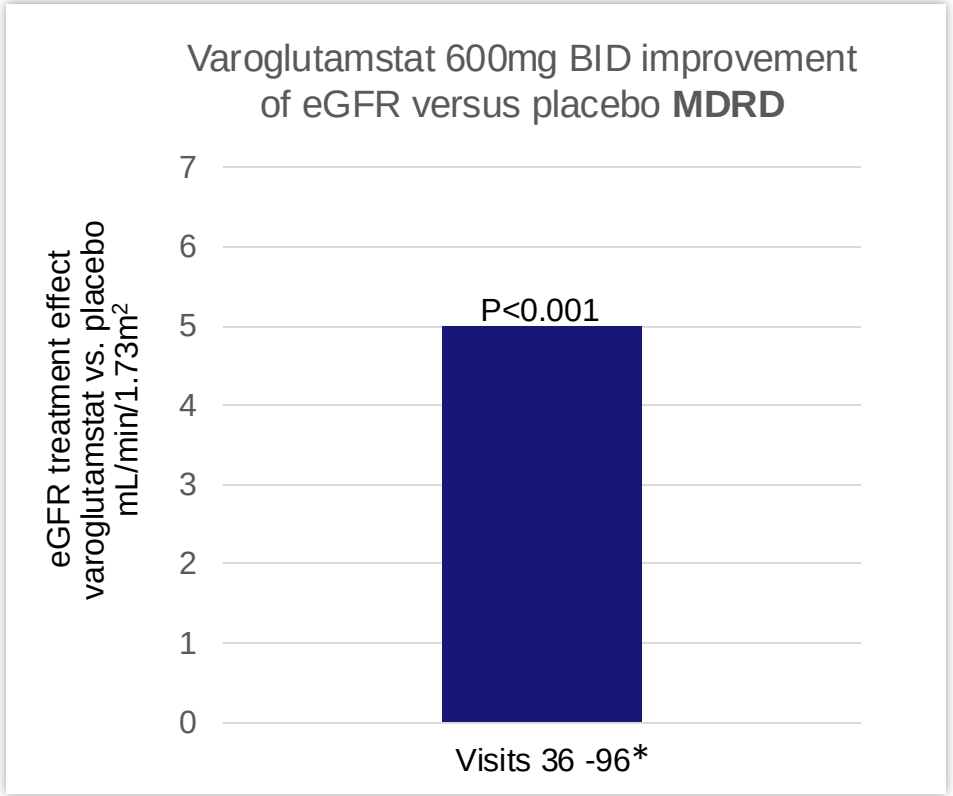
| Parameter | VIVA-MIND | VIVIAD |
|---|---|---|
| Study completion | Discontinued early<br>(no AD efficacy signal in VIVIAD) | Completed |
| Patient selection | Mild AD, mean age 72 | Mild AD, mean age 68 |
| Number of patients treated | 109 | 259 |
| Varoglutamstat dose investigated | 600mg BID | 300 and 600mg BID |
| Dose escalation | Fast, starting at 150mg BID | Slow, starting at 50mg |
| Mean treatment duration | ~46 weeks | ~76 weeks |
| Number of patients with eGFR results week 36 and later | 73 | 246 |

# eGFR Results Comparison VIVA-MIND – VIVIAD

**VIVA-MIND**




**VIVIAD**

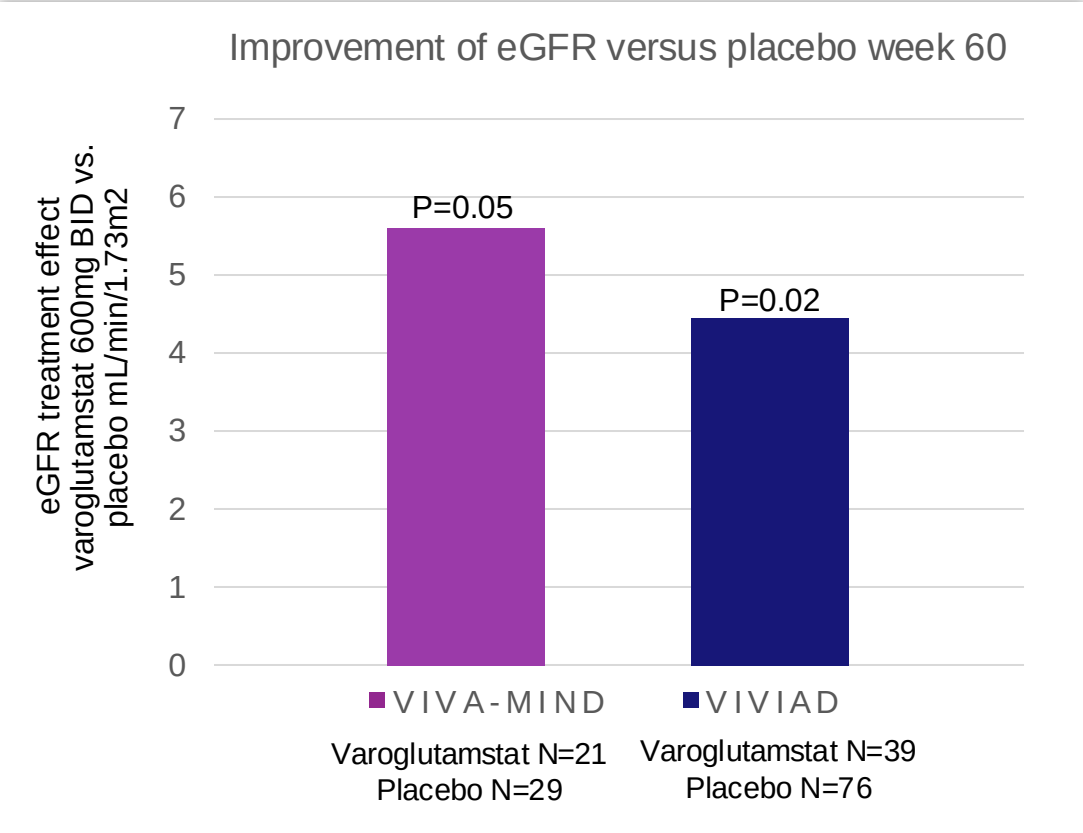


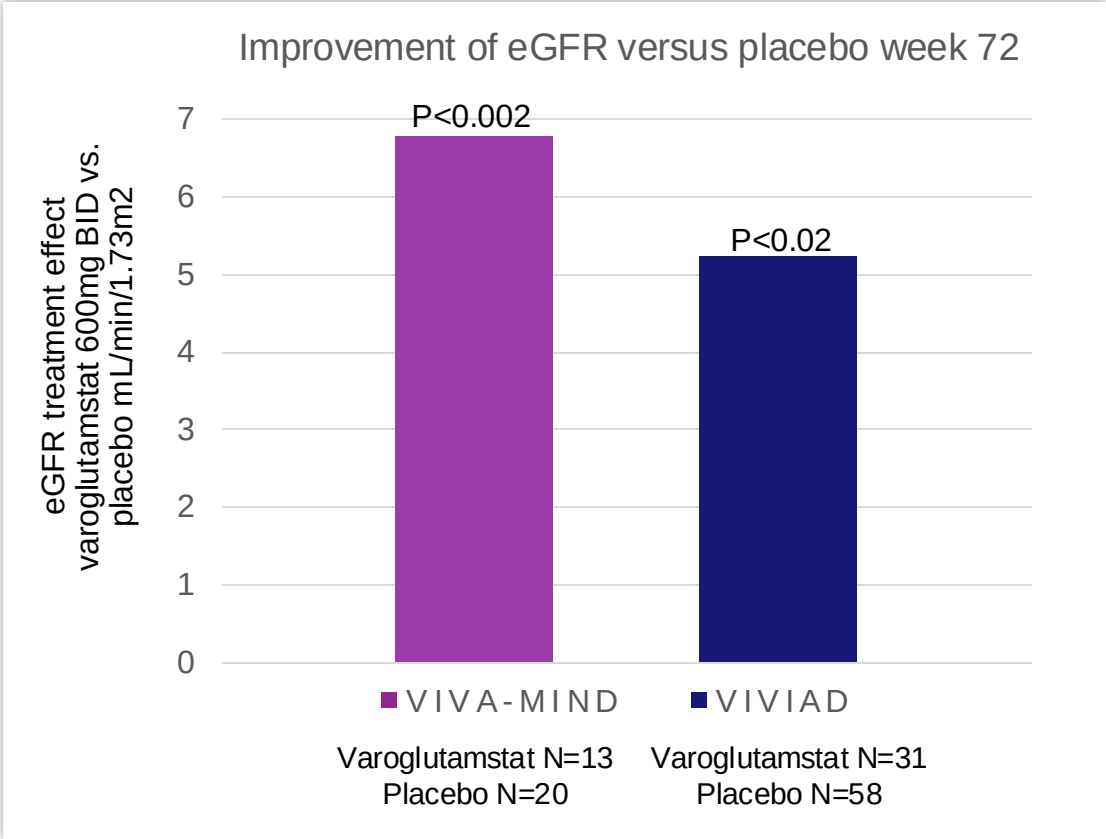

eGFR improvement of varoglutamstat versus placebo was consistent and statistically significant and clinically meaningful in both studies



*Data includes all patients and all visits with data in the observation period; * Periods adjusted to slower dose escalation and longer treatment duration in VIVIAD. MDRD calculation for eGFR, effect size calculated as weighted average; [a] Corrected from the previously reported p<0.001*

# Cross study comparison VIVA-MIND and VIVIAD
# eGFR Results – weeks 60 and 72 – Last two visits on treatment VIVA-MIND




**Difference of eGFR change between varoglutamstat and placebo shows significant and clinically meaningful efficacy sustained until week 72 in VIVA-MIND consistent with results observed in VIVIAD**

*eGFR – estimated glomerular filtration rate based on creatinine and calculated using modification of diet in renal disease (MDRD) formula*

# Summary of kidney function data from varoglutamstat Phase 2 program

- ✓ Two double blind placebo-controlled studies - one conducted in Europe and one in US - showed consistent statistically significant and clinically meaningful improvement of eGFR for varoglutamstat versus placebo
- ✓ In both studies eGFR was improved above baseline and stabilized across the whole treatment period of 96 weeks (VIVIAD) and 72 weeks (VIVA-MIND)
- ✓ The results provide robust evidence of a treatment benefit
- ✓ Good safety results in VIVA-MIND with the accelerated dose escalation scheme provide pathway for a convenient and commercially viable dosing schedule
- ✓ VIVA-MIND results fully support the sample size planning with 120 or fewer patients and previously communicated target effect size of 5mL/min/1.73m$^2$ for visits between week 24 and 72 for the planned Phase 2 study in DKD patients
- ◆ Analysis of VIVA-MIND data will continue

# Financial Results & Outlook

# Financials reflect prudent spending while refocusing on kidney disease

| In €k | Nine months ended Sept. 30, 2024 | Nine months ended Sept. 30, 2023 |
|---|---|---|
| Revenue | 0 | 0 |
| Research & Development expenses | (12,582) | (10,449) |
| General & Administrative expenses | (4,897) | (6,803) |
| Net loss for the period | (17,143) | (17,120) |

| In €k | Sept. 30, 2024 | Dec. 31, 2023 |
|---|---|---|
| Cash & cash equivalents | 12,467 | 18,562* |
| Financial assets | 59 | 10,165* |

Updated cash runway into Q3 2025 – driven by cash utilization reduction through lower spending on clinical development and efforts to optimize operating expenses while supporting kidney disease strategy

Further funding and/or partnerships required to support potential future clinical studies and/or to extend cash runway beyond current guidance



** Liquid funds in amount of EUR 10m have been deposited on a short-term basis with banks as term deposits. Thus, total liquid funds include cash & cash equivalents of EUR 18.6m and term deposits of EUR 10m.*

# Looking ahead: Upcoming value drivers

## 2024

- **VIVIAD data readout** ✓
- **Strategic shift to kidney disease** ✓
- **VIVIAD kidney data at ASN** ✓
- **VIVA-MIND data readout** ✓

## 2025

- **MoA/biomarker data**
- **Orphan kidney pre-clinical data**
- **Start Ph. 2 DKD study[1]**
- **Potential to start small orphan disease study[1]**

## 2026+

- **Ph. 2 DKD study interim data**
  (~15 months post P2 initiation)
- **Ph. 2 DKD study full data**
  (~15 months post P2 interim)

[1] *Subject to funding / partnership*

# Vivoryon: Phase 2 program confirms varoglutamstat as a leading compound for further development in kidney disorders including DKD

- Strong scientific base; novel MoA (QPCT/L inhibition); pE-CCL2 data confirms target engagement
- Two independent studies; compelling long-term kidney function improvement; clear dose response
- Extensive safety data package for varoglutamstat with convenient dose escalation scheme
- Focused development plan for significant commercial opportunity in DKD and beyond
- Additional potential orphan indications e.g. Alport Syndrome / Fabry Disease
- Composition of matter patent protection[1] expected to 2044+
- Cash runway into Q3 2025; actively pursuing funding and BD opportunities

[1] *Current composition of matter patent to 2031 with additional potential for Hatch-Waxman extension of up to 5 years, new patent filings being evaluated.*

# Q&A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