



Transforming the Treatment of Kidney Disease

Consistent eGFR Improvement
Signal in Two Independent Phase 2
Studies Supports Proposed DKD
Development Path



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**Developing new
therapies that aim to
preserve kidney
function and prevent
progression to kidney
failure**



Investment Summary

Strong clinical evidence base

First in class QPCT/L inhibitor varoglutamstat:

- Statistically significant eGFR improvement vs. placebo in two independent Phase 2 studies; excellent safety profile¹
- Additional potential applications beyond DKD

Poised to address medical need

Planned Phase 2 DKD study:

- Data in 15 and 24 months post study start²
- Subject to financing / partnership

Deliver for patients

Transforming the treatment of kidney disease

Aiming to stabilize or improve kidney function, and prevent progression to kidney failure and the need for dialysis / transplant

Defined pathway to value creation

Funding needed for Phase 2 start:

- €15M to interim value inflection point; €30M total to full data readout / Phase 3 / partnership³

Long IP runway

Strong intellectual property portfolio:

- U.S. composition of matter patent to 2044, with potential for Hatch-Waxman extension

Deliver for shareholders

Developing new therapies with the aim of preserving kidney function and preventing progression to kidney failure



Significant unmet need in kidney disease

Patients urgently need better outcomes

Aim to stabilize or improve kidney function, and prevent progression to kidney failure and the need for dialysis / transplant



Compelling data with lead program varoglutamstat

First oral agent to show improvement in kidney function

Demonstrated in two independent Phase 2 studies¹



Attractive opportunity with defined value-creation steps

Substantial market and key value inflection points within 24 months

Defined clinical path with interim data in DKD within 15 months & full data within 24 months²

Varoglutamstat: Phase 2 data showed stabilization / improvement in kidney function in elderly adults supporting strategy to develop in DKD



Promising kidney signal observed in Alzheimer's program

- ◆ Kidney function assessed as prospectively defined safety / exploratory endpoint
- ◆ Robust treatment benefit on eGFR observed in VIVIAD Phase 2b study¹
- ◆ Excellent safety profile in >400 subjects over more than 2 years



Evidence-based pivot to DKD

- ◆ Compelling kidney function data confirmed in second Phase 2 study & meta-analysis¹
- ◆ Substantially larger treatment effect in diabetes subgroup
- ◆ Dose response connected to a plausible MoA targeting inflammation / fibrosis
- ◆ Results in patients consistent with animal study outcomes



Clear strategy to develop varoglutamstat in DKD

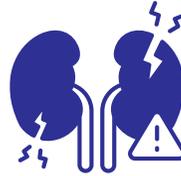
- ◆ Clearly defined Phase 2b trial for varoglutamstat in stage 3b/4 DKD (subject to financing)
- ◆ Interim data within 15 of study start; primary data within 24 months
- ◆ U.S. composition of matter patent to 2044, with potential for Hatch-Waxman extension²

Diabetic kidney disease

Diabetes is a leading cause of chronic kidney disease



Diabetes can lead to structural and functional damage of the kidneys



→ **High risk of kidney failure** in advanced disease (stage 3b/4)



→ **Dialysis and/or transplant needed** to replace function if kidney's fail

Current standard of care can delay disease progression but does not stabilize or reverse impaired kidney function

Primary goal of new treatments is to extend kidney lifespan by stabilizing and/or improving kidney function

~1.5M patients

DKD stage 3b/4
in the US

~2.4M patients

DKD stage 3b/4
in the EU

~65-75%

of stage 4 patients will
start dialysis within 5 years

~20-30%

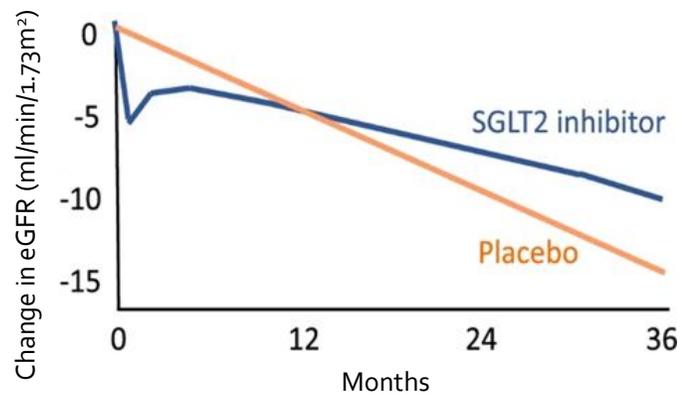
of stage 4 patients die
before dialysis

Significant unmet need for new products that stabilize or improve kidney function

Current standard of care (SGLT2i, GLP-1RA) delays disease progression but leaves significant room for improvement in kidney and cardiovascular outcomes

SGLT2i

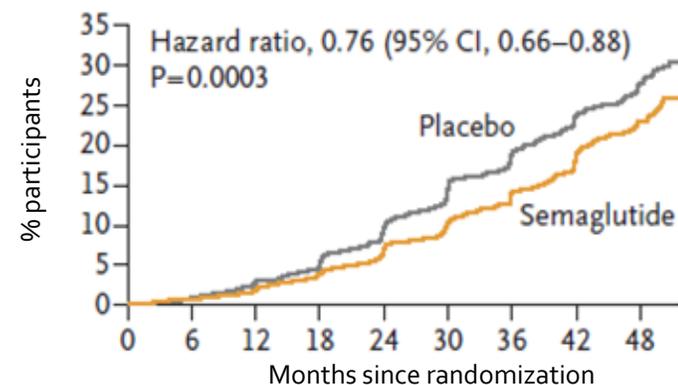
Typical changes in eGFR following introduction and long-term use of SGLT-2 inhibitors in T2 diabetes¹



Kidney function continues to decline

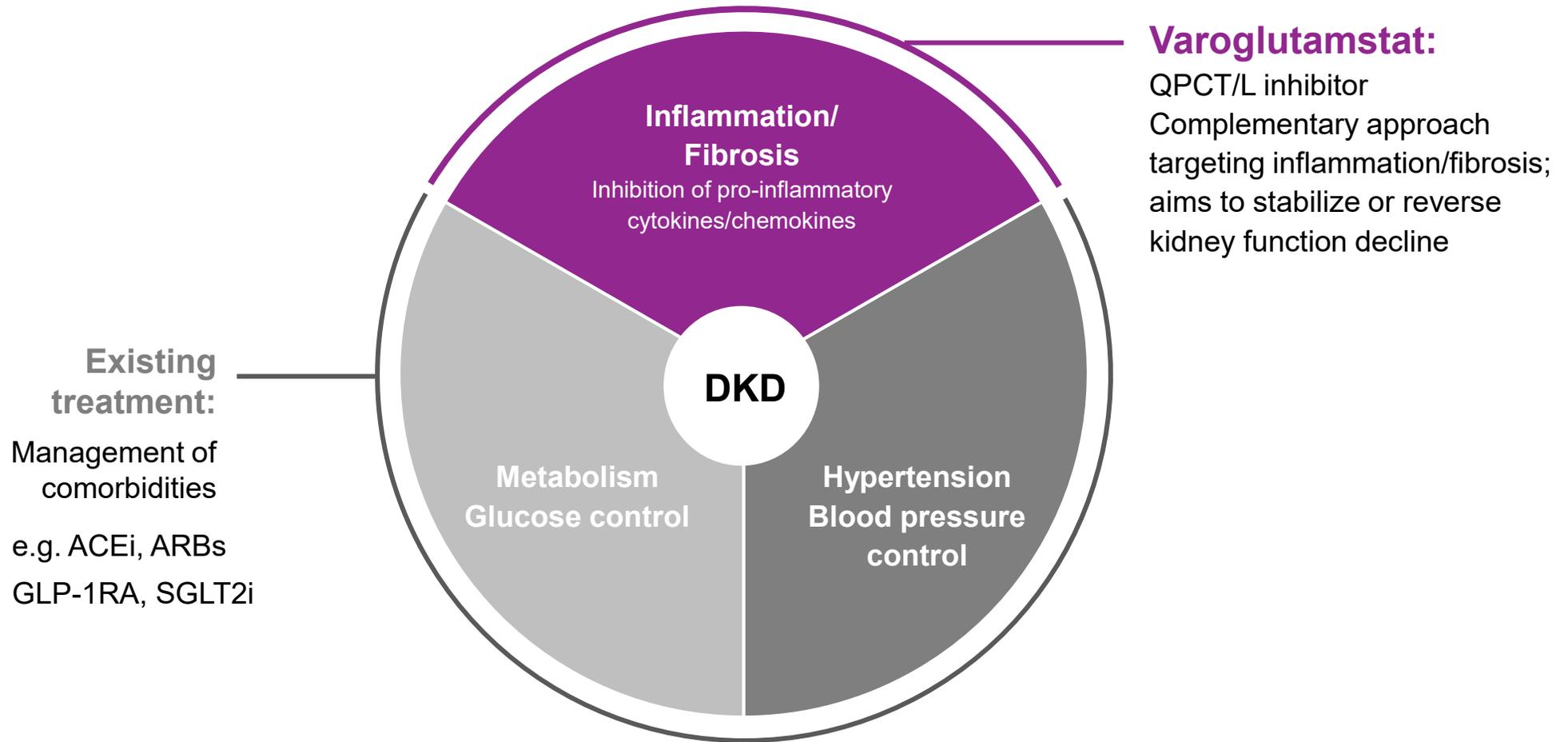
GLP-1RA

Reduction in major kidney disease events shown in FLOW trial (patients with CKD and T2 diabetes)²

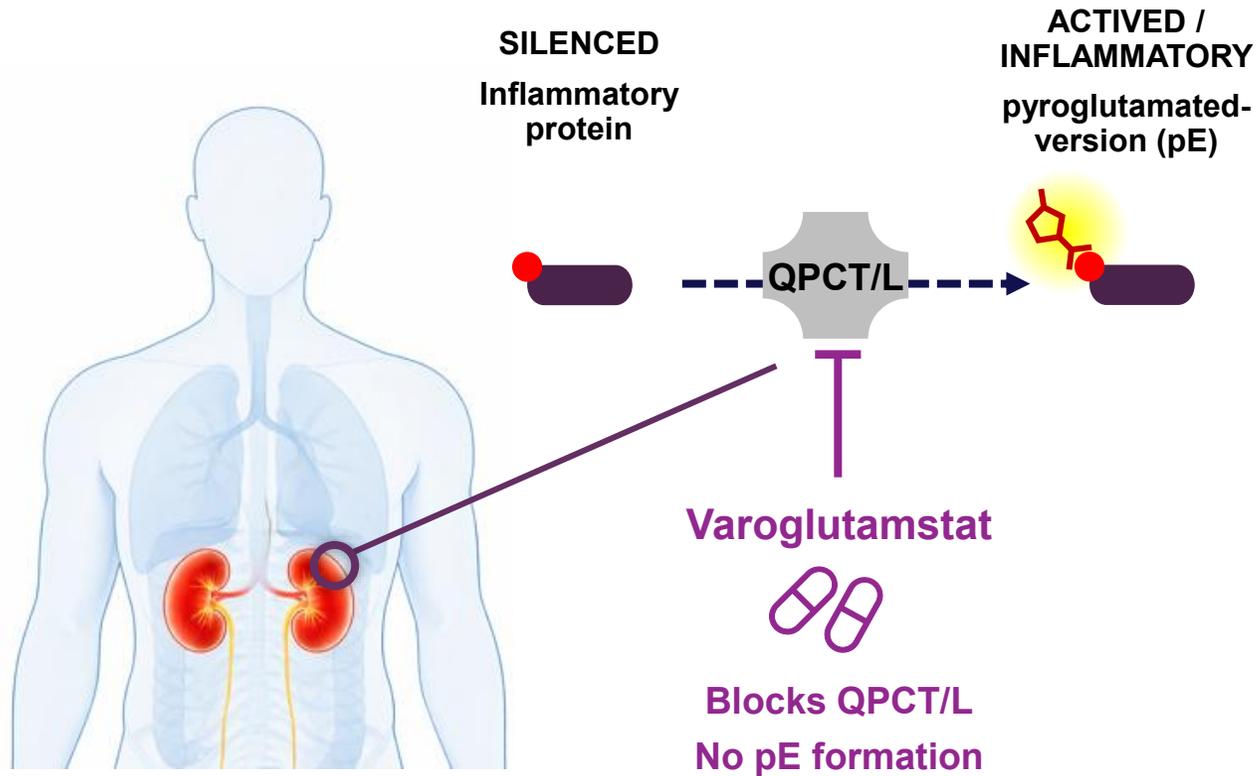


Risk of a major kidney event still exists

Targeting inflammation and fibrosis offers a complementary approach to existing therapies by tackling DKD at its roots



Varoglutamstat reduces pro-inflammatory signaling by destabilizing key inflammatory molecules



Varoglutamstat targets pro-inflammatory and pro-fibrotic pathways in kidney disease

Impaired kidney	Varoglutamstat treated
	
Kidney function 	Kidney function 
Fibrosis 	Fibrosis 
Inflammation 	Inflammation 

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

VIVIAD Phase 2b (Europe)



VIVA-MIND Phase 2 (USA)

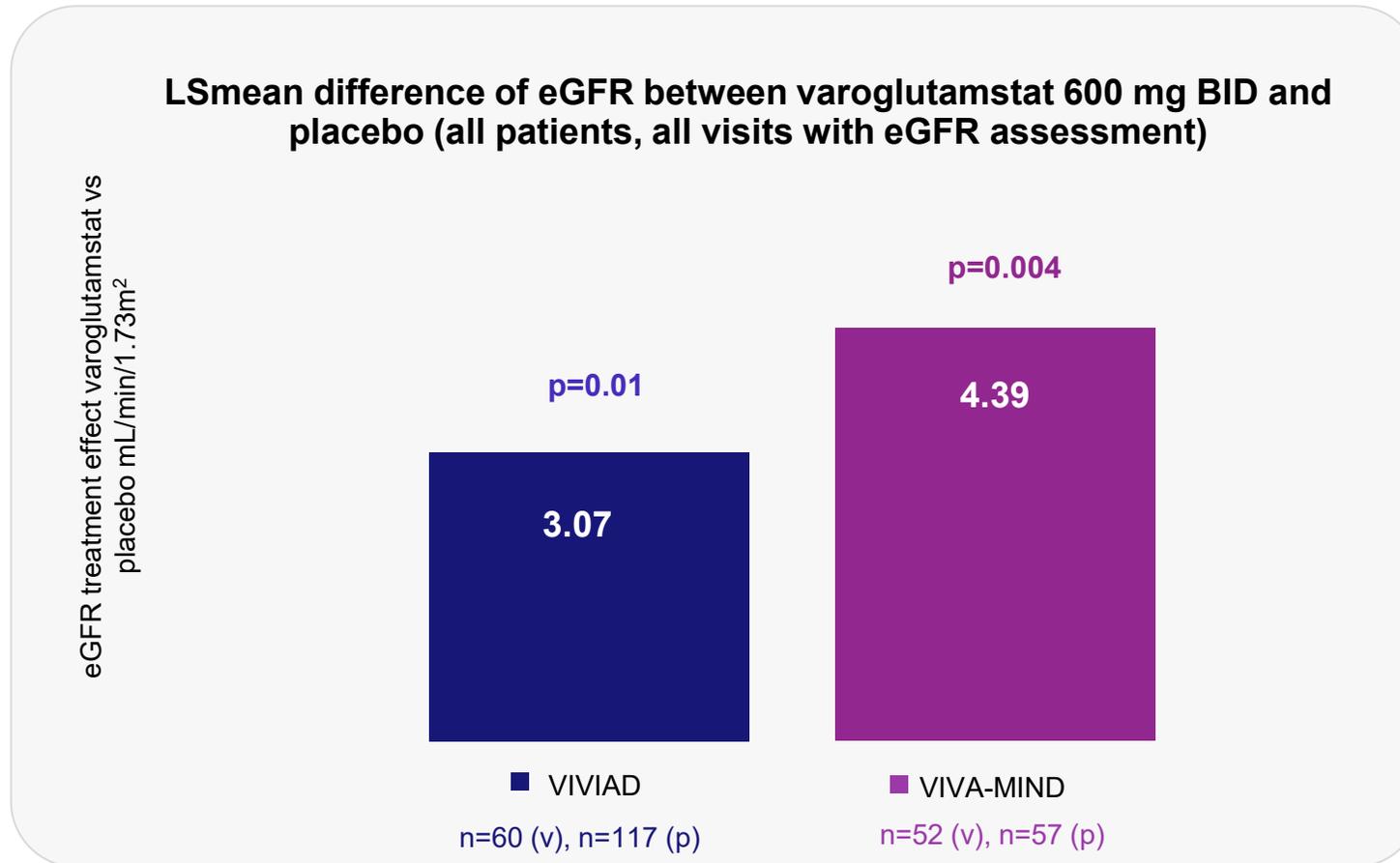


Parameter	VIVIAD (Europe)	VIVA-MIND (U.S.)
Patient selection	Mild AD, mean age 68 yrs	Mild AD, mean age 72 yrs
No. of patients treated	n=259	n=109
Varoglutamstat dose	300 and 600 mg BID	600 mg BID
Dose escalation period	Slow: 600 mg start week 13	Fast: 600 mg start week 9
Treatment duration	76 wks (mean) / 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
Baseline eGFR	81.5 mL/min/1.73m ²	77.5 mL/min/1.73m ²
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

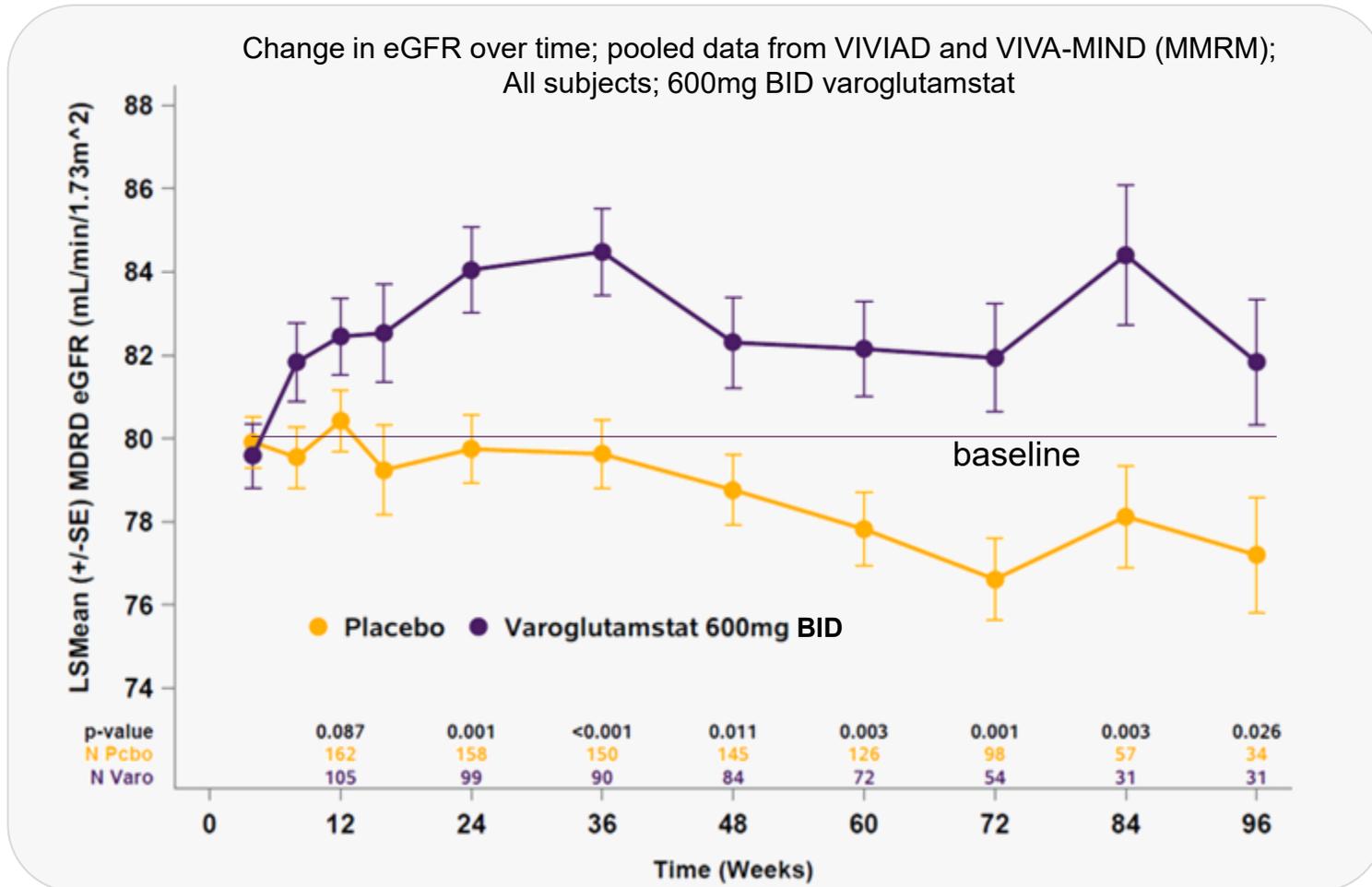
Beneficial kidney function effect consistently observed in VIVIAD and VIVA-MIND

Two independent studies confirm statistically significant and clinically meaningful improvement in eGFR



eGFR: estimated glomerular filtration rate, based on serum 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 as well as additional co-variates same as used for the respective primary endpoints as defined in the SAP using data from patients randomized to 600 mg BID and placebo of all visits on treatment, for VIVIAD (4 – 96 weeks) and VIVA-MIND (4 – 72 weeks)

Compelling beneficial effect on kidney function in subjects treated with varoglutamstat compared to placebo



Varoglutamstat

Clear and consistent separation of curves after 24 weeks

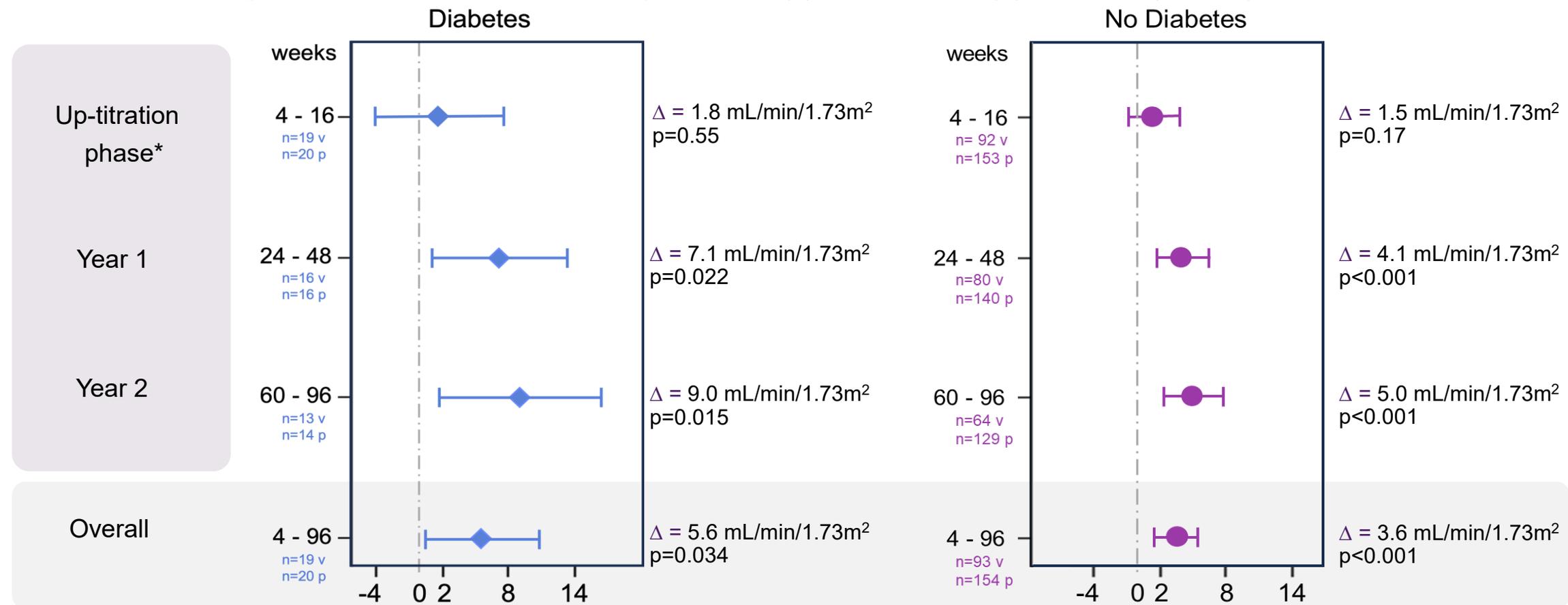
Effect stable and maintained above baseline for 2 years

Placebo patients decline mildly

eGFR: estimated glomerular filtration rate, based on serum creatinine and calculated using the modification of diet in renal disease (MDRD) method; BID: twice daily; eGFR data were analyzed over time using MMRM (mixed model for repeated measures) modelling including fixed effect terms for study, treatment, visit window and treatment-by-visit interaction as well as baseline and study using data from patients randomized to 600 mg BID and placebo of all visits on treatment, for VIVIAD (4–96 weeks) and VIVA-MIND (4–72 weeks). Within subject error modelled using an unstructured covariance matrix

VIVIAD and VIVA-MIND: Meta-analysis confirms a robust treatment effect and a larger effect size in patients with diabetes versus without diabetes

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



Treatment effect and 95% confidence intervals (mL/min/1.73m²)

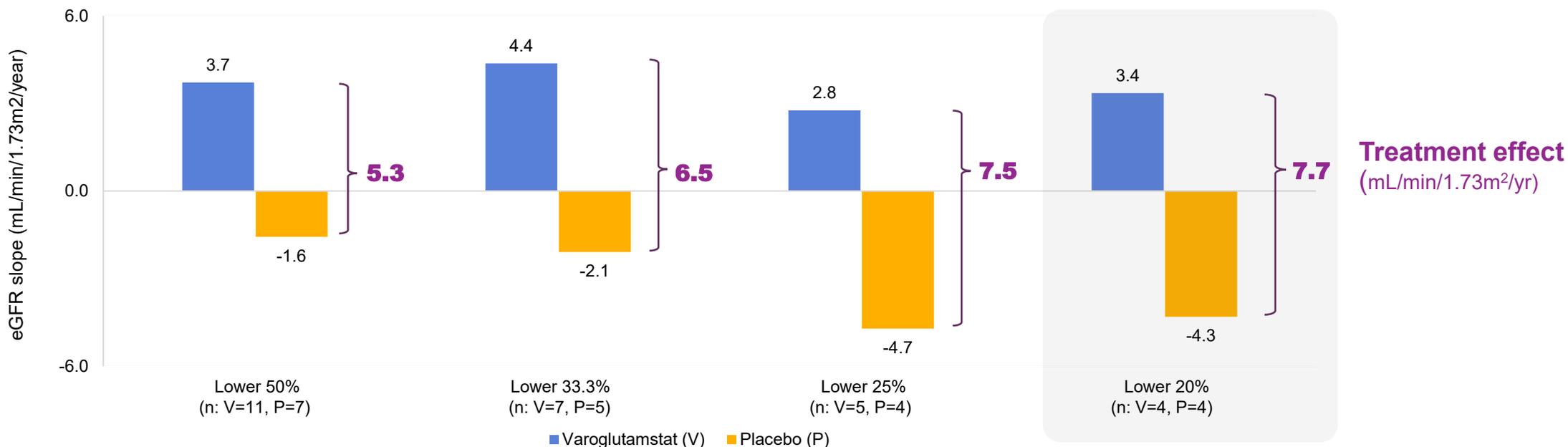
0: No treatment effect; > 0: Improvement of eGFR (MDRD);

n: Number of patients in the varoglutamstat (v) and placebo (p) group with a least one data point in the indicated time span

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 serum creatinine, calculated using modification of diet in renal disease (MDRD) method; Meta analysis of change from baseline (MMRM) in varoglutamstat-treated patients vs. placebo; * Up-titration phase: includes weeks 4, 8 (DE only), 12 in VIVIAD, weeks 4, 8 in VIVA-MIND, full-dose weeks 12, 16 in VIVA-MIND

Varoglutamstat showed consistent and strong improvement of eGFR in patients with lower baseline eGFR values and diabetes

Participants with diabetes & reduced kidney function
 (baseline eGFR levels in lower percentiles within the diabetes subgroup*;
 Treatment effect (annualized rate of change in eGFR / eGFR slope) 600 mg BID varoglutamstat vs. placebo)



Mean baseline eGFR (mL/min/1.73m²)

65.2

60.5

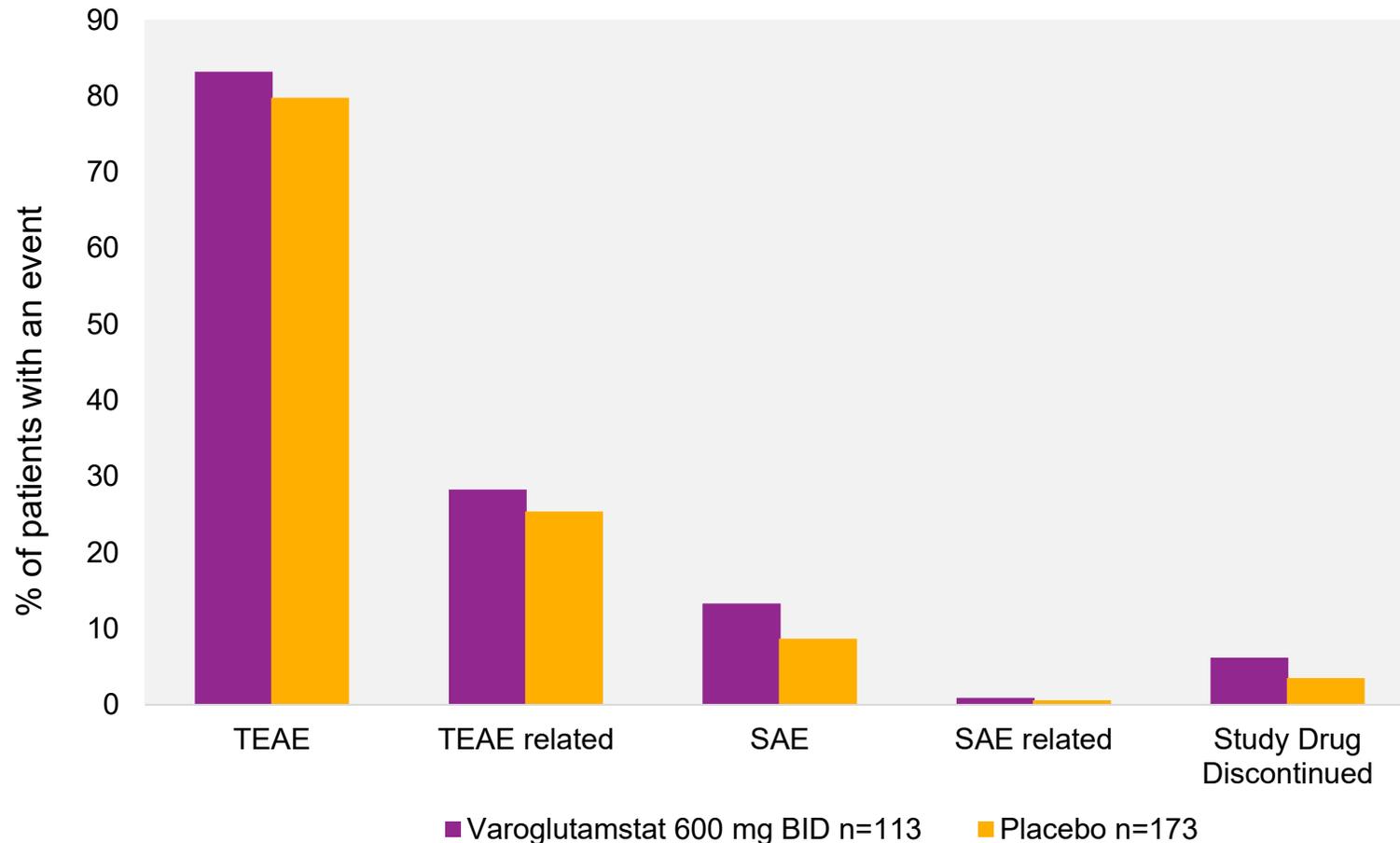
56.6

55.8

more impaired kidney function,
 more pronounced treatment effect

Varoglutamstat was well tolerated in VIVIAD and VIVA-MIND

Pooled safety analysis; all patients randomized to 600mg 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

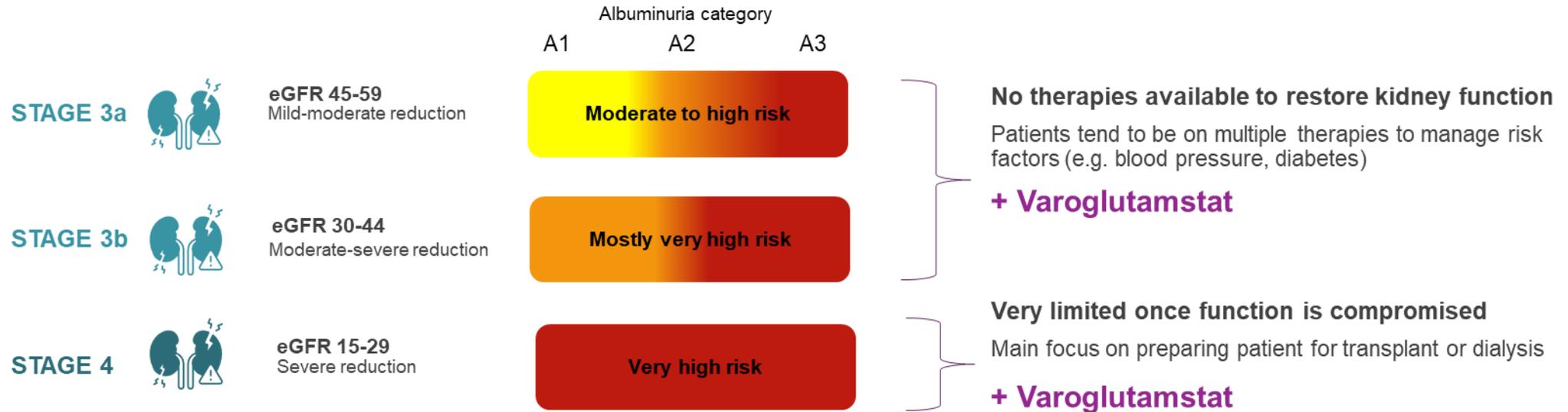
Phase 2 double-blind, placebo-controlled

Phase 2a study: 120 patients, 12 weeks
VIVIAD Phase 2b study: 259 patients, mean treatment duration 76 weeks
VIVA-MIND Phase 2 study: 109 patients treated, mean treatment duration 46 weeks

Varoglutamstat has potential to significantly improve patient outcomes by preserving kidney function

Current SoC	Varoglutamstat
 <p data-bbox="188 675 547 761">Kidney function continues to decline</p> <p data-bbox="188 851 547 989">~30–50% of patients ineligible for SGLT2i and/or GLP-1RA</p> <p data-bbox="188 1079 547 1218">High discontinuation rates of ~65% for SGLT2i and GLP-1RA</p>	 <p data-bbox="1057 475 1663 511">Shown to improve kidney function</p> <ul data-bbox="1156 568 1875 668" style="list-style-type: none">• Data from 2 independent Phase 2 studies• Prominent effect in patients with diabetes <p data-bbox="1174 746 1875 782">Well-tolerated convenient oral medicine</p> <ul data-bbox="1245 846 2359 882" style="list-style-type: none">• Excellent safety profile in >400 subjects over more than two years <p data-bbox="1296 982 1913 1018">Differentiated mechanism of action</p> <ul data-bbox="1342 1061 2226 1218" style="list-style-type: none">• Targets pro-inflammatory & pro-fibrotic pathways• Complementary to existing therapies• IP to 2044+ with U.S. composition of matter patent¹ <p data-bbox="708 675 1001 811">Stabilizes or improves kidney function</p> <p data-bbox="715 889 993 975">Excellent safety profile</p> <p data-bbox="670 1053 1039 1189">Potential to significantly improve outcomes</p>

Varoglutamstat well-positioned to address people with advanced disease where treatment options are limited

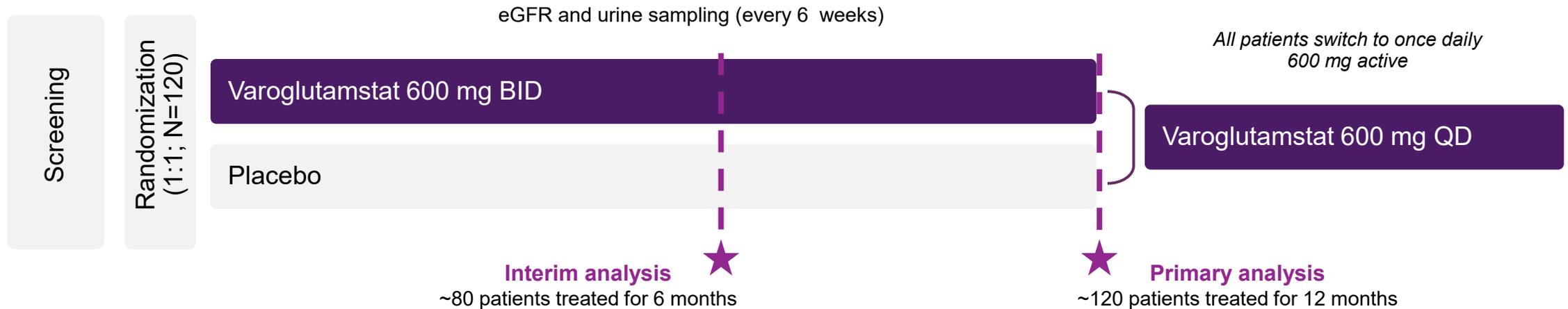


High unmet need in advanced DKD creates unique opportunity for varoglutamstat

- Patients with DKD stage 3b/4 have high risk of progression to end-stage kidney disease and dialysis
- Varoglutamstat aims to stabilize kidney function and prevent disease progression
- Phase 2b study planned to generate robust clinical evidence in a large, multibillion-dollar market

Study design to generate robust clinical evidence in patients with kidney disease and unlock asset value

Double-blind placebo-controlled Phase 2b study in stage 3b/4 DKD on top of standard of care¹



Patient population

- ◆ Patients with DKD (stage 3b/4 plus high-risk stage 3a)
 - ◆ eGFR 20-60 mL/min/1.73m²
 - ◆ Albuminuria >30 mg/g UACR (> 300 mg/g for stage 3a)
- ◆ All patients on standard of care medicines (SGLT2i + ACEi or ARBs)
- ◆ Sites in US and Western Europe

Key endpoints

- ◆ Primary: eGFR (CKD EPI) mean change from baseline [at 48 weeks]*
- ◆ Secondary: UACR (albuminuria)
- ◆ Biomarkers inflammation/fibrosis
- ◆ Safety

* eGFR slope is an accepted surrogate endpoint²

Varoglutamstat has potential to drive significant value creation



Complementary new MoA with potential to transform treatment of advanced kidney disease

Large unmet need: Urgent need for therapies that stabilize or improve kidney function to prevent progression to kidney failure

Compelling data: First oral product to show improvement in kidney function; observed in two-independent Phase 2 trials with excellent safety profile over two years¹

Predictable clinical path: key value inflection points within next 15 - 24 months²

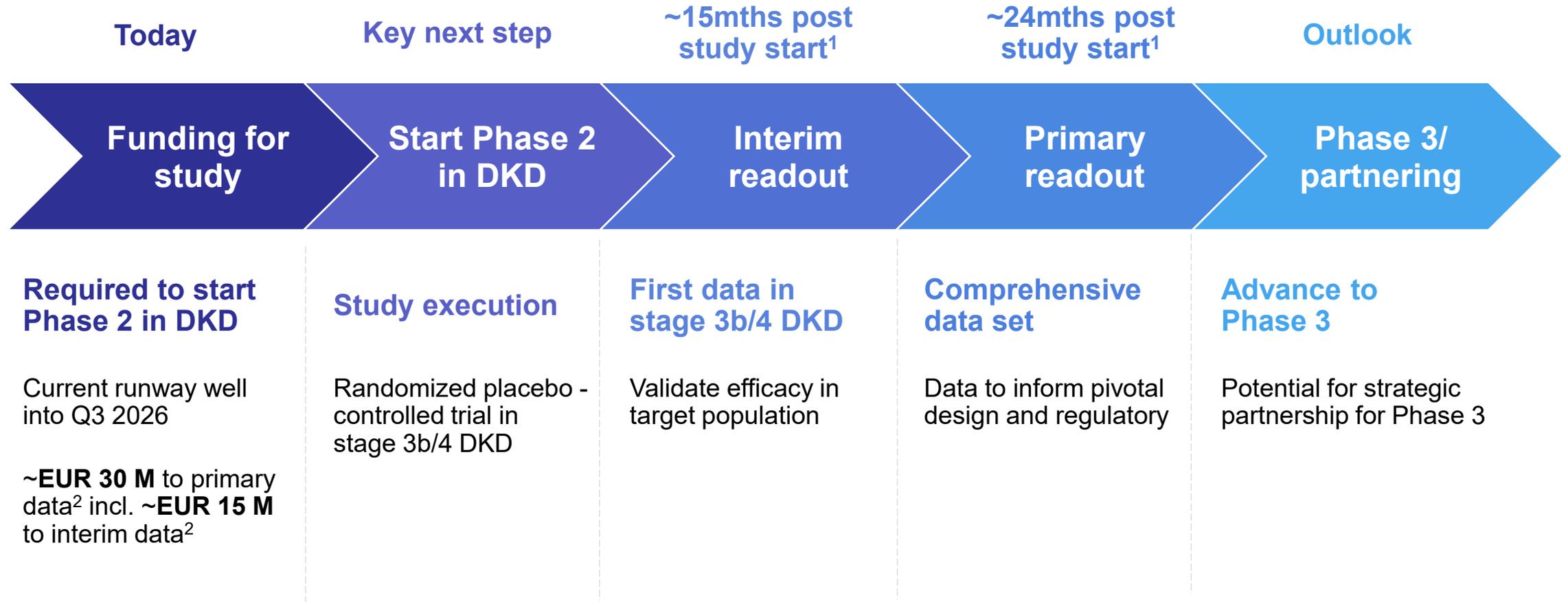


Addresses a large unmet need in a substantial patient population, creating blockbuster potential

Millions of people affected in key markets: ~1.5M patients DKD stage 3b/4 in the US and ~2.4M patients DKD stage 3b/4 in the EU

Large and growing global problem: # patients with kidney disease and burden of disease expected to increase significantly in next decade

Clear roadmap towards value creation





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Appendix

Broad potential for QPCT/L inhibitors: Multiple avenues to value generation

Therapeutic applications for QPCT/L inhibitors range across many immune-mediated diseases characterized by inflammation and fibrosis, providing additional development and partnership opportunities

Primary focus

Diabetic kidney disease

Varoglutamstat shown to effectively reduce inflammation and fibrosis and to stabilize/ partially recover kidney function:

Diabetic kidney disease
(Phase 2b planned)¹

Near-term opportunities

Rare kidney diseases

MoA and preclinical evidence provide strong rationale for exploring QPCT/L inhibitors beyond DKD, e.g.:

- ◆ Fabry disease (initial podocyte data)
- ◆ Alport disease
- ◆ FSGS
- ◆ Cystic kidney diseases (e.g. ADPKD)

Mid-term opportunities

Other immune-mediated diseases

Strong evidence for benefit of QPCT/L inhibitors on inflammation and fibrosis supports expansion into other organ systems, e.g.:

- ◆ MASH / MASLD
- ◆ Cardiovascular diseases
- ◆ IBD
- ◆ Septic arthritis
- ◆ MS