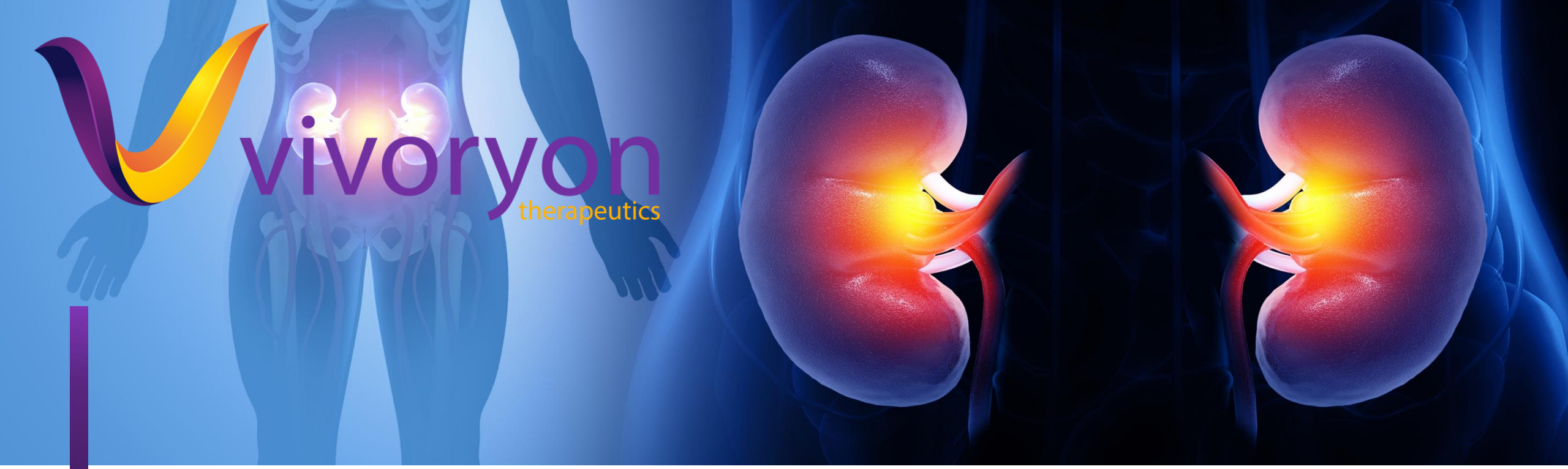

Improving Kidney Health Outcomes
Lead Program: Varoglutamstat in Diabetic Kidney Disease

January 2025

Vivoryon Therapeutics N.V.

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Forward-looking statements speak only as of the date they are made, and we do not undertake any obligation to update them in light of new information or future developments or to release publicly any revisions to these statements in order to reflect later events or circumstances or to reflect the occurrence of unanticipated events or otherwise, except as required by applicable law.

Vivoryon: Poised to improve kidney health with varoglutamstat's novel mechanism of action and breakthrough clinical results

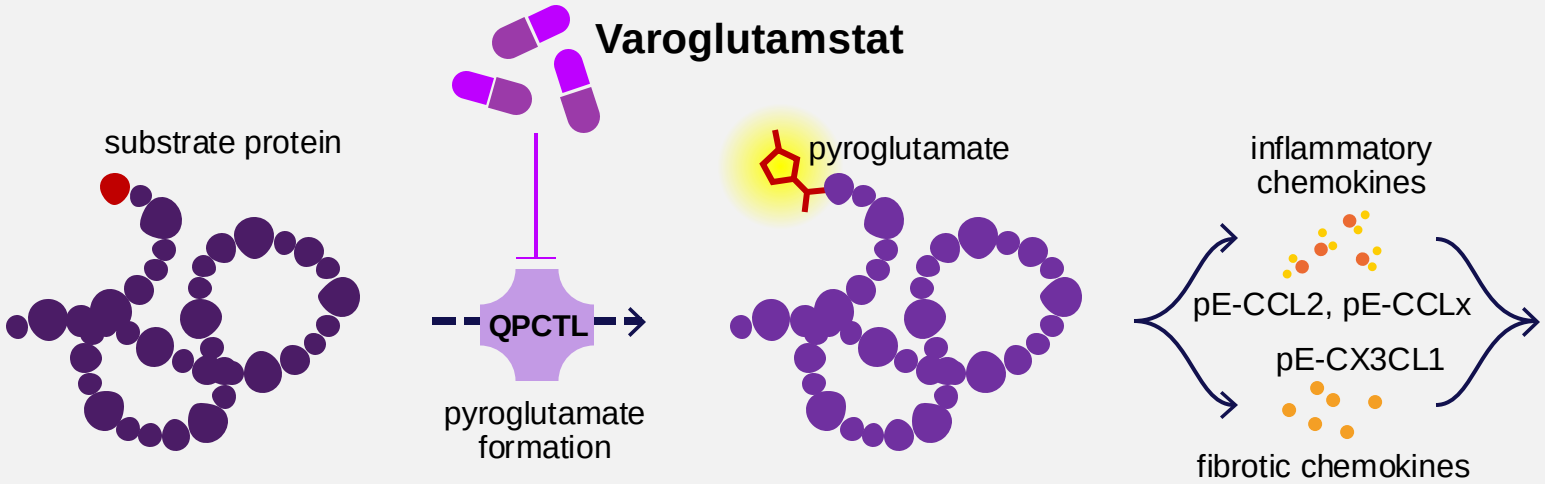
- Strong scientific base; novel MoA (QPCT/L inhibition); pE-CCL2 data confirms target engagement
- Two independent Phase 2 studies[1]; compelling long-term kidney function improvement
- Extensive safety data package for varoglutamstat with convenient dose escalation scheme
- Focused development plan for significant commercial opportunity in DKD and beyond
- Additional potential orphan indications e.g. Alport syndrome / Fabry disease
- Composition of matter patent protection[2] expected to 2044+
- Cash runway into Q3 2025; actively pursuing funding and BD opportunities

[1] *VIVIAD and VIVA-MIND Phase 2 studies in early Alzheimer's disease (AD) included prospectively defined measures of kidney function as safety and other exploratory endpoints, the primary and secondary endpoints in early AD were not met;*

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

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	↓

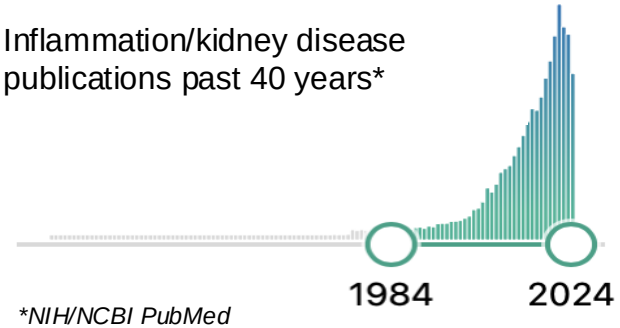
Fibrosis	
Collagen 3	↓
α-SMA	↓
CX3CL1	↓

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 chemokynes; Notes: Graphic is for illustrative purposes only.

Robust research supports development of QPCTL inhibitors in inflammatory and fibrotic kidney and liver disorders

Inflammation/kidney disease publications past 40 years*



*NIH/NCBI PubMed

Pharmacological inhibition of the chemokine CCL2 (MCP-1) diminishes liver macrophage infiltration and steatohepatitis in chronic hepatic injury

Baeck et. al. 2012

N-terminal pyroglutamate formation in CXC3CL1 is essential for its full biologic activity

Kehlen et. al. 2017

Inhibition of Glutaminyl Cyclases alleviates CCL2-mediated inflammation of non-alcoholic fatty liver disease in mice

Cynis et al., 2013

Chronic treatment with the (iso-)glutaminyl cyclase inhibitor PQ259 is a novel and effective approach for glomerulonephritis in chronic kidney disease

Kanemitsu et. al. 2021

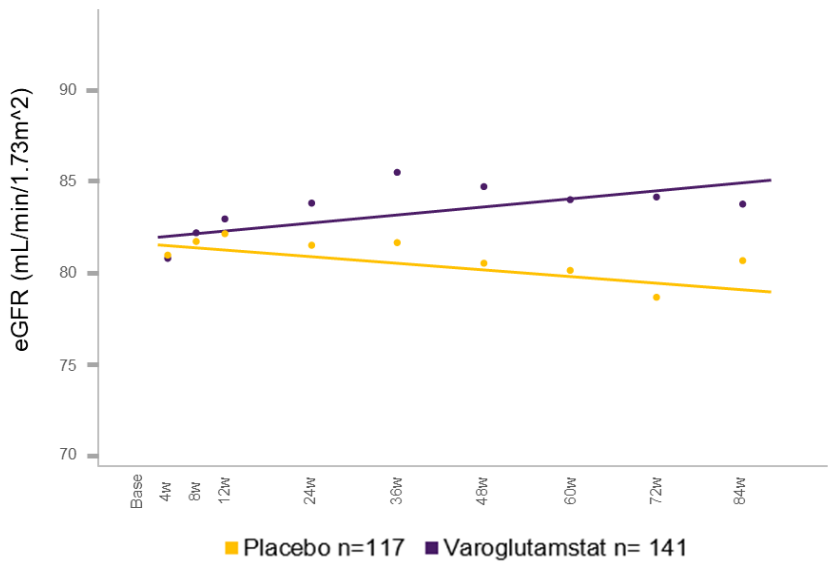
- Discovered and established pE-CCL2 as direct biomarker for QPCTL engagement
- Dose-dependent decrease of pE-CCL2 levels directly correlates with eGFR improvement

Cynis et.al. Int, J of Exp Pathol, 2013; Baeck et.al., Gut, 2012; Chang et.al. Int J Mol Sci., 2020; Kanemitsu et al., Naunyn Schmiedebergs Arch Pharmacol, 2021; Kehlen et al, Biosci Rep, 2017

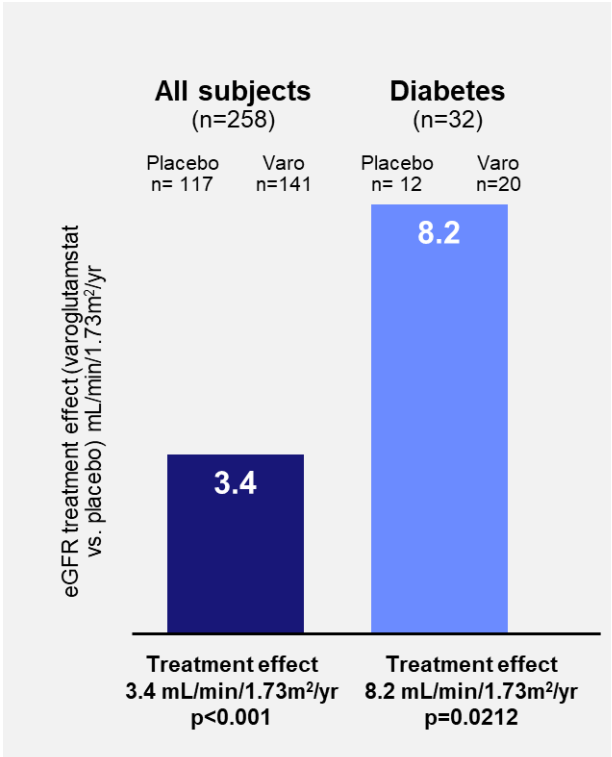
VIVIAD: Breakthrough clinical results show statistically significant improvement in prospectively defined eGFR over two years

Validated regulatory primary endpoint

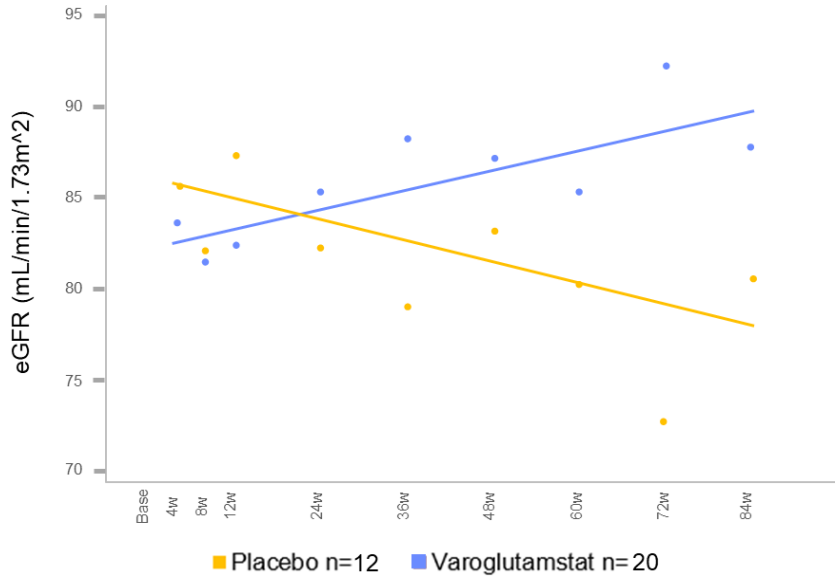
All subjects
Change in eGFR over time
Slope analysis



Magnitude of effect of slope analysis



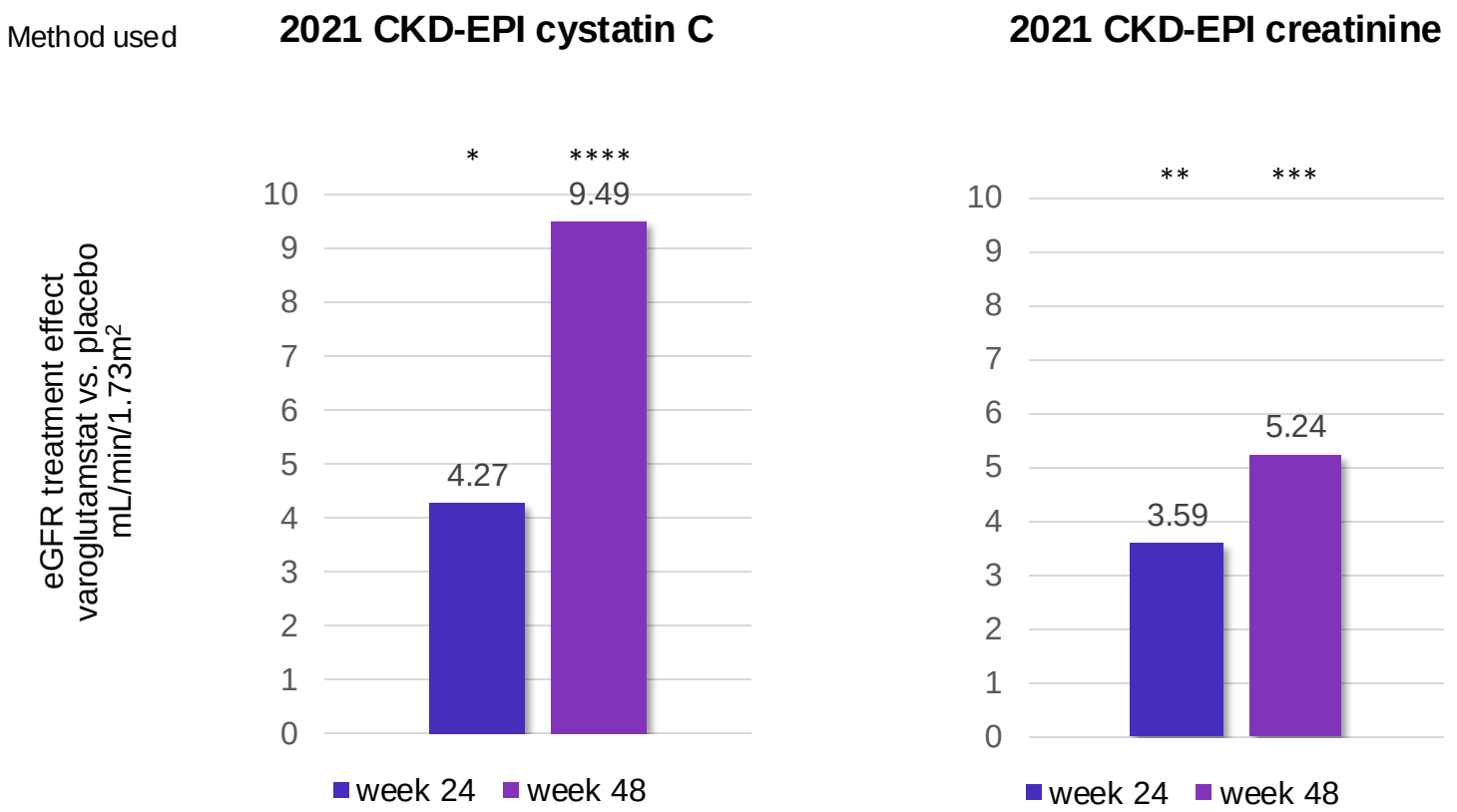
Diabetes
Change in eGFR over time
Slope analysis



Protocol for VIVIAD Phase 2b in early AD included investigation of kidney function to explore role of QPCTL inhibition; eGFR: estimated glomerular filtration rate based on creatinine, calculated using modification of diet in renal disease (MDRD) method, creatinine measured at 12-week intervals; Treatment effect: difference between eGFR slope in varoglutamstat-treated patients vs. placebo

VIVIAD: Consistency of results using diverse and validated methods for eGFR assessment

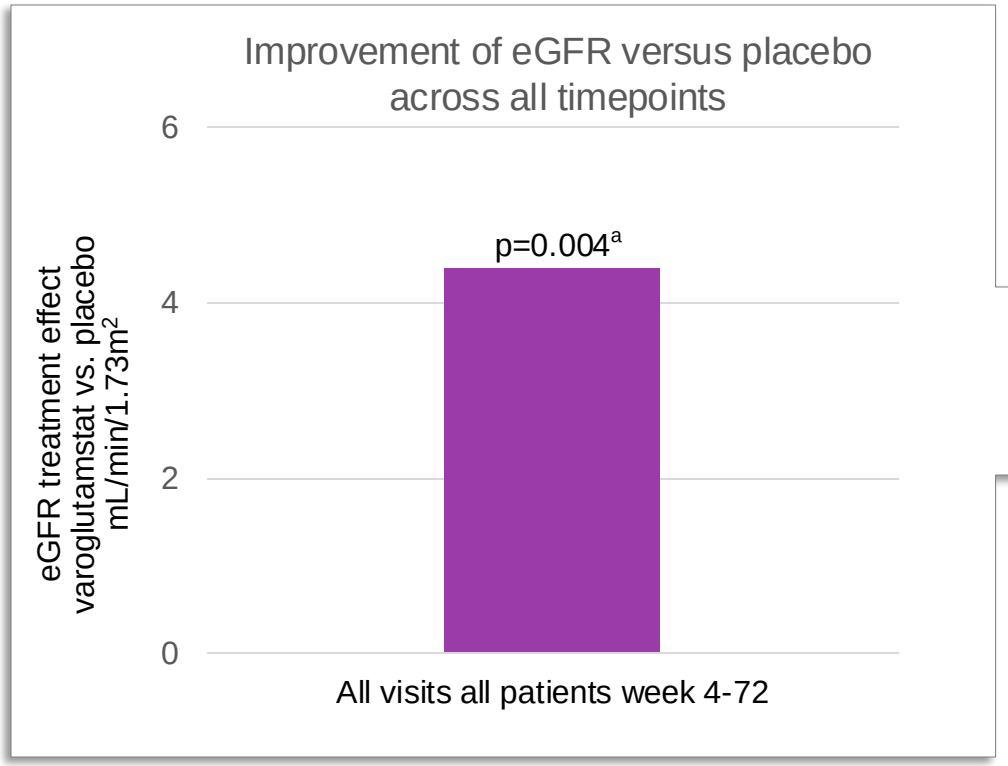
Sensitivity analysis: baseline adjusted treatment effect of varoglutamstat versus placebo



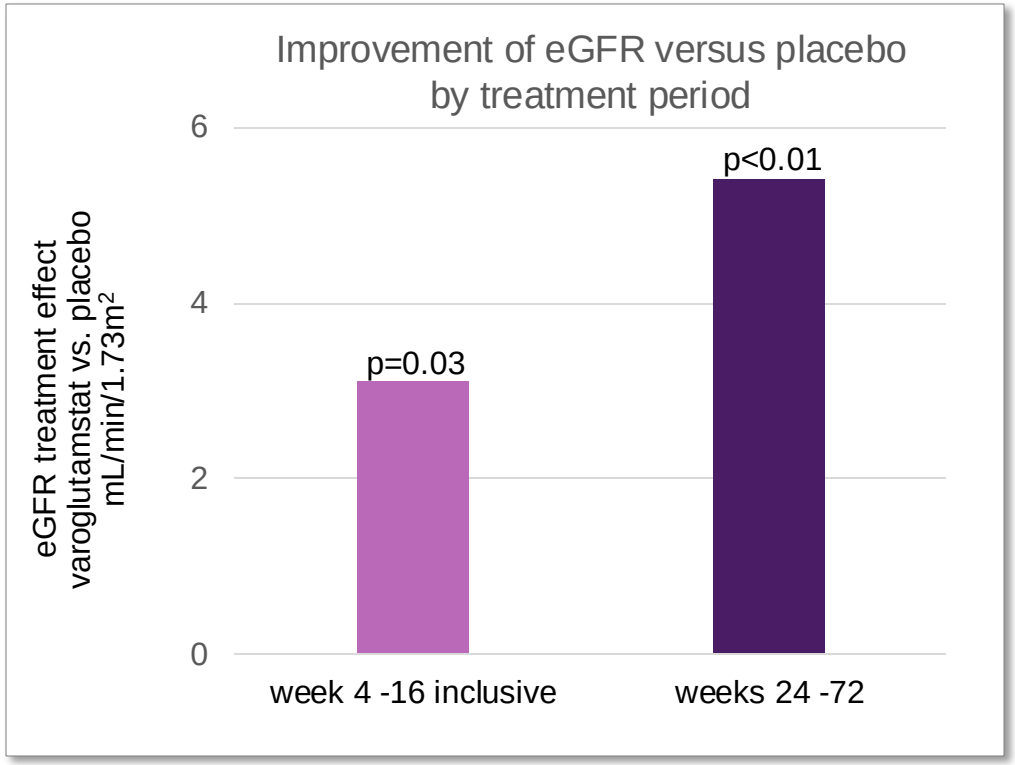
* significant difference (with p<0.05) ** significant difference (with p<0.01) *** significant difference (with p<0.001) **** significant difference (with p<0.0001)
MMRM analysis: Change from baseline difference between varoglutamstat and placebo at specific timepoints from dedicated biomarker samples

CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration); eGFR assessed by Cystatin C and additional Creatinine measurement (Atellica CH analyser)

VIVA-MIND: Statistically significant and clinically meaningful improvement vs. placebo in kidney function measured by eGFR (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

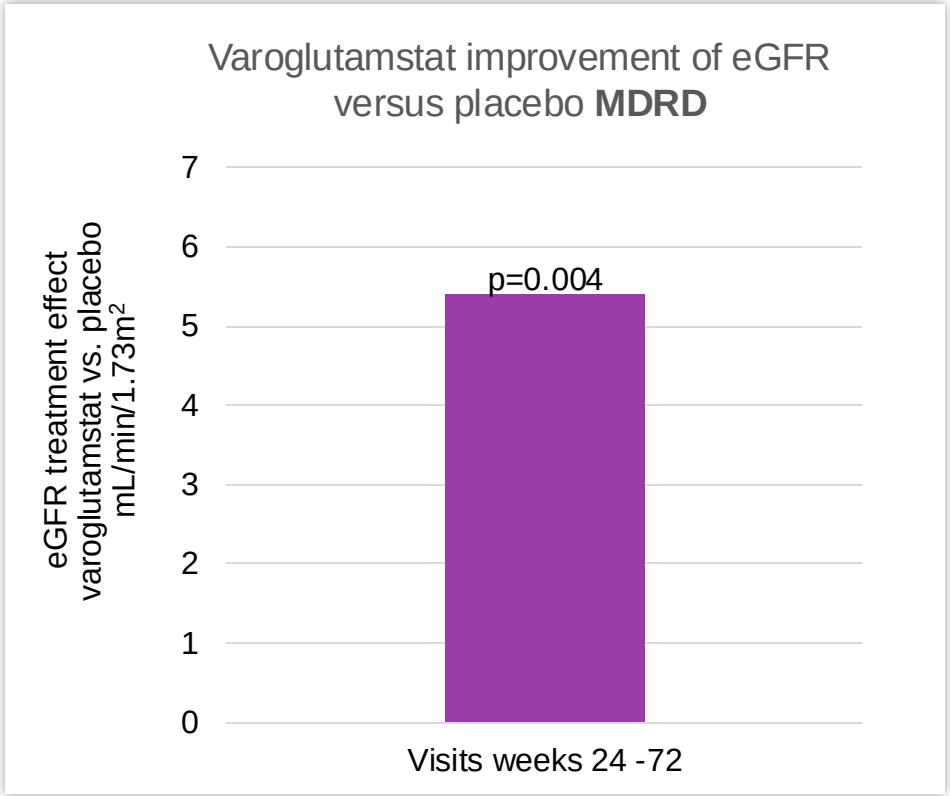
Placebo n=57, Varoglutamstat 600mg BID n=52

MMRM analysis: Change from baseline, difference between varoglutamstat and placebo

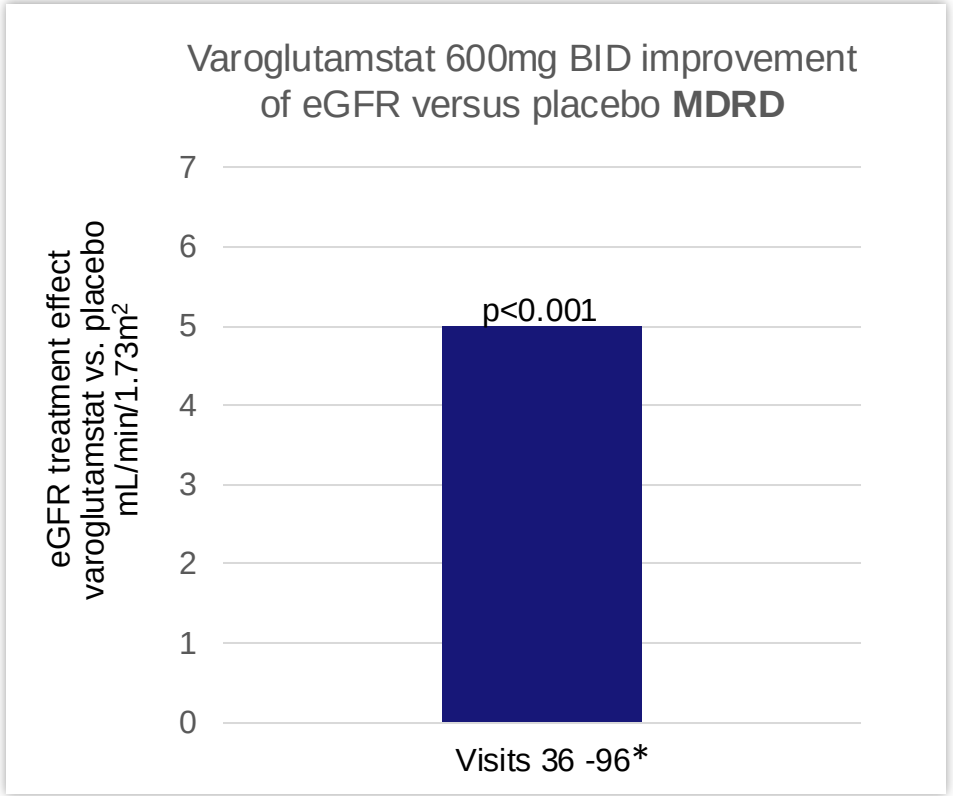
[a] *Corrected from the previously reported p<0.001; More information on VIVA-MIND Phase 2 study at clinicaltrials.gov ID NCT03919162*

eGFR Results Comparison VIVA-MIND – VIVIAD

VIVA-MIND



VIVIAD



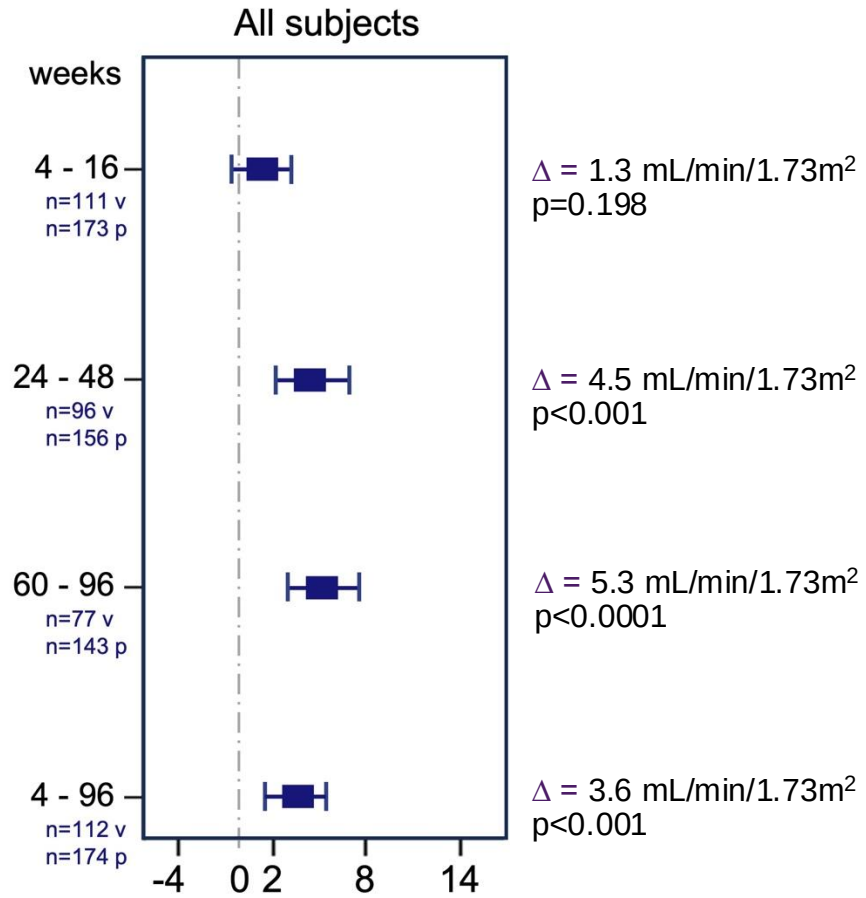
eGFR improvement of varoglutamstat versus placebo was consistent and statistically significant and clinically meaningful in both studies

MDRD calculation for eGFR, MMRM analysis: Change from baseline, difference between varoglutamstat and placebo

*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*

VIVIAD and VIVA-MIND: Meta-analysis shows strong effect on eGFR

Difference of change from baseline between varoglutamstat (v) and placebo (p) of eGFR (MDRD)



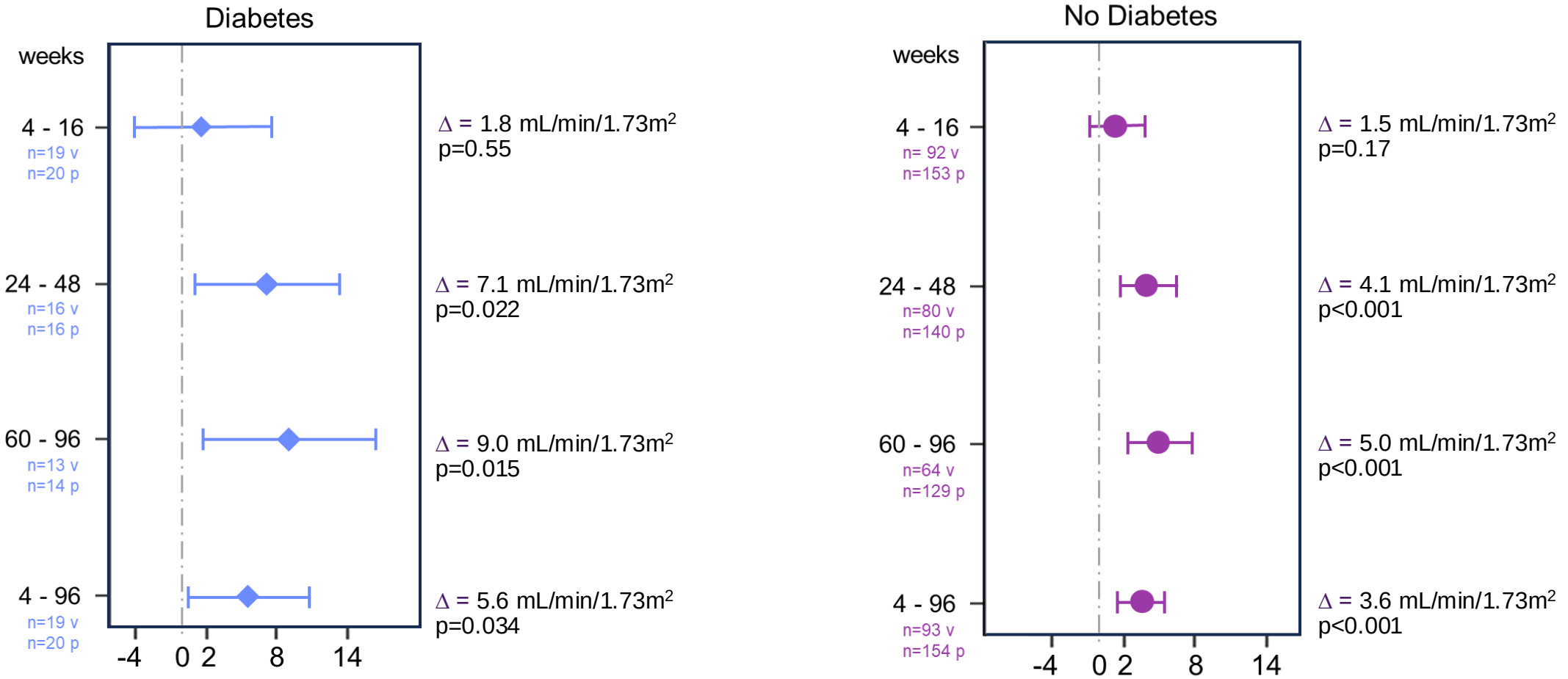
Treatment effect and 95% confidence intervals (mL/min/1.73m^2)
0: No treatment effect; >0: Improvement of eGFR (MDRD);
n: Number of patients in the varoglutamstat (v) and placebo (p) group

- Meta-analysis includes all patients on placebo and all patients randomized to 600mg varoglutamstat BID of both studies (patients randomized to 300mg BID in VIVIAD not included)
- Improvement of eGFR – kidney function is demonstrated in the total population
- Difference of change from baseline between varoglutamstat and placebo becomes significant at week 24
- Treatment effect is maintained for 2 years

VIVIAD Phase 2b in early AD included investigation of kidney function (eGFR) over up to 96 weeks; VIVA-MIND Phase 2 study in early AD included investigation of kidney function (eGFR) over up to 72 weeks; eGFR: estimated glomerular filtration rate based on creatinine, calculated using modification of diet in renal disease (MDRD) method; Meta analysis of change from baseline (MMRM) in varoglutamstat-treated patients vs. placebo

VIVIAD and VIVA-MIND: Meta-analysis shows a larger effect size in diabetes versus non-diabetes patients

Difference of change from baseline between varoglutamstat (v) and placebo (p) of eGFR (MDRD)

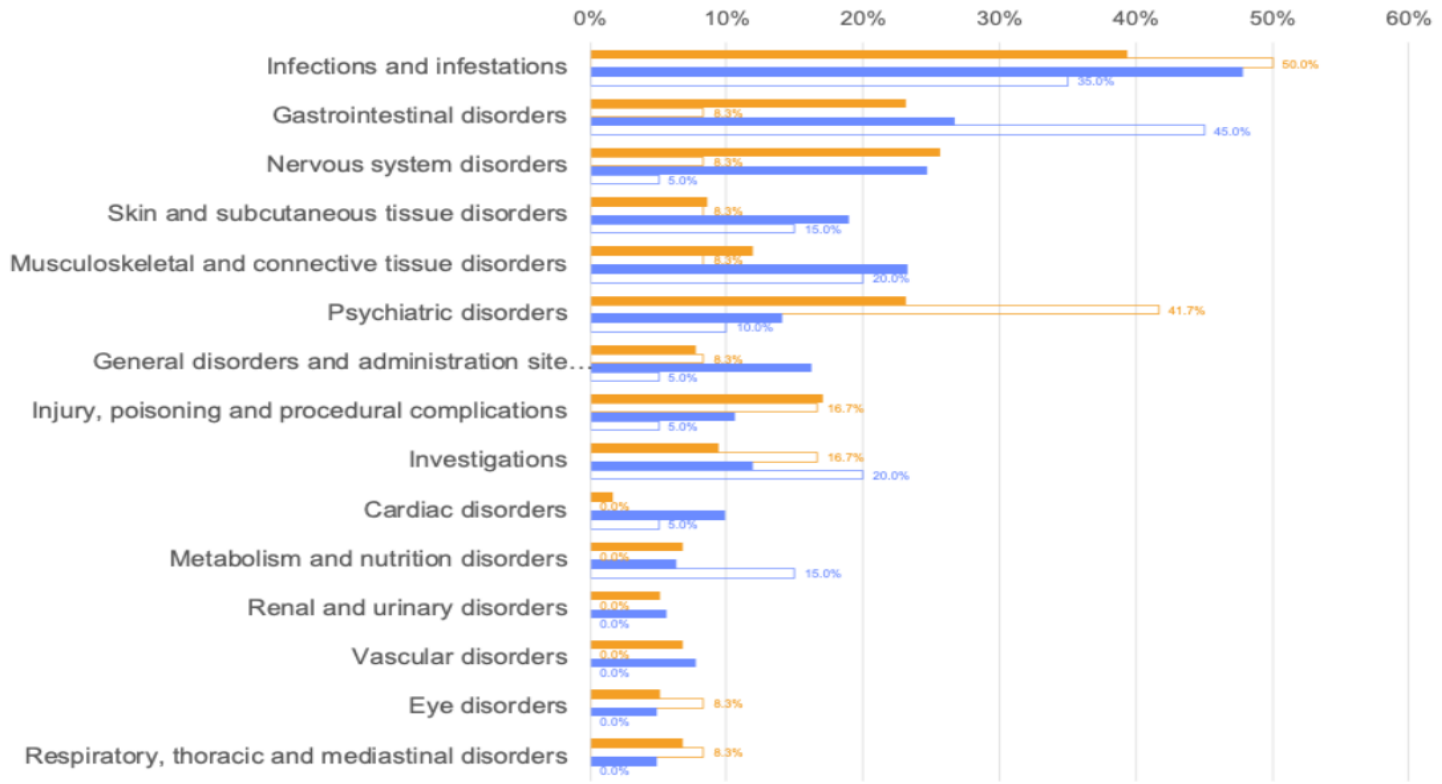


Treatment effect and 95% confidence intervals (mL/min/1.73m^2)
0: No treatment effect; >0: Improvement of eGFR (MDRD);
n: Number of patients in the varoglutamstat (v) and placebo (p) group

VIVIAD Phase 2b in early AD included investigation of kidney function (eGFR) over up to 96 weeks; VIVA-MIND Phase 2 study in early AD included investigation of kidney function (eGFR) over up to 72 weeks; eGFR: estimated glomerular filtration rate based on creatinine, calculated using modification of diet in renal disease (MDRD) method; Meta analysis of change from baseline (MMRM) in varoglutamstat-treated patients vs. placebo

VIVIAD: Excellent safety profile consistent across two years of study duration

VIVIAD Phase 2b study
% of patients with at least one TEAE[1]



[1] % of patients with at least one Treatment-Emergent Adverse Events (TEAE) in a System Organ Class, lists only occurrence > 5% in the total population; Diabetes subgroup: 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 a HbA1c > 6.5%.

VIVA-MIND: No new safety signals identified in second Phase 2 study

VIVA-MIND Phase 2 study			
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

Extensive safety package
(# / duration)

Pharmacology / Phase 1

- Phase 1 study: large trial with 205 subjects
- Human ADME / mass balance study completed

Phase 2 double-blind, placebo-controlled

- Phase 2a study: 120 patients, 12 weeks
- VIVIAD Phase 2b study: 259 patients, avg. treatment duration ~80 weeks
- VIVA-MIND Phase 2 study: 109 patients treated, avg. treatment duration ~46 weeks

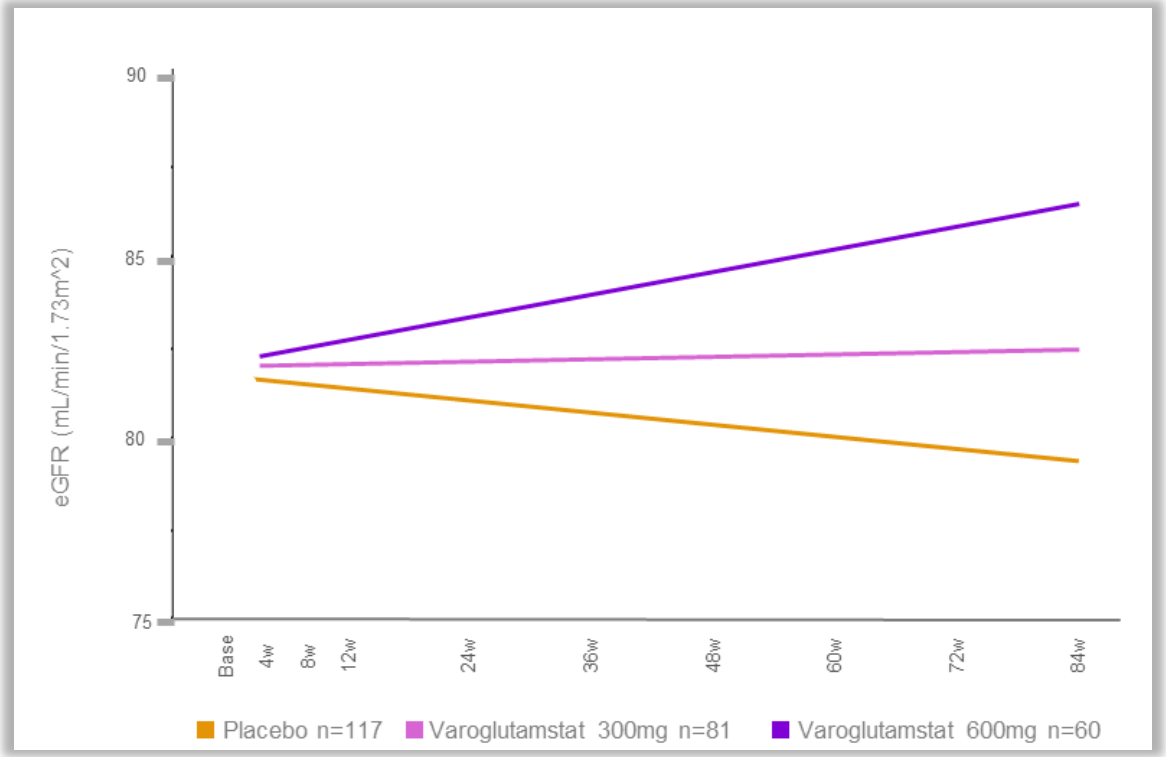
[1] One patient died after a head injury from a fall and the patient had a patient's provision to not resuscitate. A second patient had surgery for gastrointestinal bleeding after stopping study medication and died from complications of the surgery several weeks later. The deaths were considered not / 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*

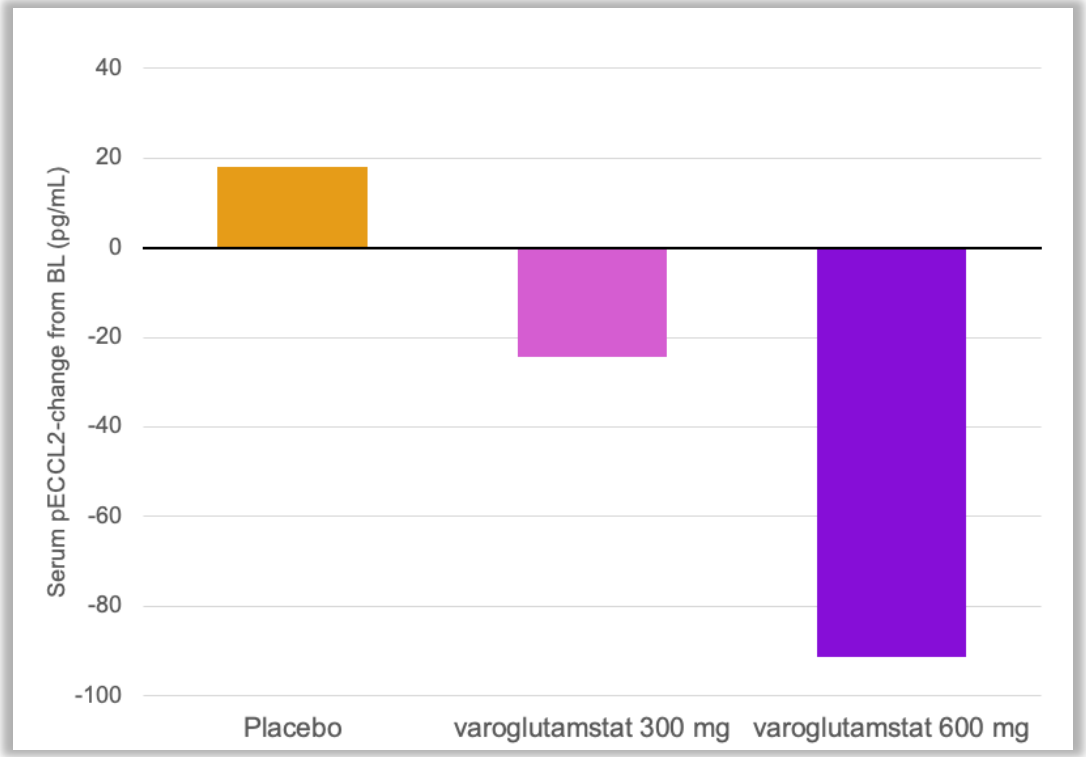
Clear dose-finding results strongly correlated with MoA and biomarker

Reduction of pE-CCL2 in VIVIAD correlates with improvement of eGFR

Varoglutamstat effect on kidney function outcomes
(total population; change in eGFR over time (MDRD)[1])



Median reduction in pE-CCL2 levels at week 48 compared to baseline with varoglutamstat
(total population)

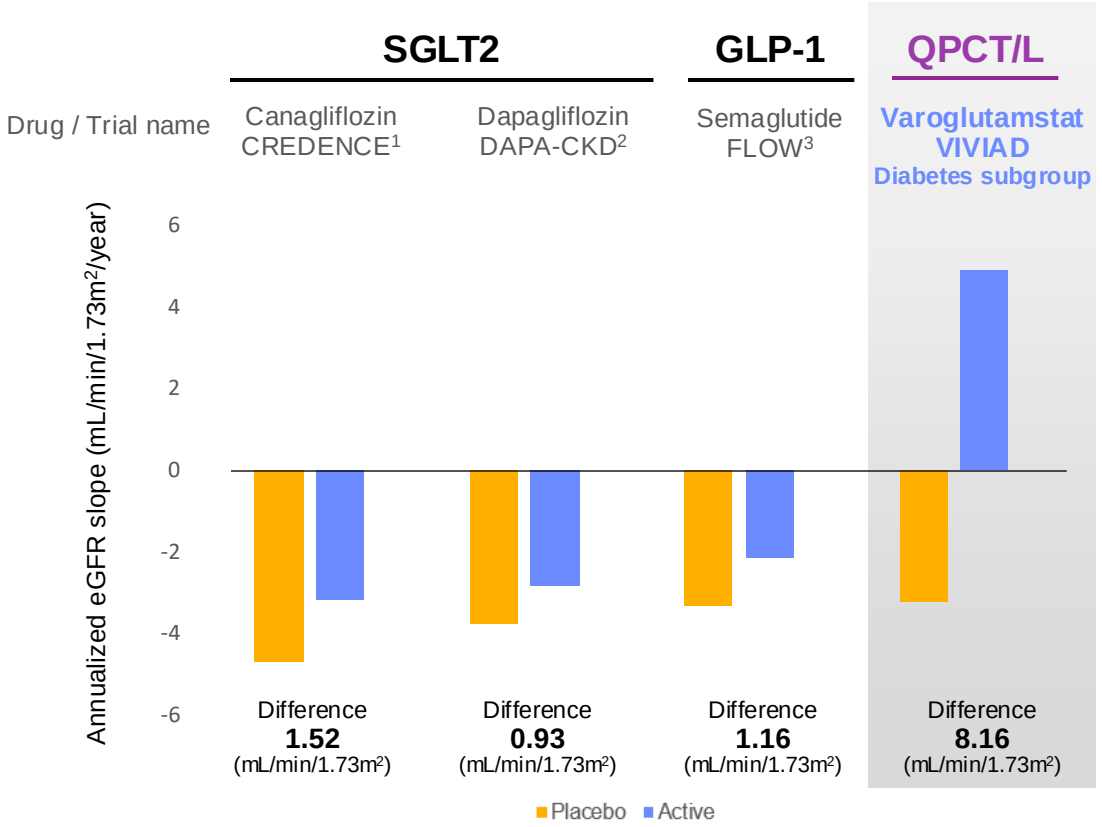


[1] *Chart shows change in eGFR (estimated glomerular filtration rate) over time based on creatinine and calculated using modification of diet in renal disease (MDRD) method*

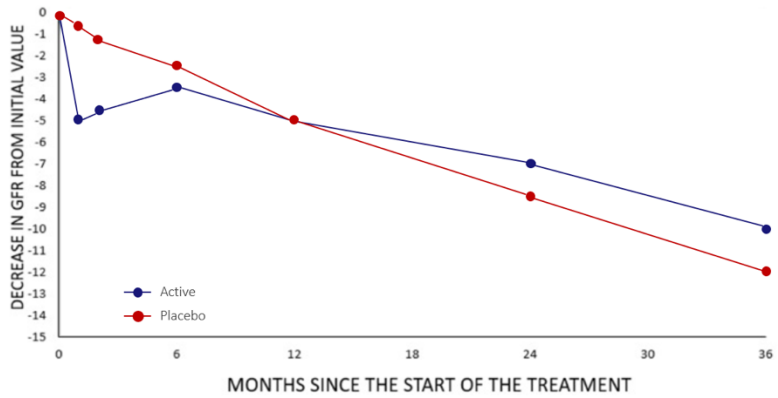
Summary of kidney function data from varoglutamstat Phase 2b program

- ✓ Two double blind placebo-controlled studies - one conducted in Europe and one in U.S. - 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)
- ✓ Meta-analysis shows an approximately two times larger effect size in the diabetes population versus the non-diabetes population
- ✓ 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 2b study in DKD patients
- ◆ Analysis of VIVA-MIND data will continue

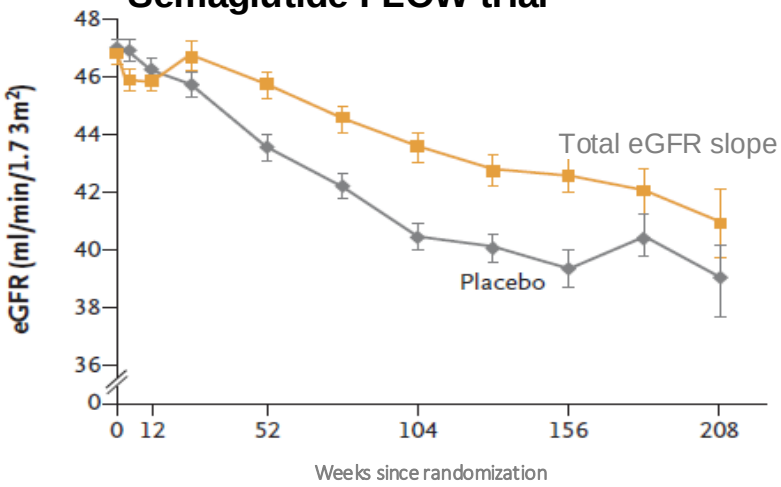
Outstanding commercial potential: Currently available, highly successful medicines only slow disease progression in DKD



SGLTi eGFR (compiled)[4]



Semaglutide FLOW trial

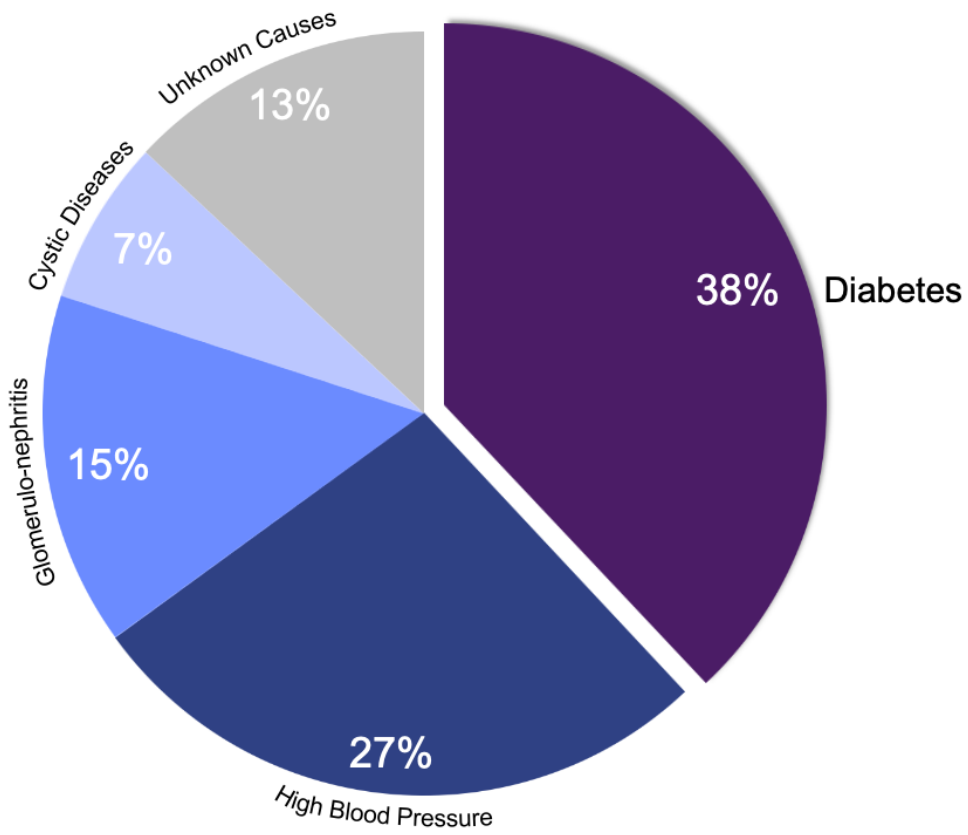


[1] Perkovic et al., N Engl J Med, 2019; [2] Heerspink et al. N Engl J Med, 2020; [3] Perkovic et al., N Engl J Med, 2024; [4] schematic based on Costanzo et al., Int. J. Mol. Sci. 2023; SGLT2 – sodium glucose cotransporter-2 inhibitor class; GLP-1 Glucagon-like peptide class (semaglutide is a GLP-1 receptor agonist); QPCT/L – varoglutamstat inhibits the glutaminyl cyclases QPCT and QPCTL; Note: Graphics and charts are for illustrative purposes, not intended to be direct comparisons between studies

DKD[1] is the leading cause of end stage kidney disease (ESKD)

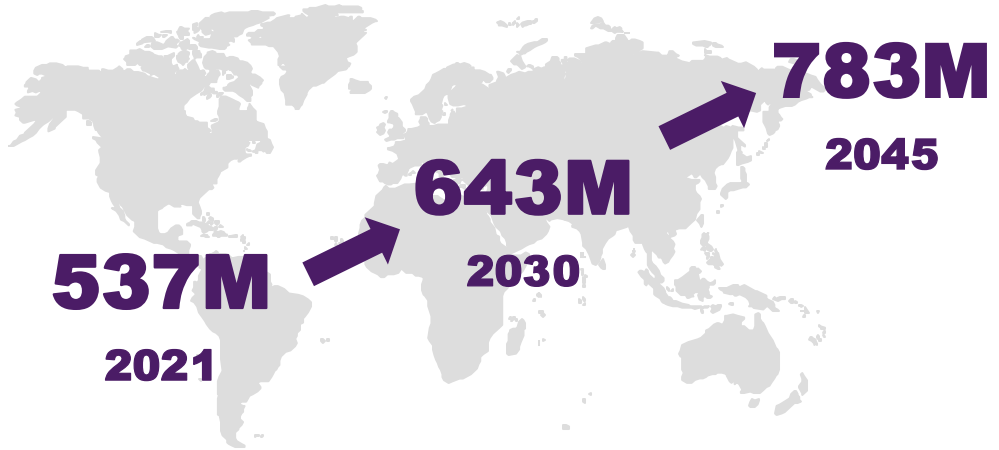
Inflammation and fibrosis are key underlying pathways in DKD

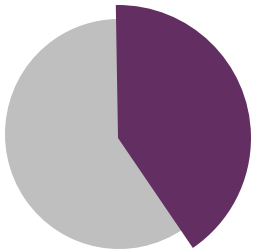
Diabetes is a leading cause of end-stage kidney disease[2]



Diabetes is a significant and growing global challenge

(adults aged 20-79 years with diabetes, worldwide)[3]





~40%

of people with diabetes may develop diabetic kidney disease (DKD)[4]

1 in 10

people with diabetes may end up with end-stage kidney disease[4]

[1] *Diabetic Kidney Disease (DKD): typically, DKD is defined by the presence of CKD characterized by persistently (≥ 3 months) elevated urinary albumin excretion (albumin-to-creatine ratio [ACR] ≥30 mg/g) and/or low eGFR (< 60mL/min/1.73 m²) in a person with diabetes (Levin et al., Kidney Int. Suppl. 2013, KDIGO group);*
[2] *U.S. Renal Data System;* [3] *International Diabetes Federation (IDF) Atlas 2021;* [4] *Qazi et al., EMJ Nephrol, 2022.*

Planned Phase 2b study in stage 3b/4 DKD on top of standard of care[1]

Draft study design, with anticipated interim analysis at 15 months after study start

Enrollment:

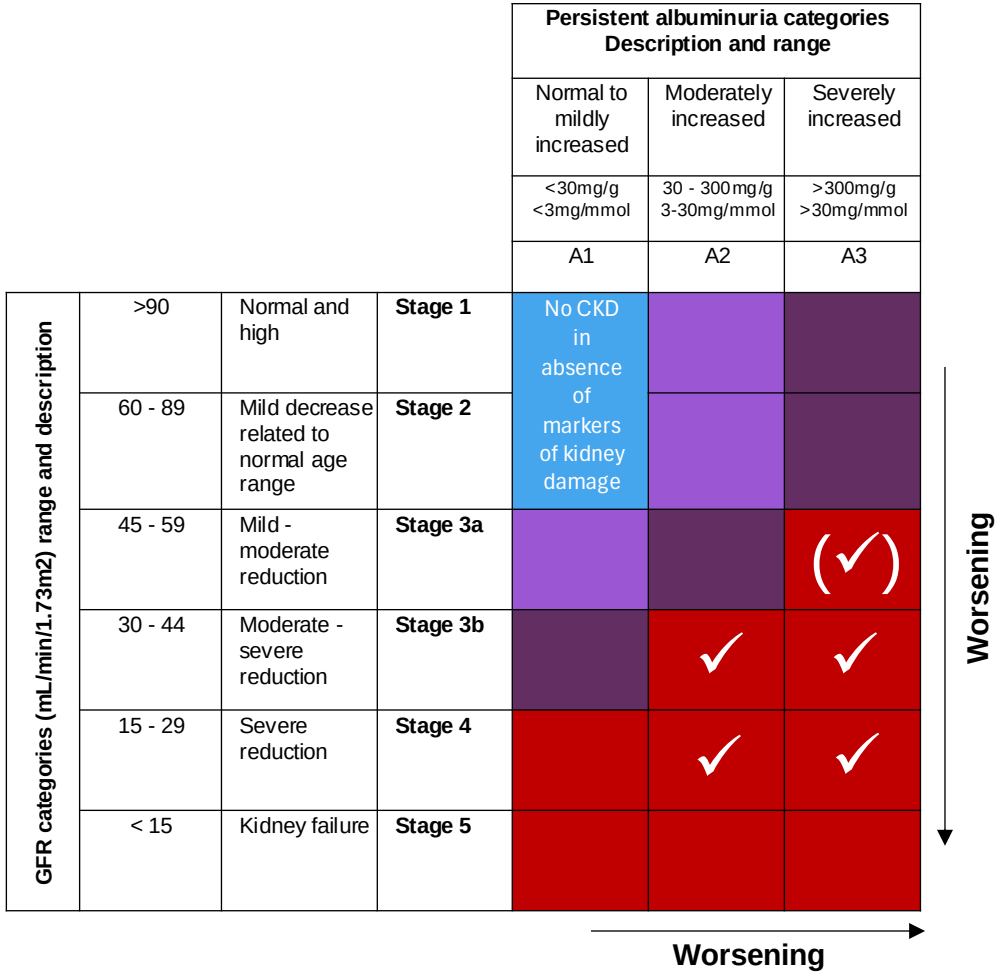
- Patients: Diabetes patients with CKD 3b/4 eGFR
- Number of patients: up to 120
- Regions: U.S. and Western Europe

Draft design:

- Double-blind placebo-controlled
- Powered to confirm effect size of at least 3.5mL/min eGFR slope; 80% power to detect a difference of 5mL/min eGFR slope

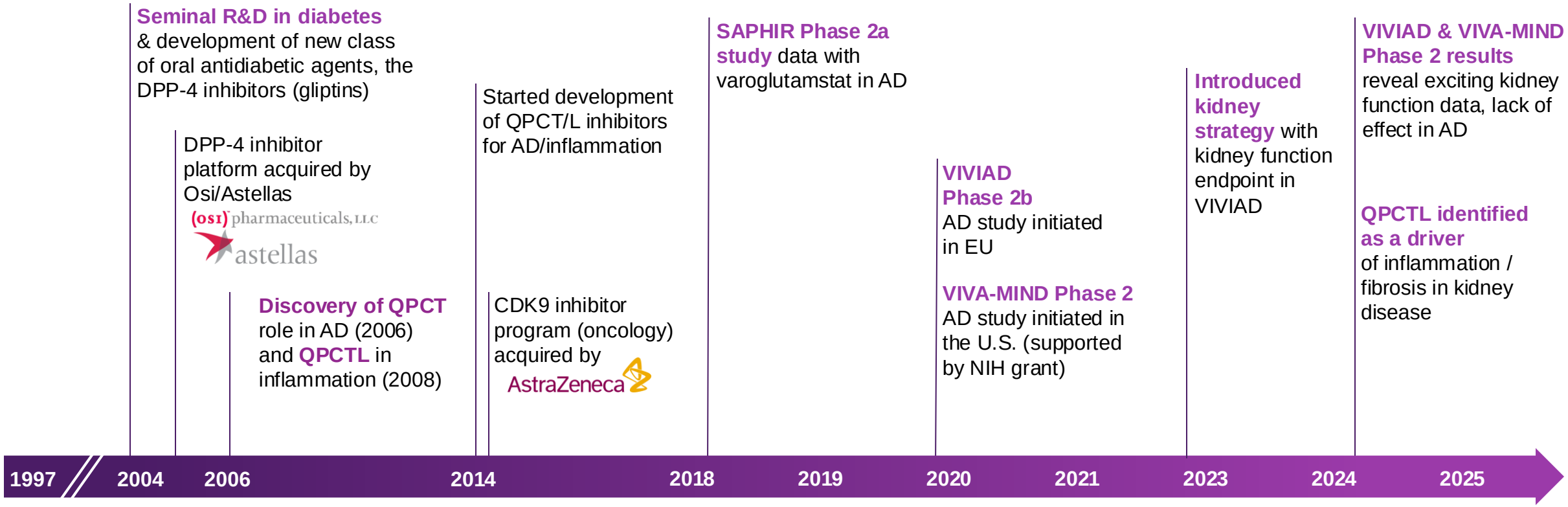
Duration/potential costs:

- Interim: until confirmation of effect size, ~15 months (~ 60 patients)
- Full: study completion approx. 2.5 yrs; typical trial cost approx. EUR 10 – 12m [2]



[1] *Clinical trial subject to further funding / partnership;*
[2] *Based on typical industry costs for Phase 2 in similar indications*

Vivoryon: A history of groundbreaking discoveries and developments



AD: Alzheimer's disease

A trusted company: Senior management team with a strong track record

Executive Directors

Frank Weber, MD
Chief Executive Officer

InterMune · Merck · ZBiotech Zambon Biotech

Anne Doering, CFA
Chief Financial Officer

BioNTech · Merck · Franklin Templeton

Michael Schaeffer, PhD
Chief Business Officer

Sirean · Crelux a WuXi AppTec company · Crenano

Non-executive Directors

Erich Platzer, MD, PhD
Chairman of the Board

Charlotte Lohmann

Claudia Riedl, PhD
Chair Audit Committee

Samir Shah, MD

Decades of collective experience in biopharma industry, e.g.:

First approved drug in pulmonary fibrosis

Successful development of biomarker driven oncology & diabetes programs

M&A and business development **expertise** from transactions with large biopharma

Know-how in life science research & development, biophysical and structure-based drug discovery

Strong financial, capital markets and legal **experience**

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. 2b DKD study[1]**
- **Potential to start small orphan disease study[1]**

2026+

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

[1] *Subject to funding / partnership*

Pipeline focused on kidney disorders and inflammatory/fibrotic diseases

	Program	Approach	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Status
Inflammatory/fibrosis incl. kidney	DKD (Varoglutamstat/PQ912)	SMI QPCT/L				*POC in VIVIAD & VIVA-MIND results*		Preparing for Phase 2b DKD study
	Kidney orphan diseases (Varoglutamstat/PQ912)	SMI QPCT/L			Pre-IND			Pre-clinical orphan disease models
	Kidney disorders, fibrotic/inflammatory (VY2149)	SMI QPCT/L			Pre-IND			
	Fibrotic indications (NCE)	SMI Meprin			Research program			
Alzheimer's disease	Varoglutamstat (PQ912)	SMI QPCT/L				*Phase 2 (high dose) under evaluation*		AD program: under evaluation after negative topline data March 2024 (VIVIAD) & December 2024 (VIVA-MIND)
	Varoglutamstat (SIM0408, PQ912)	SMI QPCT/L				*CTA approval in China*		Partnered with Simcere in Greater China
	PBD-C06	mAb N3pE amyloid			Pre-IND			Partnered with Simcere in Greater China

DKD: diabetic kidney disease; SMI: small molecule inhibitor; IND: investigational new drug; NCE: novel chemical entity; CTA: Clinical Trial Application; mAb: monoclonal antibody

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

Groundbreaking discovery	Inhibition of QPCTL reduces kidney inflammation and fibrosis
Breakthrough clinical results	Varoglutamstat – first in class QPCT/L inhibitor – shows a large and statistically significant improvement of eGFR versus placebo in two independent Phase 2 studies
Outstanding commercial potential	Substantial market opportunity in DKD with potential to prolong time before kidney replacement therapy – further potential in other kidney and liver indications
Actionable clinical plan	Completion of Phase 2 DKD program requires only one additional study
Trusted organization	Management with track record in fibrosis and business development

QPCTL: iso-glutaminyl cyclase enzyme or glutaminyl peptide cyclotransferase-like protein; DKD: Diabetic Kidney Disease

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