

The top half of the slide features a blue-toned background. On the left, there is a stylized logo consisting of a purple and yellow ribbon-like shape. In the center, the word "vivoryon" is written in a purple, lowercase, sans-serif font, with "therapeutics" in a smaller, yellow, lowercase font below it. To the right of the logo, there are two anatomical illustrations of human kidneys. The left kidney is shown in a frontal view, and the right kidney is shown in a side view. Both kidneys are rendered in a realistic style with a reddish-brown color and a glowing yellow light emanating from the renal pelvis area. The background also includes faint silhouettes of human figures showing the internal organ systems.

vivoryon
therapeutics

Improving Kidney Health Outcomes

Lead Program: Varoglutamstat in Diabetic Kidney Disease

May 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 studies¹; 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 protection in US until 2044²; expansions to ROW due end 2025



Cash runway into January 2026; actively pursuing funding and BD opportunities



Inhibiting QPCTL has potential to halt the progressive course of kidney disease through unique approach to tackle inflammation and fibrosis

Huge unmet medical need



Current treatments do not stabilize / improve kidney function leaving significant risk of ESRD (dialysis, transplant) or cardiovascular event

Inflammation a key underlying driver



Inflammation and fibrosis have long been known as key drivers of disease yet attempts to develop effective therapeutics selectively targeting key pathways have had limited success

Targeting QPCTL to unlock inflammatory approach



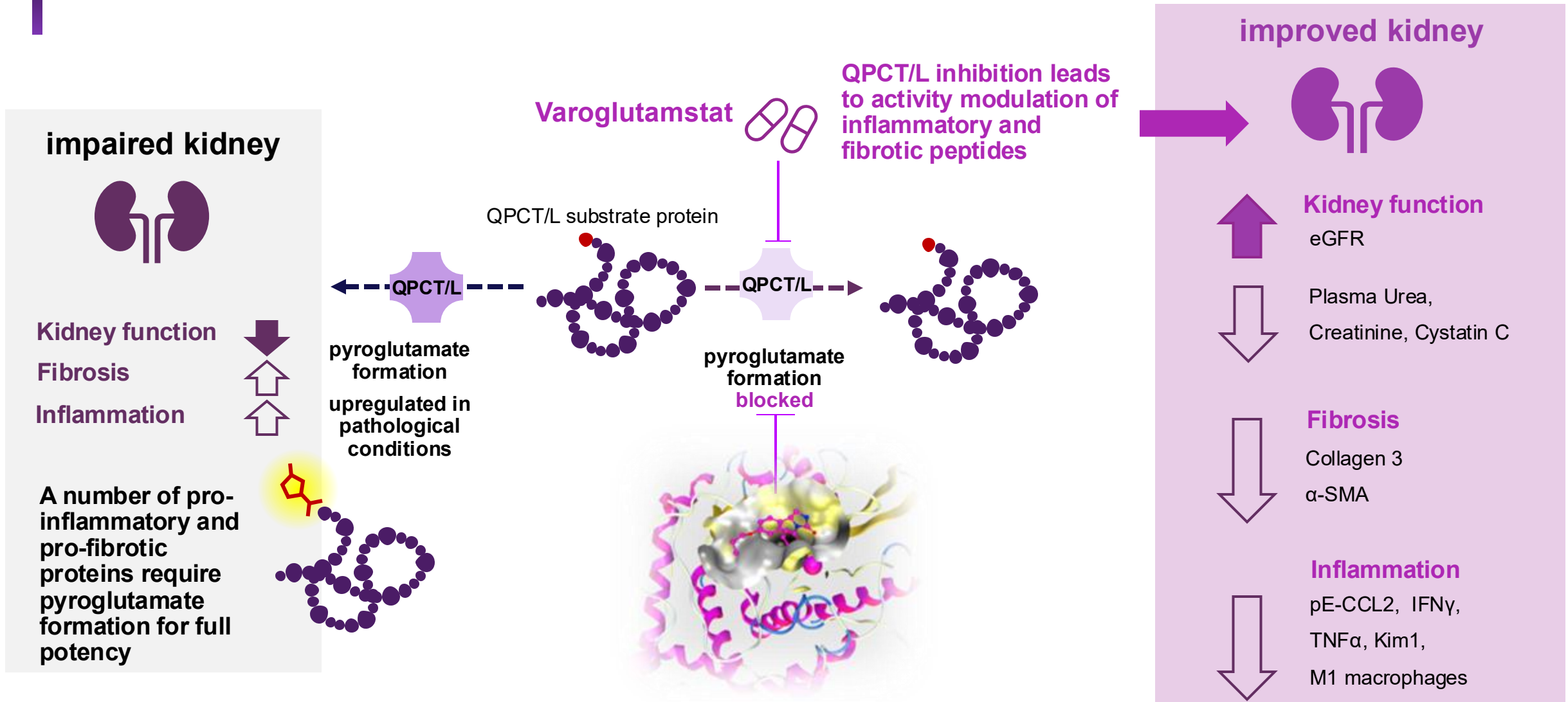
Vivoryon has identified QPCTL, an enzyme that creates pro-inflammatory pE-versions of key inflammatory proteins, as a promising target with potential to stabilize disease

Varoglutamstat

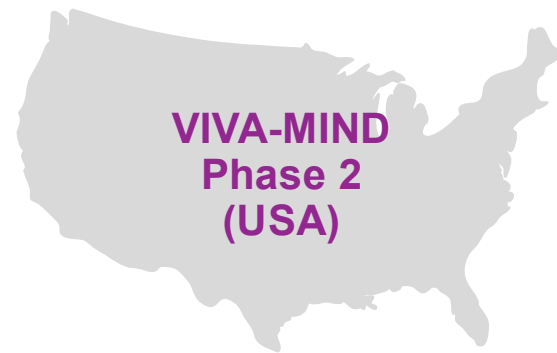
- Oral, selective QPCTL inhibitor
- Significantly improved kidney function¹ in two independent Phase 2 studies²
- Unprecedentedly large and sustainable effect size over two years



Groundbreaking discovery: Inhibition of QPCT/L reduces kidney inflammation and fibrosis, and improves pathophysiology and kidney function



Vivoryon has evaluated varoglutamstat's effect on kidney function in two independent randomized double-blind placebo-controlled Phase 2 studies



Similarities and differences between VIVIAD & VIVA-MIND

Parameter	VIVIAD (Europe)	VIVA-MIND (U.S.)
Patient selection	Mild AD, mean age 68 yrs	Mild AD, mean age 72 yrs
No. of patients treated	n=259	n=109
Varoglutamstat dose	300 and 600 mg BID	600 mg BID
Dose escalation period	Slow: 600 mg start week 13	Fast: 600 mg start week 9
Treatment duration	76 wks (mean) / 96 wks (max.)	46 wks (mean) / 72 wks (max.)
eGFR ¹ sampling	Every 12 weeks plus week 4	Every 12 weeks plus weeks 4, 8, 16
No. of patients with diabetes	n=32 (12.4%)	n=16 (14.7%)

Kidney function, measured using eGFR, was a pre-specified safety / exploratory endpoint



VIVIAD: ClinicalTrials.gov IDNCT04498650; VIVA-MIND: ClinicalTrials.gov IDNCT03919162; BID: twice daily; eGFR: estimated glomerular filtration rate, based on serum creatinine samples and calculated using the modification of diet in renal disease (MDRD) method; AD: Alzheimer's disease; Diabetes subgroup defined as patients having at baseline either medical history of diabetes (type 1 or 2, and glucose tolerance impaired, hyperglycaemia in VIVA-MIND) and/or comedication with drugs used in diabetes and/or untreated with a HbA1c > 6.5%.

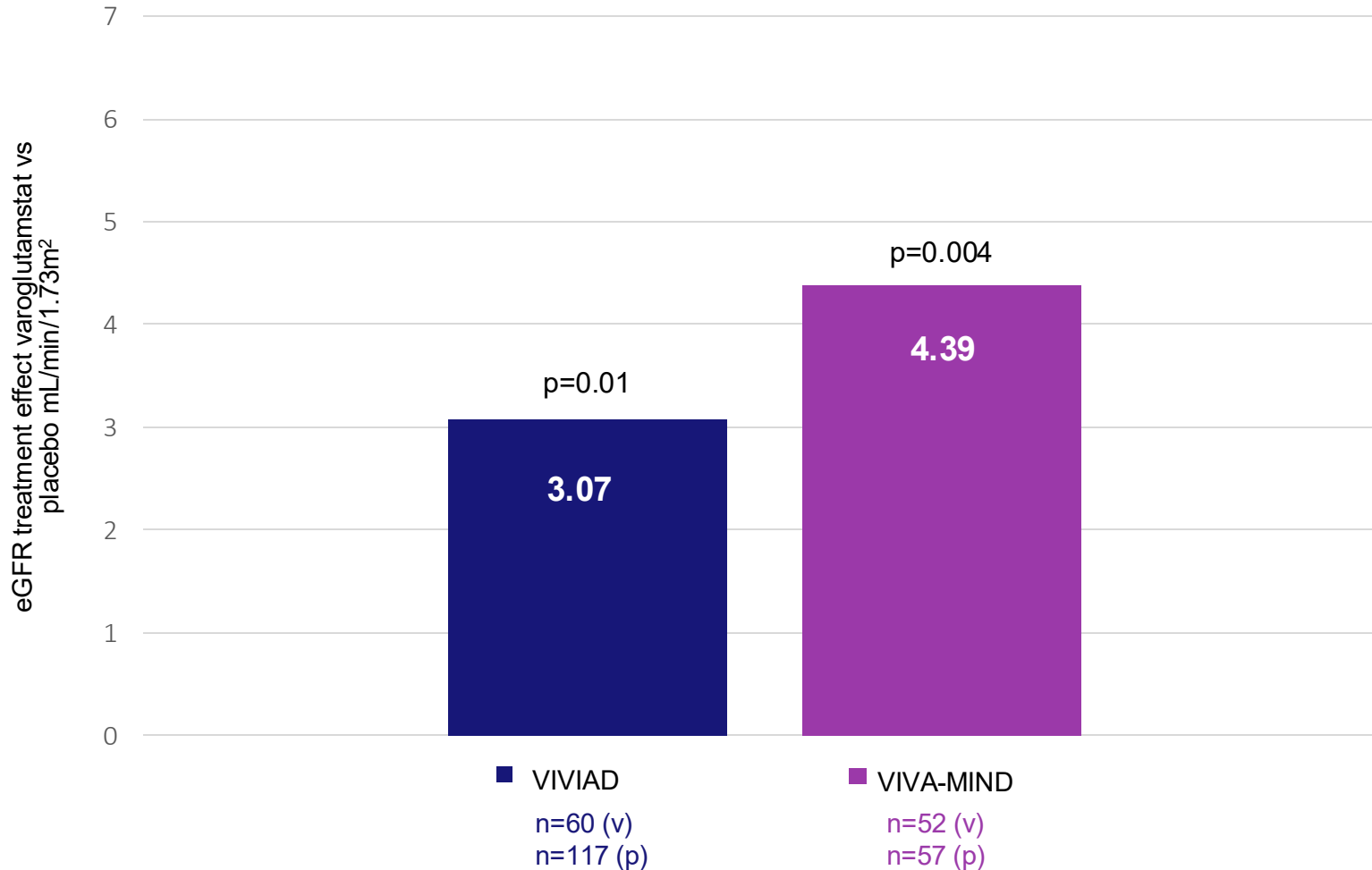
VIVIAD and VIVA-MIND both show a statistically significant and clinically meaningful improvement in eGFR over baseline

eGFR results (MDRD); all patients randomized to 600 mg BID varoglutamstat (v) and placebo (p)

eGFR treatment effect:

Difference between varoglutamstat and placebo (LSmean change from baseline)

Total population, 600 mg BID patients only, all visits

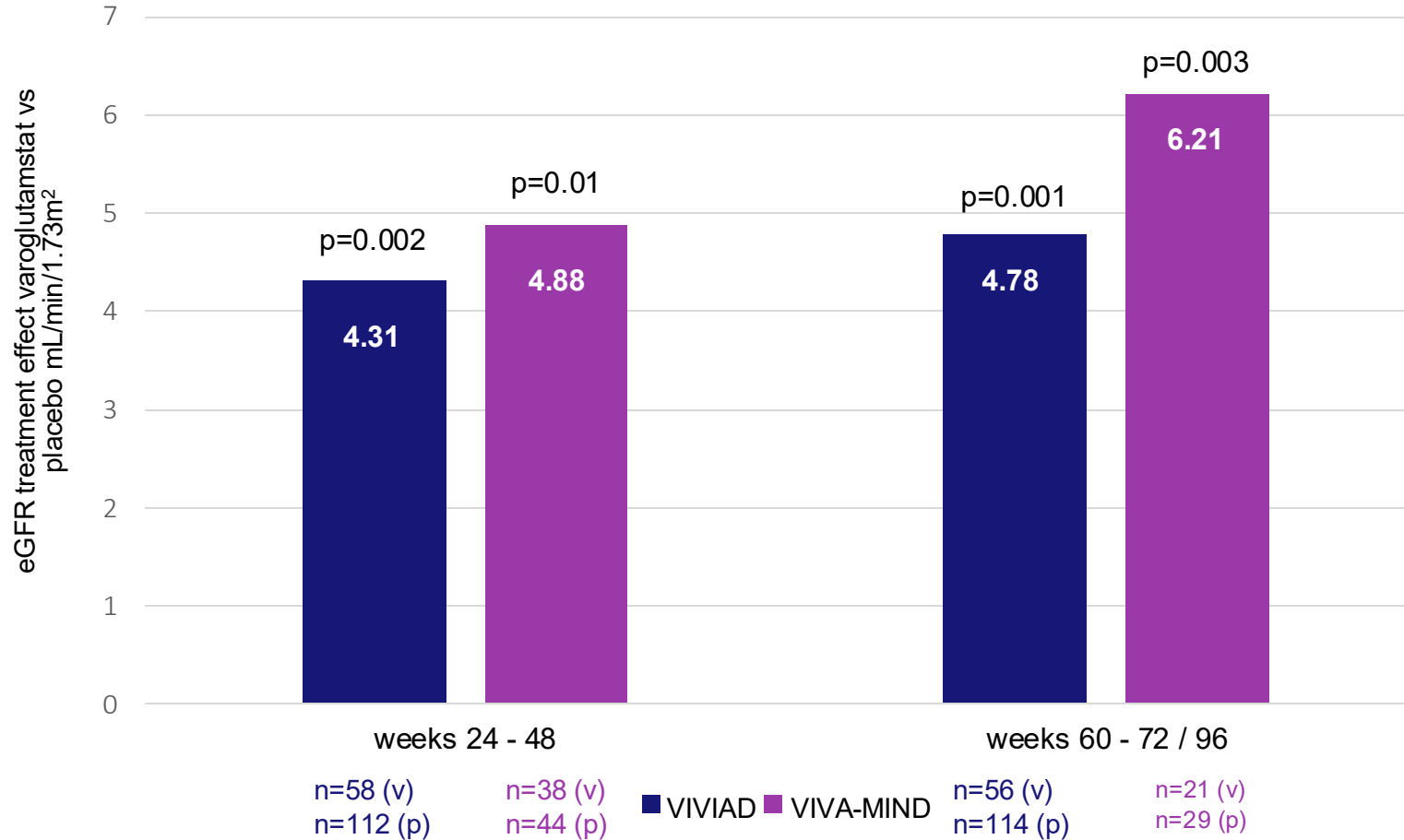


Consistent improvement in kidney function and effect size across distinct treatment periods in both studies

Sensitivity analysis; all patients randomized to 600 mg BID varoglutamstat (v) and placebo (p)

eGFR treatment effect:

Difference between varoglutamstat and placebo (LSmean change from baseline)



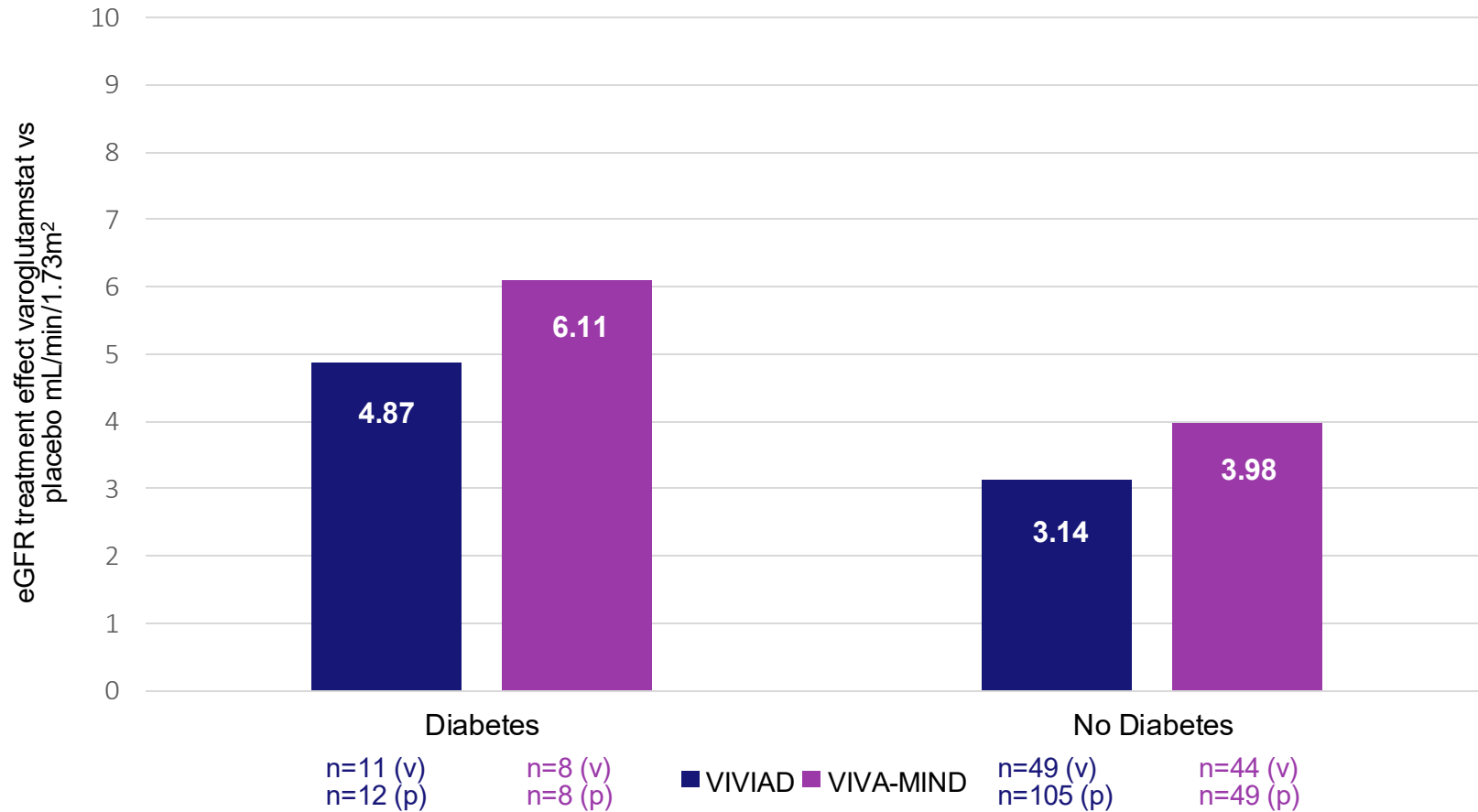
eGFR: estimated glomerular filtration rate, based on creatinine and calculated using the modification of diet in renal disease (MDRD) method. eGFR data were analysed over time using MMRM (mixed model for repeated measures) modelling including fixed effect terms for treatment, visit window and treatment-by-visit interaction using data from patients randomized to 600 mg and all visits on treatment, for VIVIAD (4 – 96 weeks) and VIVA-MIND (4 - 72 weeks); LSmean: least squares mean

Results are nearly identical between studies when comparing treatment effect in patients with or without diabetes, with consistently higher effect in diabetes

Subgroup analysis; with and without diabetes; 600 mg BID varoglutamstat (v) and placebo (p)

eGFR treatment effect:

Difference between varoglutamstat and placebo (LSmean change from baseline)

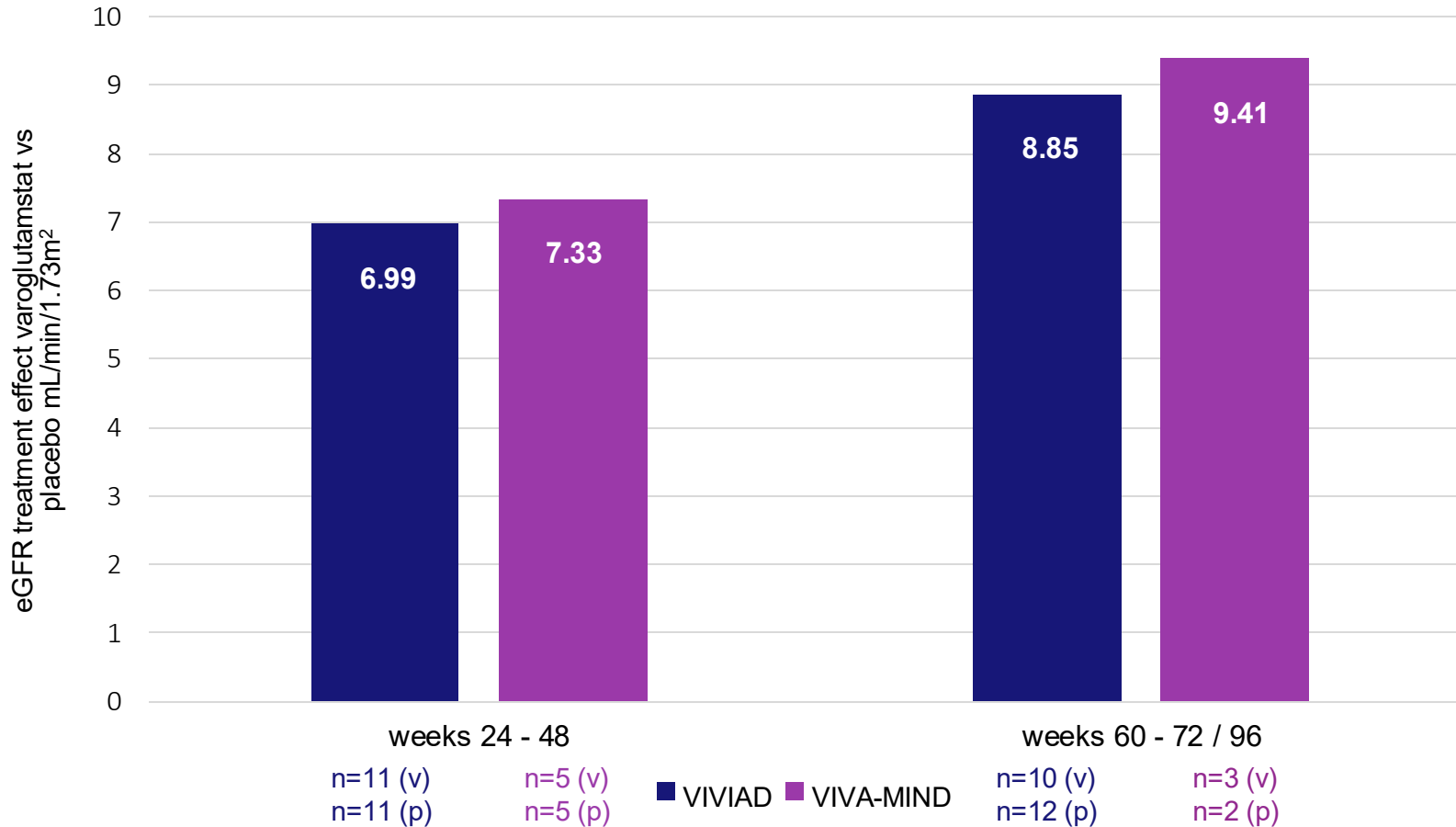


Consistent and very strong efficacy signal and large treatment effect observed in both studies in patients with diabetes at different timepoints

Subgroup analysis; patients with diabetes; 600 mg BID varoglutamstat (v) and placebo (p)

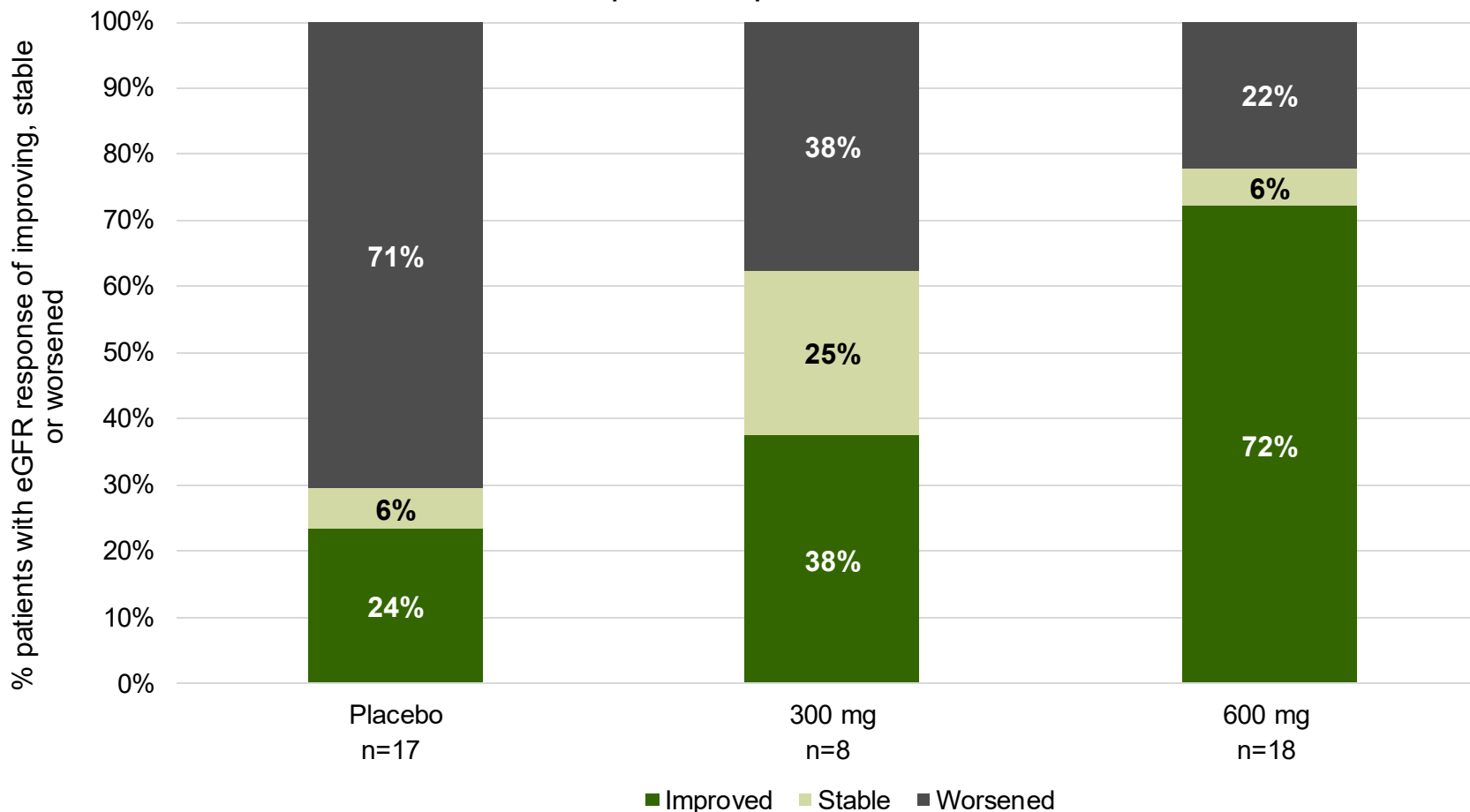
eGFR treatment effect:

Difference between varoglutamstat and placebo (LSmean change from baseline)



Responder analysis: kidney function predominantly improved or stabilized in varoglutamstat treated patients compared to a decline in the placebo group

Diabetes patients pooled VIVIAD & VIVA-MIND



Classification of eGFR response (change vs. baseline, mL/min/1.73m²)

- Improved: ≥ 2 mL above baseline
- Stable: $\geq 0 - < 2$ mL above baseline
- Worsened: < 0 mL below baseline

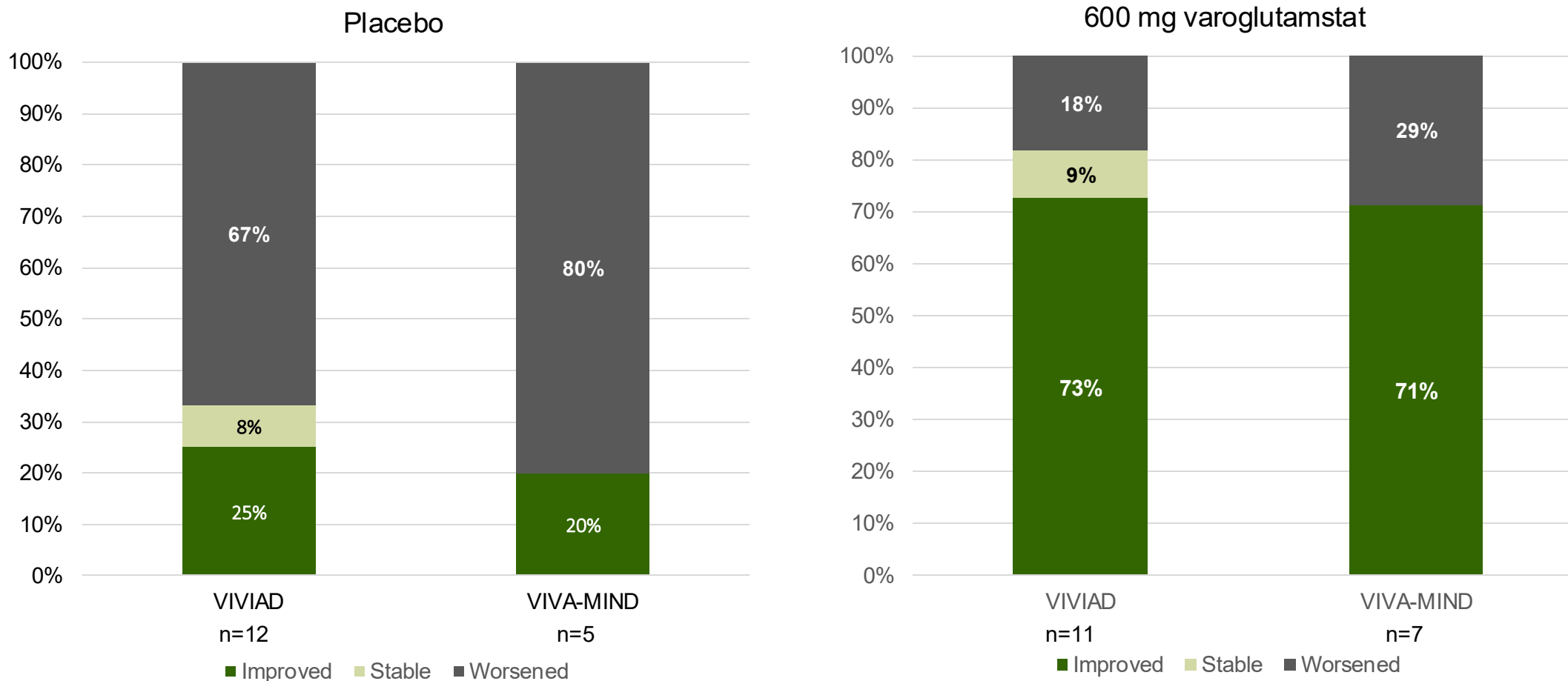
Response analysis (proportional odds)

300 mg vs placebo
2.91, 95% CI (0.55, 15.53), p=0.2106

600 mg vs. placebo
9.20, 95% CI (2.14, 39.50), p=0.028



Sensitivity analysis: side by side comparison of responder analysis in diabetes patients shows high consistency between studies in diabetes patients

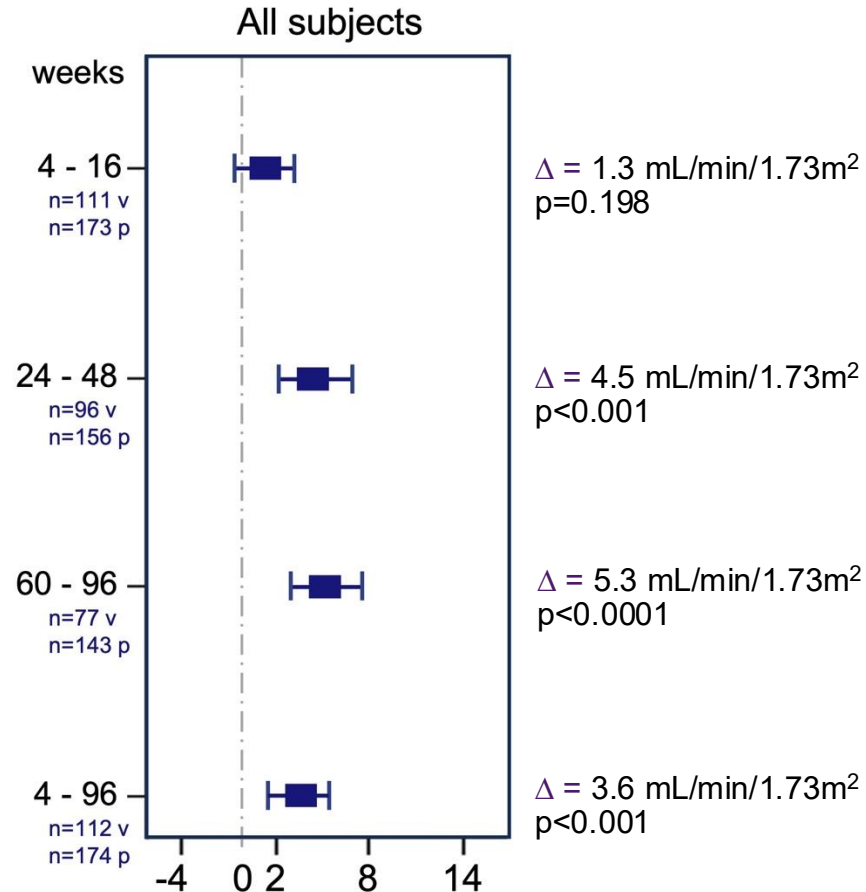


Classification of eGFR response (change mean eGFR (week 12-EOT) vs. baseline, mL/min/1.73m²):
 Improved: ≥ 2 mL above baseline, Stable: ≥ 0 - < 2 mL above baseline, Worsened: < 0 mL below baseline



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)



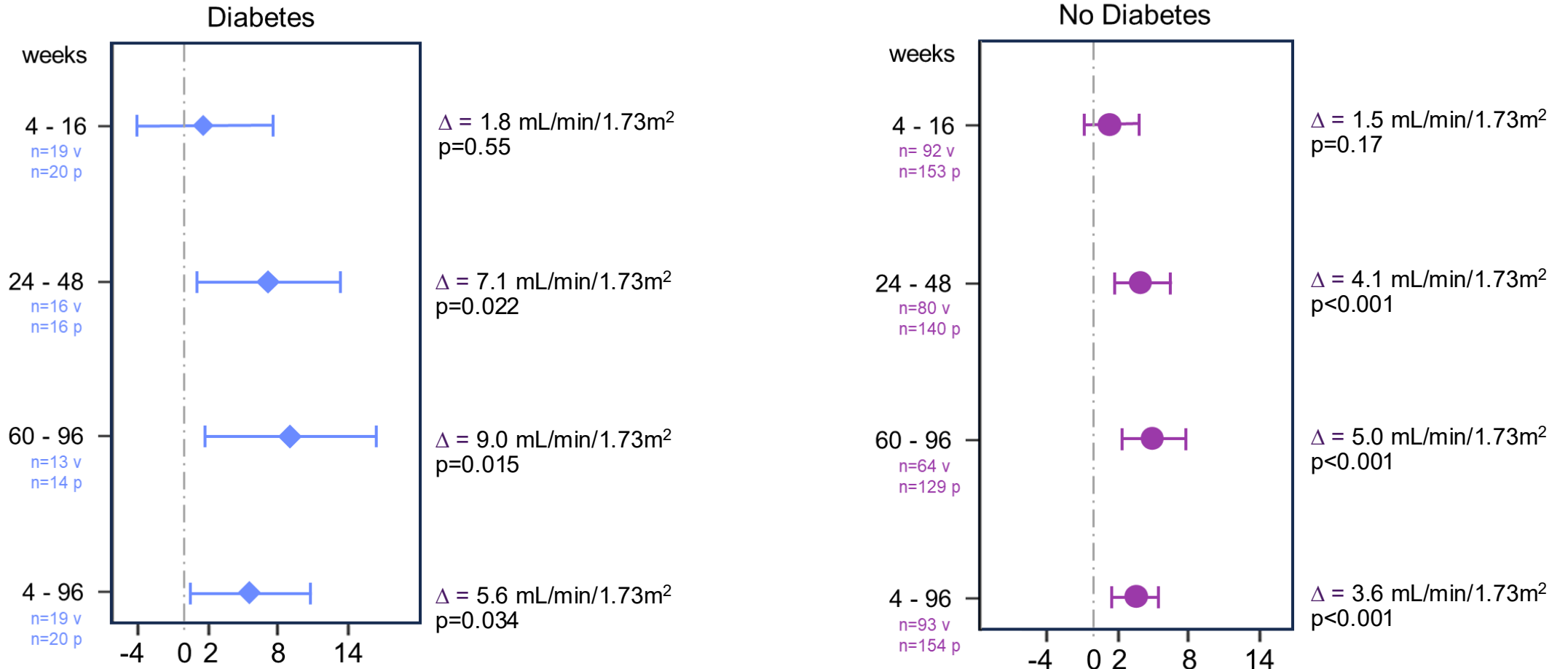
Treatment effect and 95% confidence intervals (mL/min/1.73m²)
0: No treatment effect; > 0: Improvement of eGFR (MDRD);
n: Number of patients in the varoglutamstat (v) and placebo (p) group

- ◆ Meta-analysis includes all patients on placebo and all patients randomized to 600 mg varoglutamstat BID of both studies (patients randomized to 300 mg 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 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)



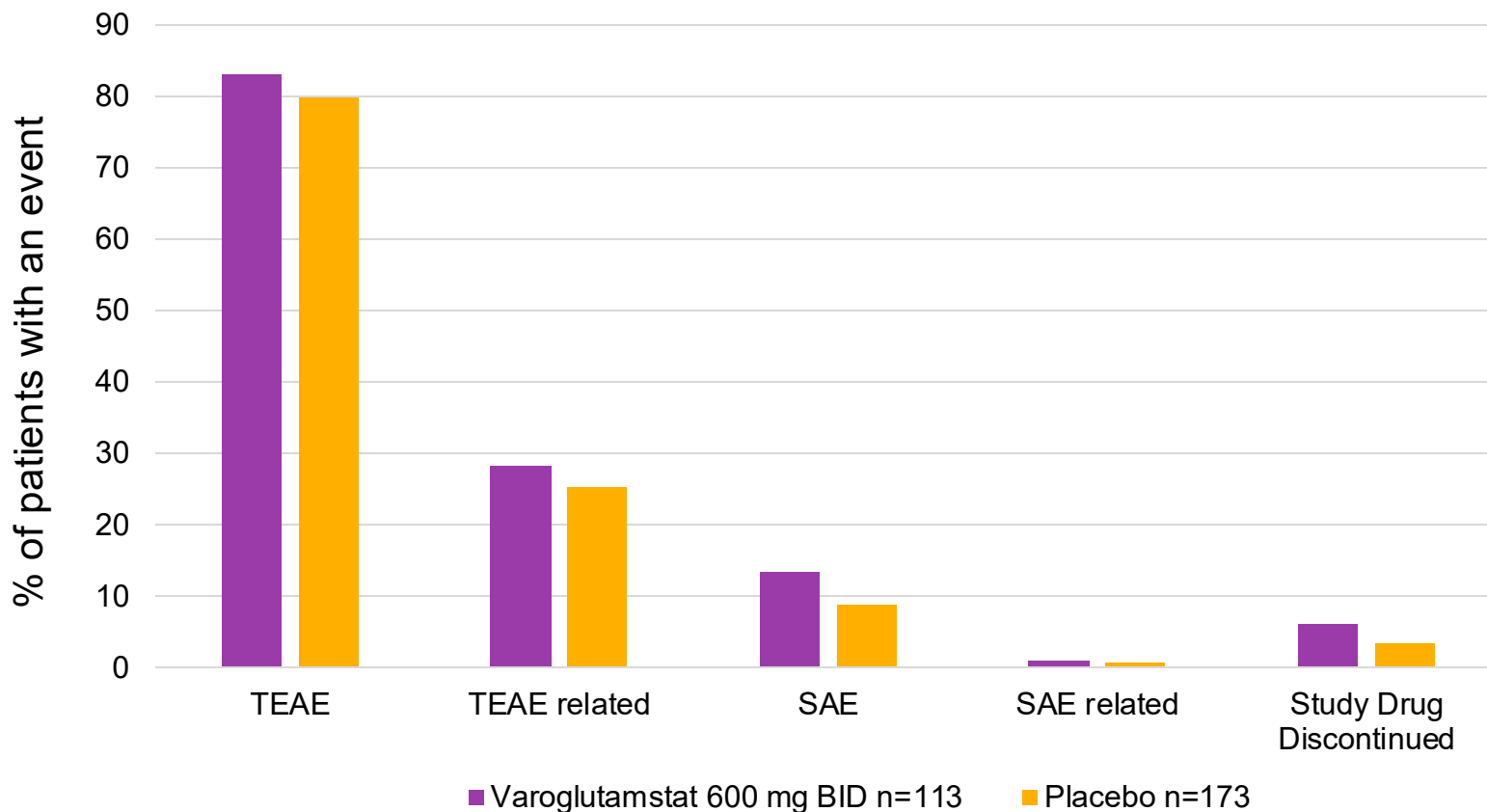
Treatment effect and 95% confidence intervals (mL/min/1.73m²)
 0: No treatment effect; > 0: Improvement of eGFR (MDRD);
 n: Number of patients in the varoglutamstat (v) and placebo (p) group



Safety: pooled analysis of VIVIAD and VIVA-MIND

600 mg varoglutamstat is well tolerated

All patients randomized to 600 mg varoglutamstat BID and placebo



Extensive safety package (# / duration)

Pharmacology / Phase 1

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

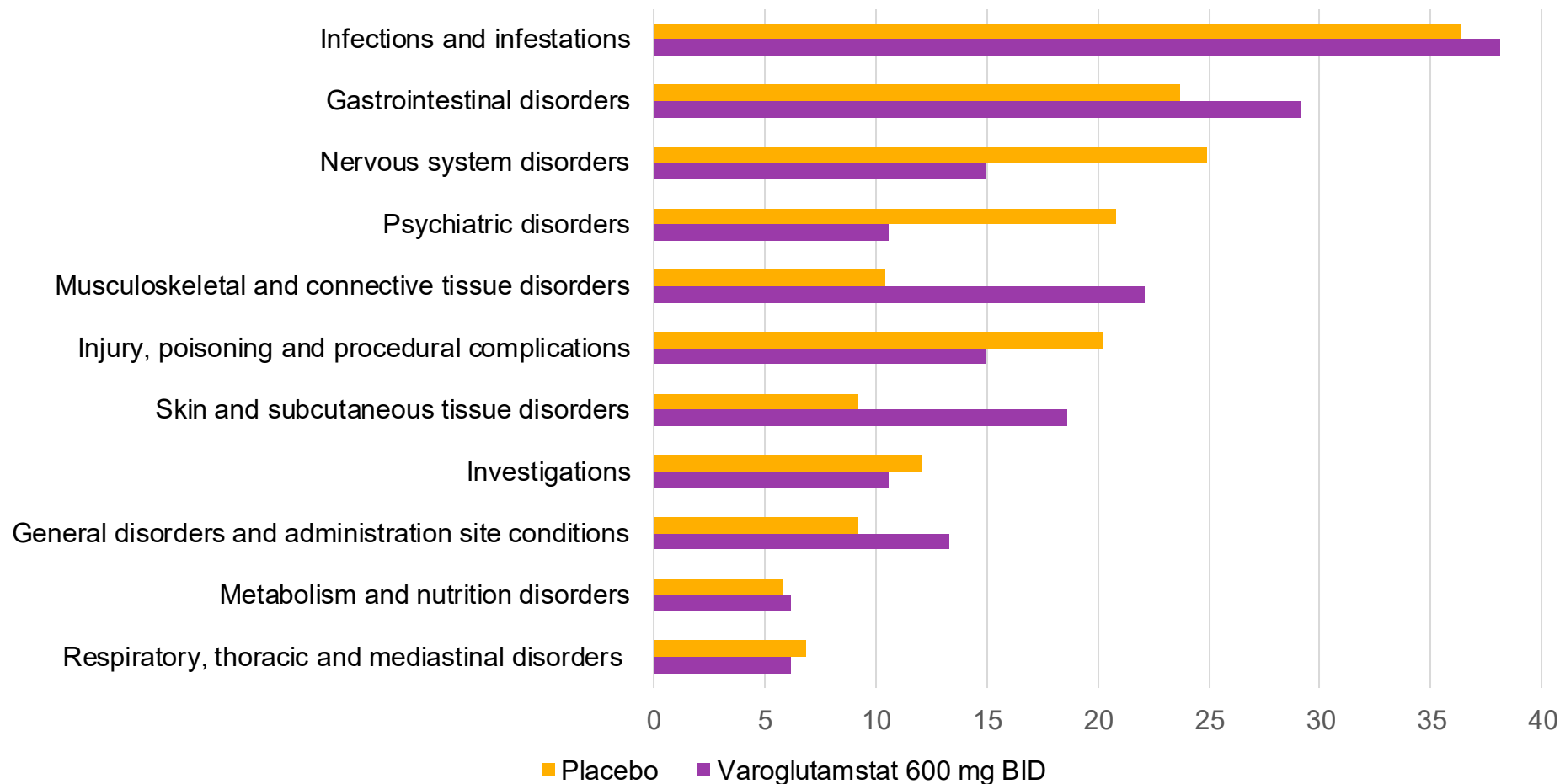
Phase 2 double-blind, placebo-controlled

- ◆ 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

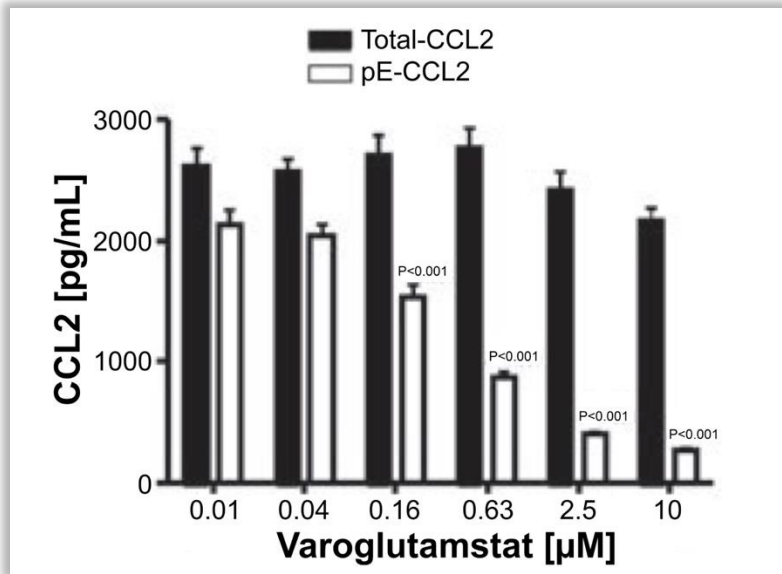


Pooled safety analysis VIVIAD and VIVA-MIND: TEAE by system organ class

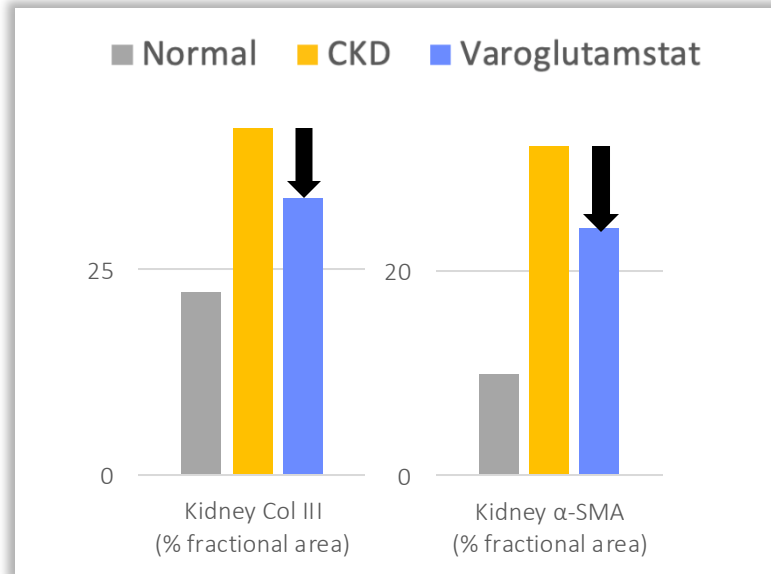
All patients randomized to 600 mg varoglutamstat BID and placebo
All events independent of relationship assessment



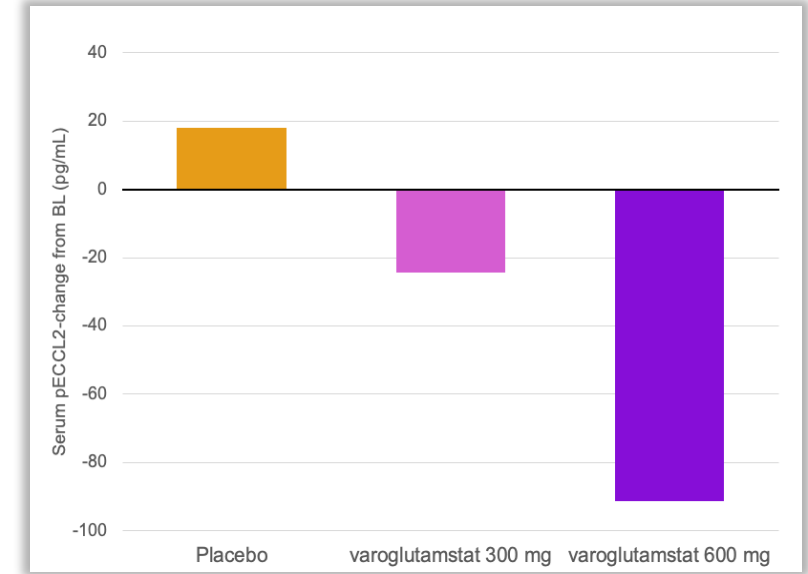
Robust evidence demonstrating inhibition of intracellular QPCTL decreases activity of pro-inflammatory cytokines and kidney fibrosis



Decrease of pE-CCL2 levels by QPCTL inhibitor application. LPS-stimulation of RAW264.7 cells. Analysis of varoglutamstat effect on total-CCL2 and pE-CCL2.



Histological changes show improvement of kidney Col-III and α-SMA. Adenine-induced mouse model of CKD.



Median reduction in pE-CCL2 levels compared to baseline with varoglutamstat. VIVIAD, total population, at week 48.



A convenient new treatment option to fill the existing gap in kidney diseases

Varoglutamstat has the potential to stabilize/counteract continuous decline in kidney function



Single agent oral compound



First-in-class mechanism of action addressing key pathways in inflammation / fibrosis



Consistent, statistically significant and clinically meaningful improvement of eGFR over placebo in two independent Phase 2 double-blind placebo-controlled studies in Europe and U.S.



Effect size substantially larger in diabetes population vs. non-diabetes population



Clearly differentiated profile with >70% patients showing improvement or stabilization of eGFR in diabetes subgroup



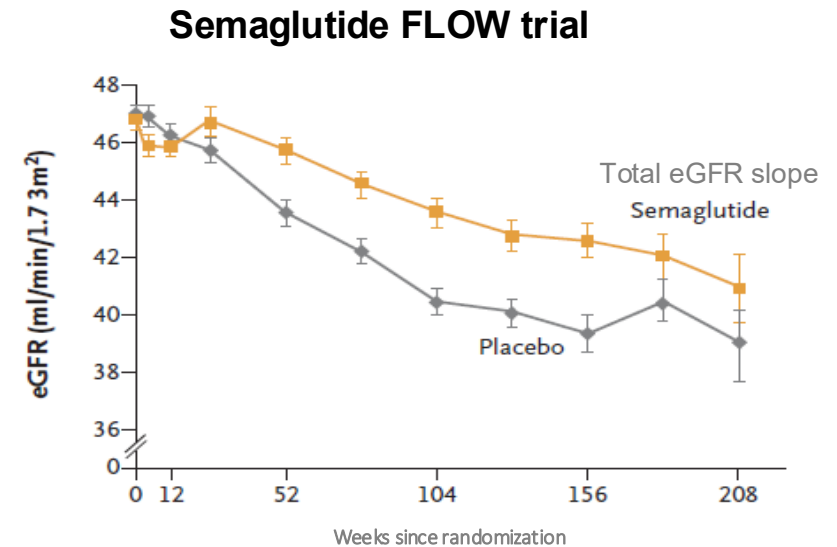
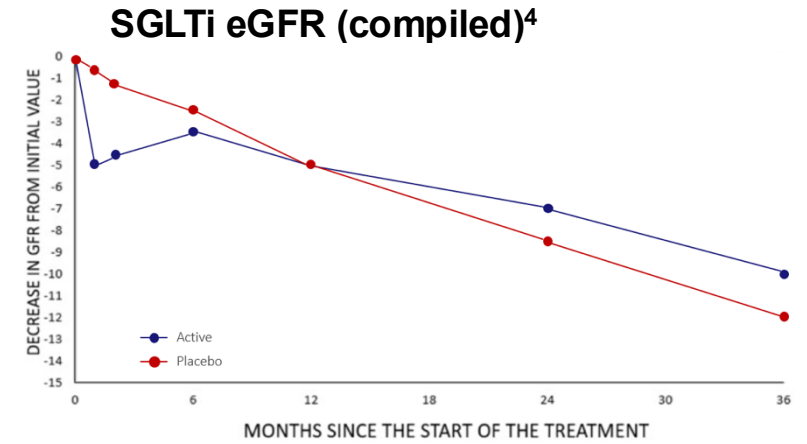
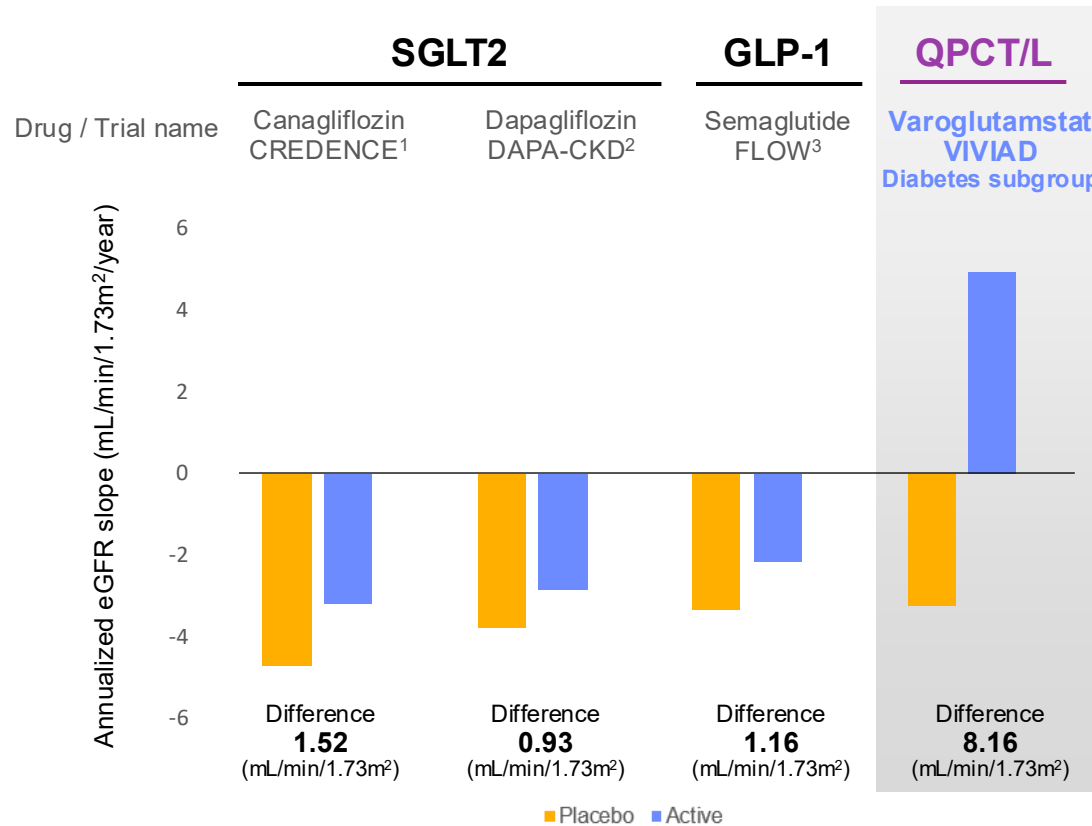
Excellent safety profile consistent across two years of study duration



MOA and safety make varoglutamstat suitable for treatment on top of SOC and potential combinations with other therapeutics








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



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 glutaminy cyclases QPCT and QPCTL; Note: Graphics and charts are for illustrative purposes, not intended to be direct comparisons between studies

Vivoryon's varoglutamstat is well-positioned in competitive landscape

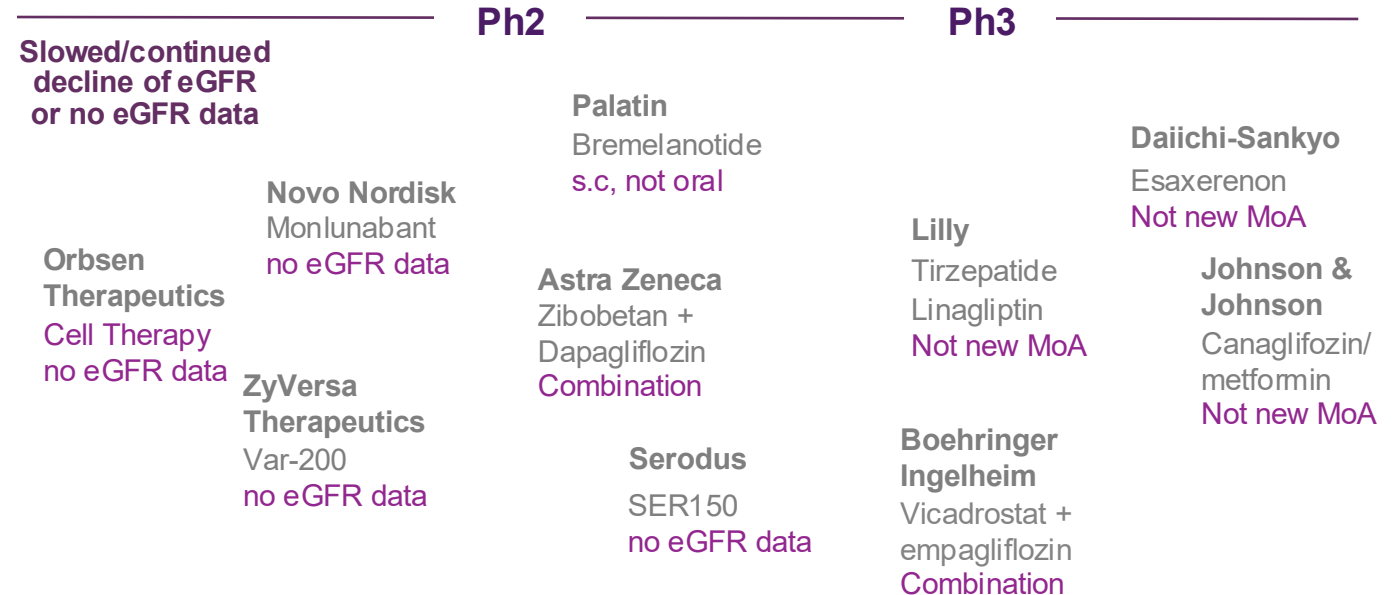
Key characteristics Varoglutamstat

	oral	✓
	Novel MoA First-in-class QPCTLi	✓
	Single agent with potential use in combination	✓
	Demonstrated long-term effect on eGFR	✓
	Long-term Safety	✓

Stabilizing or
improving eGFR


Varoglutamstat
oral

ProKidney
REACT Autologous
Cell Therapy



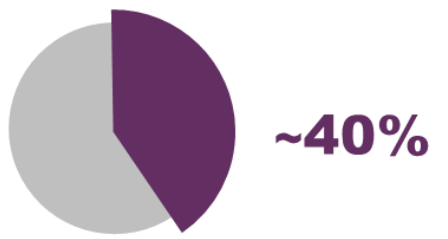
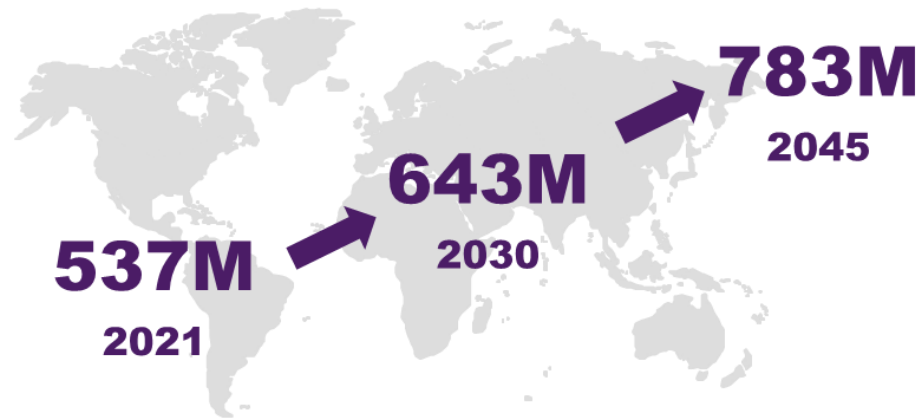
Currently marketed standard of care therapeutics including RAASi, SGLT2i, GLP-1 RA, MRA show slowing but no improvement of eGFR



Initial target market represents an attractive patient opportunity with potential label expansion to earlier stages of DKD / CKD

Diabetes is a significant and growing global challenge

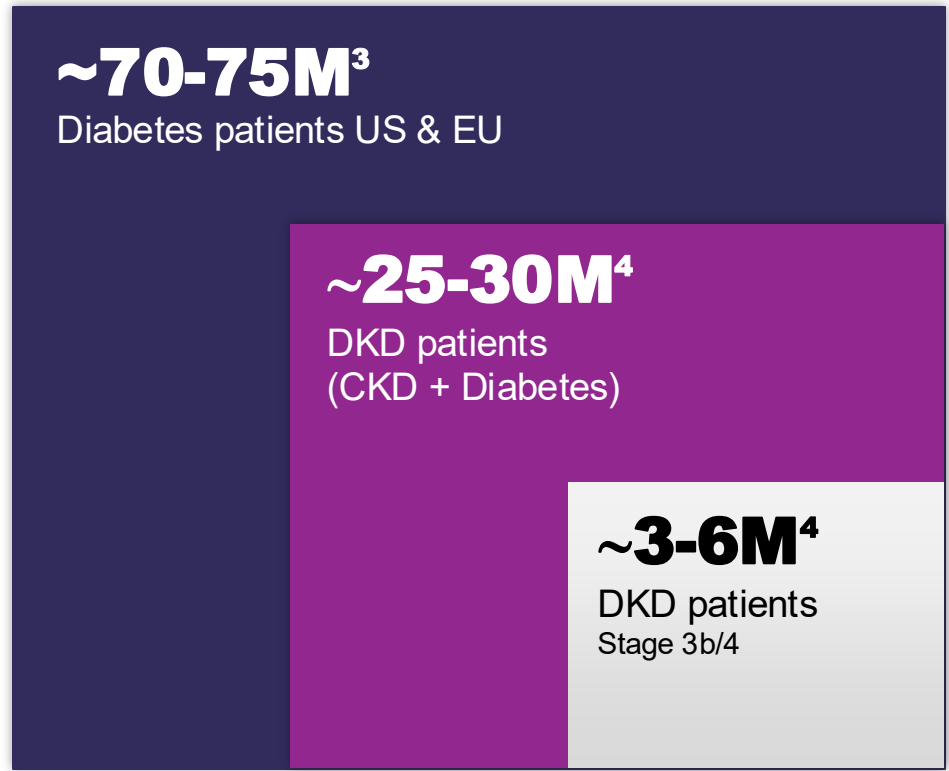
(adults aged 20-79 years with diabetes, worldwide)¹



of people with diabetes may develop diabetic kidney disease (DKD)²



people with diabetes may end up with end-stage kidney disease²



Total prevalent population



¹International Diabetes Federation (IDF) Atlas 2021; ²Qazi et al., EMJ Nephrol, 2022; ³CDC National Diabetes Statistics Report 2024; Eurostat 2017; CDC Chronic Kidney Disease in the United States, 2023; Brück et al., J Am Soc Nephrol, 2015; Sundström et al., The Lancet, Regional Health Europe, 2022; ⁴Prevalent population assumptions based on internal analyses using a combination of public sources and management estimates, including Wu et al., BMJ Open Diabetes Research and Care, 2016; Feng et al., Kidney Med, 2022, CDC Kidney Disease Surveillance System (NHANES); This information may prove to be inaccurate because this information cannot always be verified with complete certainty due to the limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties.

Double-blind placebo-controlled Phase 2b study¹ in patients with T2DM and CKD stages 3b and worse on top of standard of care (SoC)

Estimated timeline to topline readout of new Phase 2b study



Primary Objective:

Investigate the efficacy and safety of varoglutamstat on kidney function in patients with T2DM and CKD 3b and worse

Secondary Objectives

Explore the efficacy of a once daily dose of varoglutamstat

Generate further evidence of the mechanism of action

Generate data on the effect of varoglutamstat on frequently concomitantly affected organs in T2DM patients: liver, vasculature, bodyweight

Persistent albuminuria categories Description and range		
Normal to mildly increased	Moderately increased	Severely increased
<30mg/g <3mg/mmol	30 - 300mg/g 3-30mg/mmol	>300mg/g >30mg/mmol
A1	A2	A3

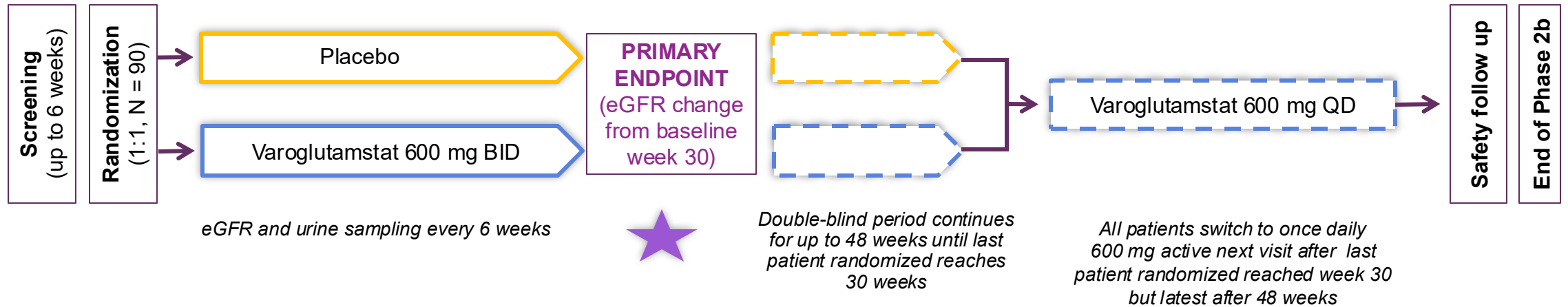
GFR categories (mL/min/1.73m ²) range and description	>90	Normal and high	Stage 1	No CKD in absence of markers of kidney damage		
	60 - 89	Mild decrease related to normal age range	Stage 2			
45 - 59	Mild - moderate reduction	Stage 3a				(✓)
30 - 44	Moderate - severe reduction	Stage 3b			✓	✓
15 - 29	Severe reduction	Stage 4			✓	✓
< 15	Kidney failure	Stage 5				

Worsening

Worsening



Draft trial design based on robust data from VIVA-MIND and Phase 2 meta-analysis



Patient characteristics

- ◆ T2DM patients with Stage 3b+ CKD; all patients on standard of care medicines (SoC)

Endpoints

- ◆ **Primary:** eGFR change from baseline to last visit
- ◆ **Secondary:** UACR (albuminuria)
- ◆ **Exploratory:** Inflammatory, metabolic and fibrotic biomarkers liver transaminases, liver ultrasound (fibroscan)

Stratification

- ◆ By CKD severity
- ◆ Patients with SGLT-2 versus no SGLT-2
- ◆ Patients with GLP-1 versus without GLP-1



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	<i>POC in VIVIAD & VIVA-MIND results</i>					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						AD program: discontinued after negative topline data March 2024 (VIVIAD) & December 2024 (VIVA-MIND)
	Varoglutamstat (SIM0408, PQ912)	SMI QPCT/L			<i>CTA approval in China</i>			Partnered with Simcere in Greater China; under evaluation
	PBD-C06	mAb N3pE amyloid			Pre-IND			Partnered with Simcere in Greater China; under evaluation



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

QPCTL inhibitors have a large market potential: Development opportunities across a range of diseases driven by underlying inflammation / fibrosis

DKD / CKD / earlier stages

Replication of a sustained improvement of kidney function in two independent Phase 2 studies¹

Initial focus on stage 3b/4 DKD given high unmet need and large effect in diabetes subgroup

Opportunity to expand market potential by moving into earlier and later stage DKD / CKD

Rare kidney diseases

e.g. Alport / Fabry disease

Novel mode of action, effect on inflammatory markers and observed effect on kidney function holds promise for QPCTL inhibitors in certain rare diseases

Disorders progressing through inflammation & fibrosis

e.g. NAFLD

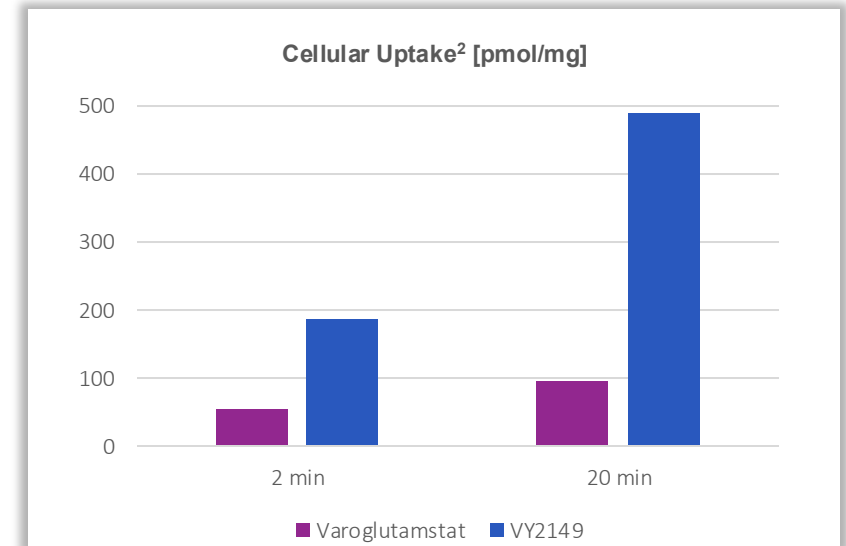
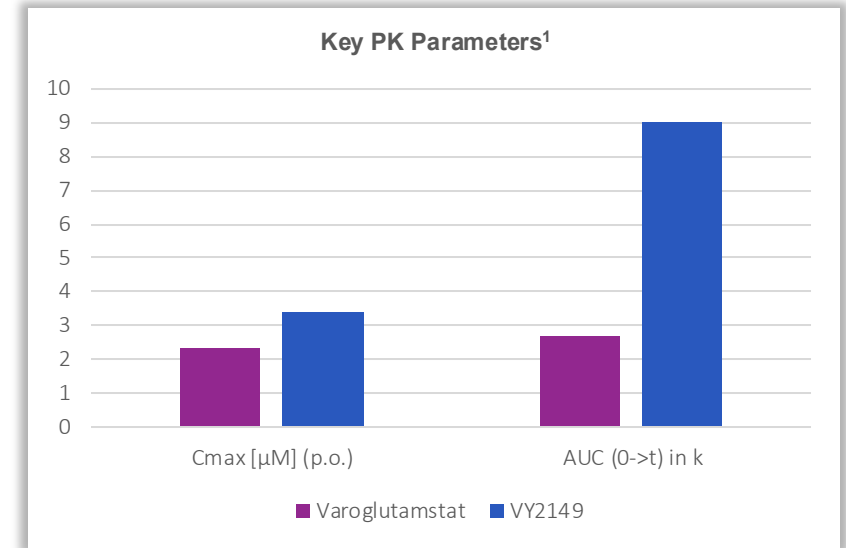
NAFLD is the most prevalent form of liver disease which may advance to metabolic dysfunction-associated steatohepatitis (“MASH”) and cirrhosis

In vivo proof of concept in NAFLD mice²



New development compound VY2149 shows improved cellular uptake, PK profile and superior outcomes in kidney animal studies

- ◆ Higher intracellular QPCTL inhibition translates to better activity, lower doses and the opportunity for once daily dosing
- ◆ Pre-clinical stage follow-on candidate VY2149, has shown improved molecular properties including
 - ◆ Improved peak concentration (C_{max}) of VY2149 compared to varoglutamstat at comparable bioavailability upon oral dosing
 - ◆ Markedly increased overall drug exposure (AUC)
 - ◆ Significantly higher passive uptake into cells
- ◆ Assessment of once daily dosing for VY2149 in an animal model has shown strong effects on eGFR, creatinine, cystatin C levels and α -SMA levels and collagens

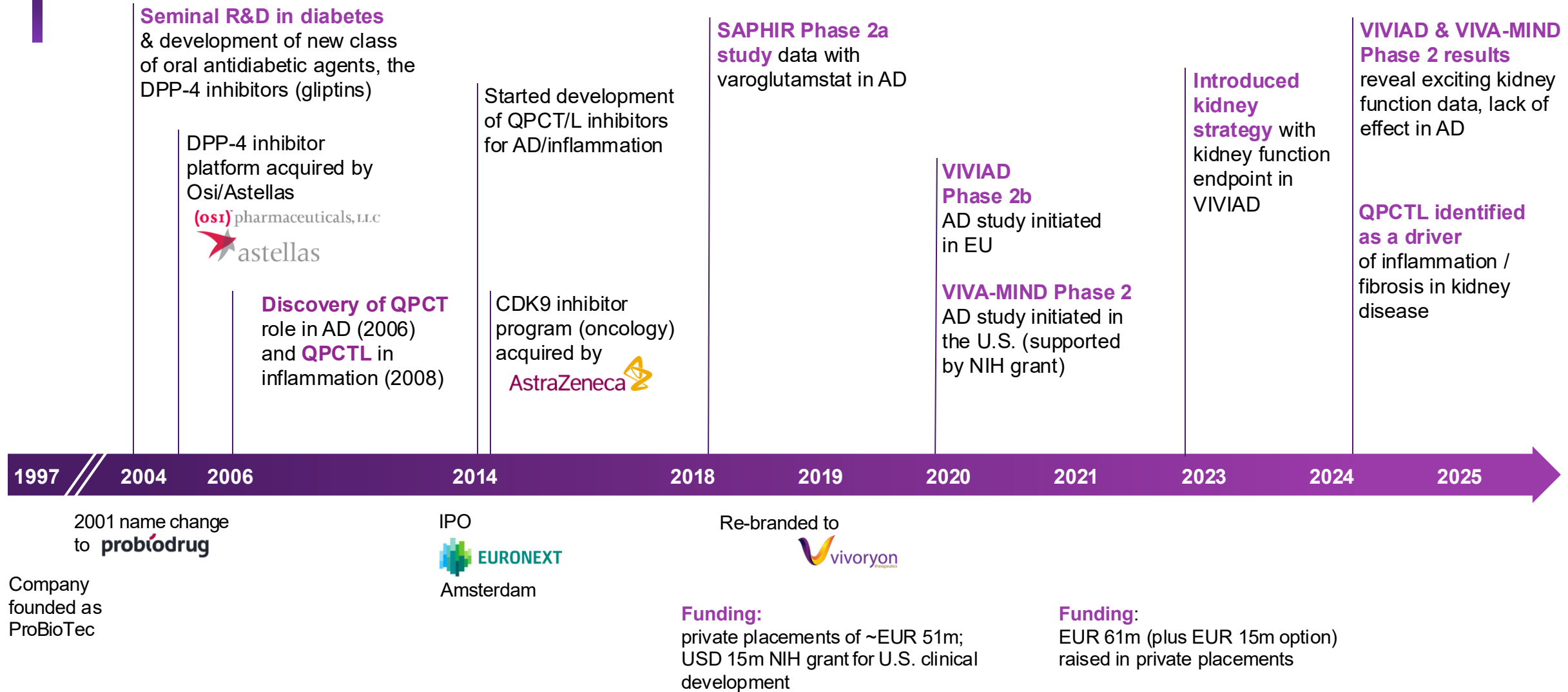


¹ Single low dose (10mg/kg); p.o.= oral; PK = pharmacokinetics; AUC = Area under the curve; C_{max} = peak concentration

² Passive uptake into HEK293 cells incubated for 2 vs. 20 min with 1 µM compound in medium (37°C); reported as pmol/mg protein of a reference protein.



Vivoryon: A history of groundbreaking discoveries and developments



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

Management

Frank Weber, MD
Chief Executive Officer



Anne Doering, CFA
Chief Financial Officer



Michael Schaeffer, PhD
Chief Business Officer



Julia Neugebauer, PhD
Chief Operating Officer



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**



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



Addressing unmet needs in areas of high commercial potential

Mission is to improve **kidney health** and ultimately reduce rate of transplant / dialysis in **DKD/CKD/other** potential indications



Unique oral asset with MOA targeting inflammation

Developed first in class oral **QPCTL inhibitor**; only one in clinic to show **improvement in kidney function** in elderly population¹



Compelling Phase 2 results replicated in two independent studies

Unprecedentedly large and sustainable improvement in kidney function, especially in 'diabetes' subgroup; **large long-term safety data base**



Actionable, risk-contained plan for Phase 2b trial in DKD²

Next steps in target population founded on statistical insights from **robust, long-term Phase 2 data**

Extensive intellectual property portfolio³; pipeline of additional early-stage QPCTL inhibitors; experienced management team with track record in inflammation and business development



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 Subject to funding / partnership; ³ Composition of matter patent protection expected to 2044+ based on current composition of matter patent to 2031 with additional potential for Hatch-Waxman extension of up to 5 years, new patent filings being evaluated



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