Transforming the Treatment of Kidney Disease

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

Vivoryon Therapeutics N.V.

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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 profile[1]
- Additional potential applications beyond DKD

Poised to address medical need

Planned Phase 2 DKD study:

- Data in 15 and 24 months post study start[2]
- 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 / partnership[3]

Long IP runway

Strong intellectual property portfolio:

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

Deliver for shareholders

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[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;
[2] Clinical trial subject to further funding / partnership; [3] company estimates; includes funding for study and company operations

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 studies[1]

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 months[2]

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[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;
[2] Based on draft trial considerations as part of scenario planning; study start and final trial design subject to additional financing / partnership; timelines refer to from study start

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 study[1]
- Excellent safety profile in >400 participants over more than 2 years

Evidence-based pivot to DKD

- Compelling kidney function data confirmed in second Phase 2 study & meta-analysis[1]
- Substantially larger treatment effect in diabetes subgroup
- Dose response connected to a plausible MoA targeting inflammation / fibrosis
- Results in study participants 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 extension[2]

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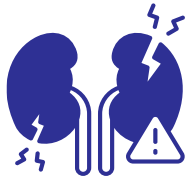
[1] VIVIAD and VIVA-MIND Phase 2 studies in early Alzheimer's disease (AD) included prospectively defined measures of kidney function as safety and other exploratory endpoints, the primary and secondary endpoints in early AD were not met; [2] Potential for Hatch-Waxman extension of up to 5 years.

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

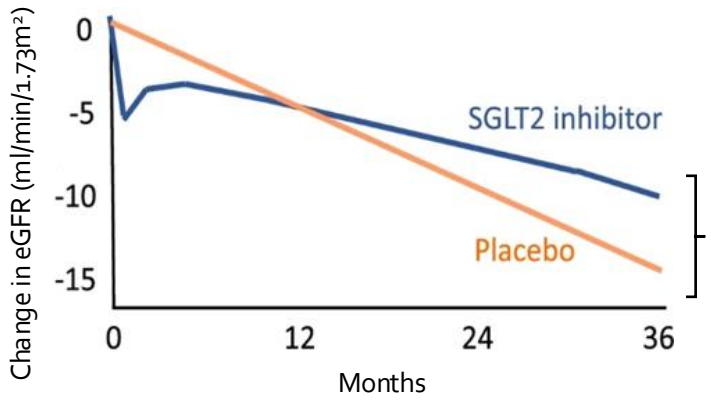
~1.5M patients	~2.4M patients	~65-75%	~20-30%
DKD stage 3b/4 in the US	DKD stage 3b/4 in the EU	of stage 4 patients will start dialysis within 5 years	of stage 4 patients die before dialysis

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

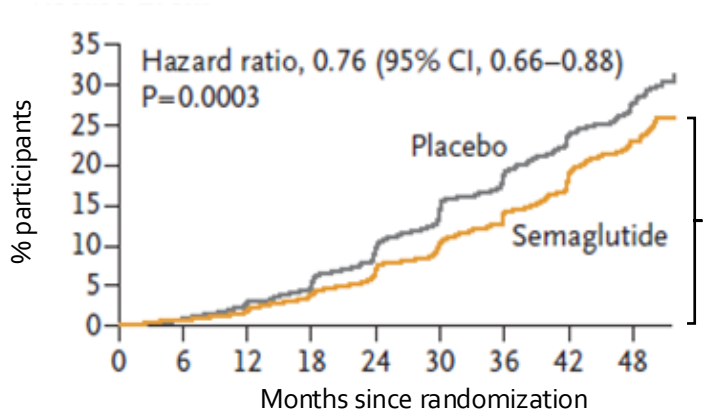
Typical changes in eGFR following introduction and long-term use of SGLT-2 inhibitors in T2 diabetes[1]



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

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[1] Bailey et al. Current Diabetes Reports (2022); [2] Perkovic et al., NEJM (2024) FLOW trial;
SGLT2i: sodium-glucose cotransporter-2 inhibitor; GLP-1RA: glucagon-like peptide 1 receptor agonist

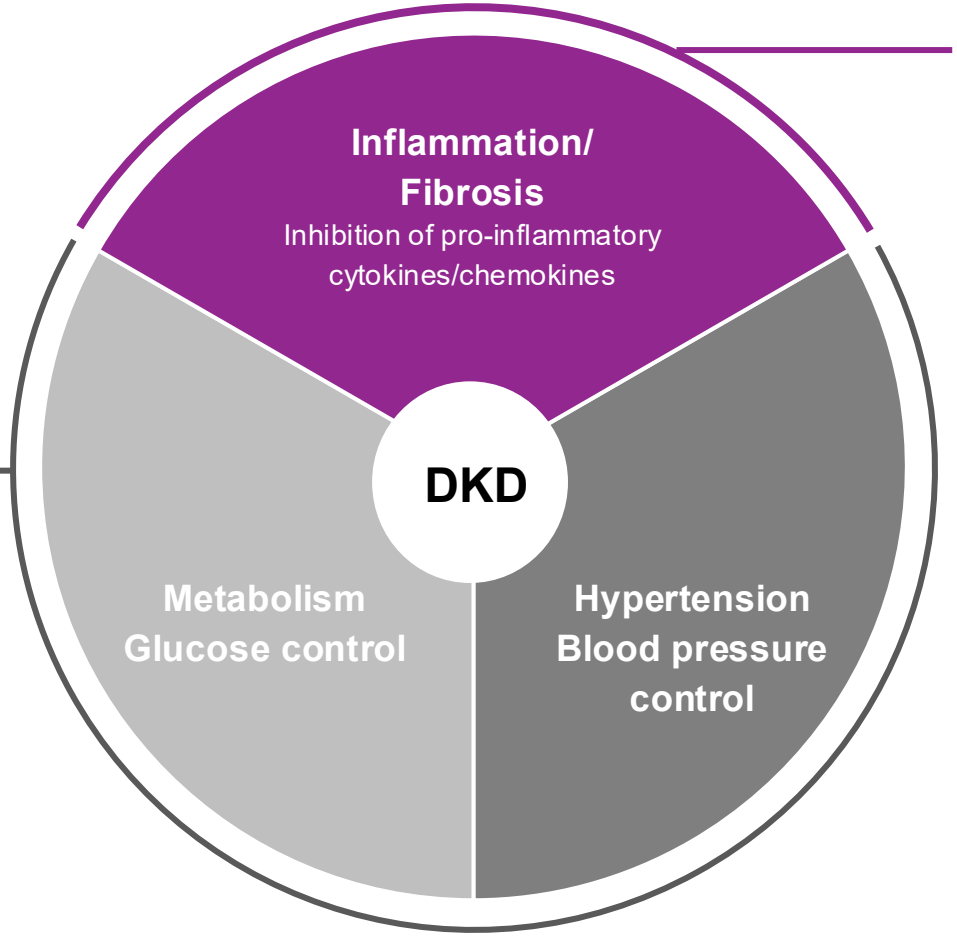
Targeting inflammation and fibrosis offers a complementary approach to existing therapies by tackling DKD at its roots

Existing treatment:

Management of comorbidities

e.g. ACEi, ARBs

GLP-1RA, SGLT2i



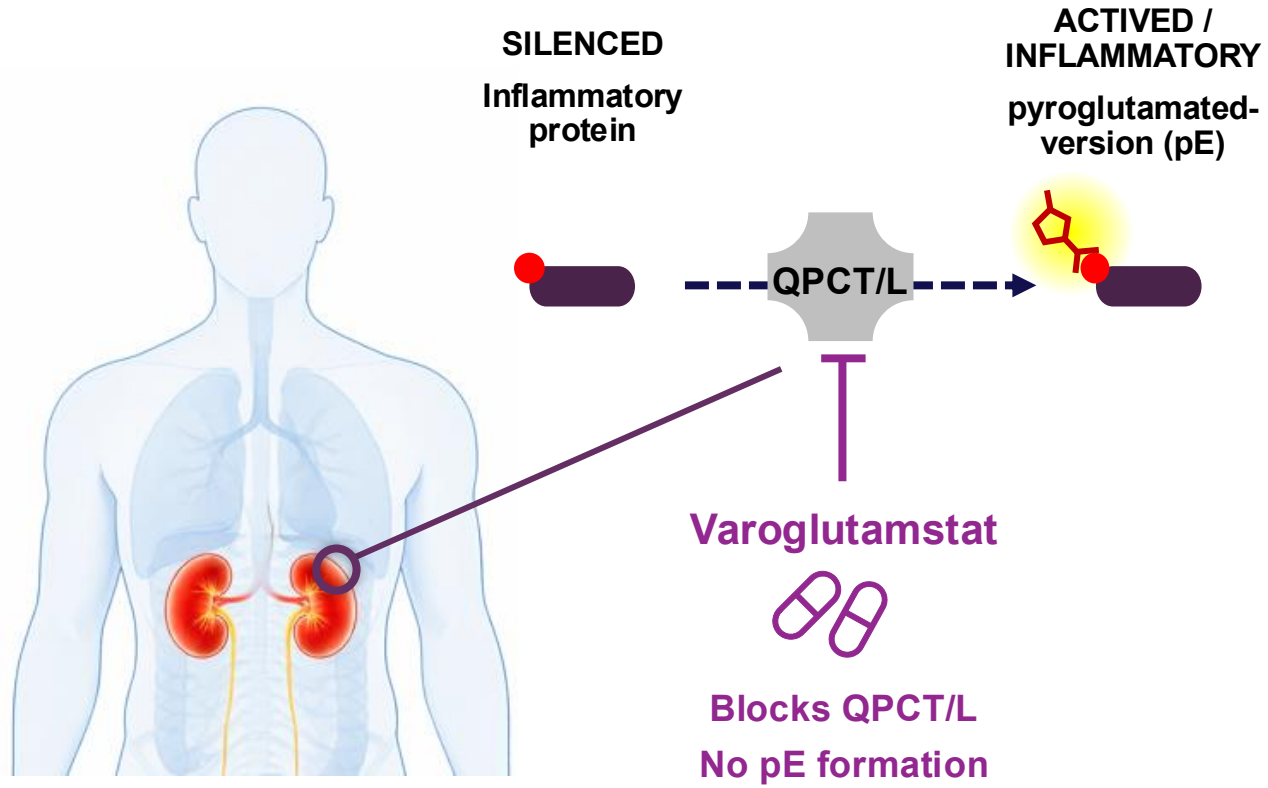
Varoglutamstat:

QPCT/L inhibitor

Complementary approach targeting inflammation/fibrosis; aims to stabilize or reverse kidney function decline

SGLT2i: sodium-glucose cotransporter-2 inhibitor; GLP-1RA: glucagon-like peptide 1 receptor agonist; ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin II receptor blocker

Varoglutamstat reduces pro-inflammatory signaling by destabilizing key inflammatory molecules



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

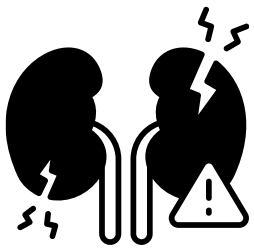
Impaired kidney	Varoglutamstat treated
Kidney function ↓	Kidney function ↑
Fibrosis ↑	Fibrosis ↓
Inflammation ↑	Inflammation ↓

Cynis et.al. EMBO, 2011; Cynis et al, Int. J Exp Path, 2013; Kanemitsu et al., 2021; Vivoryon company data, 2024; QPCT/L: Glutaminyl-peptide cyclotransferase / -like protein; Notes: Graphic is for illustrative purposes only

Varoglutamstat in kidney disease: targeting loss of kidney function at two levels simultaneously - the inflammatory and the fibrotic axis

HYPERTENSION

mechanical stress



DIABETES

advanced glycation end products (AGE), mitochondrial stress, ROS

Varoglutamstat

QPCT/L substrates

Chemokines

e.g. CCL2, CCL7, CX3CL1

Inflammatory response

TGFb signaling, NFkB activation, mitochondrial stress, apoptosis

Varoglutamstat

QPCT/L substrates

(Pro-) Collagens

I and III, fibronectin

Fibrotic response

myofibroblast activation, ECM protein secretion, tissue scarring / stiffening

Loss of Function

mitochondrial stress, apoptosis, podocyte effacement, glomerulosclerosis

tubulointerstitial fibrosis, kidney failure

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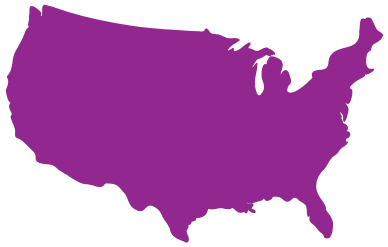
Vivoryon has evaluated varoglutamstat's effect on kidney function in two independent randomized double-blind placebo-controlled Phase 2 studies

VIVIAD Phase 2b (Europe)

VIVA-MIND Phase 2 (USA)



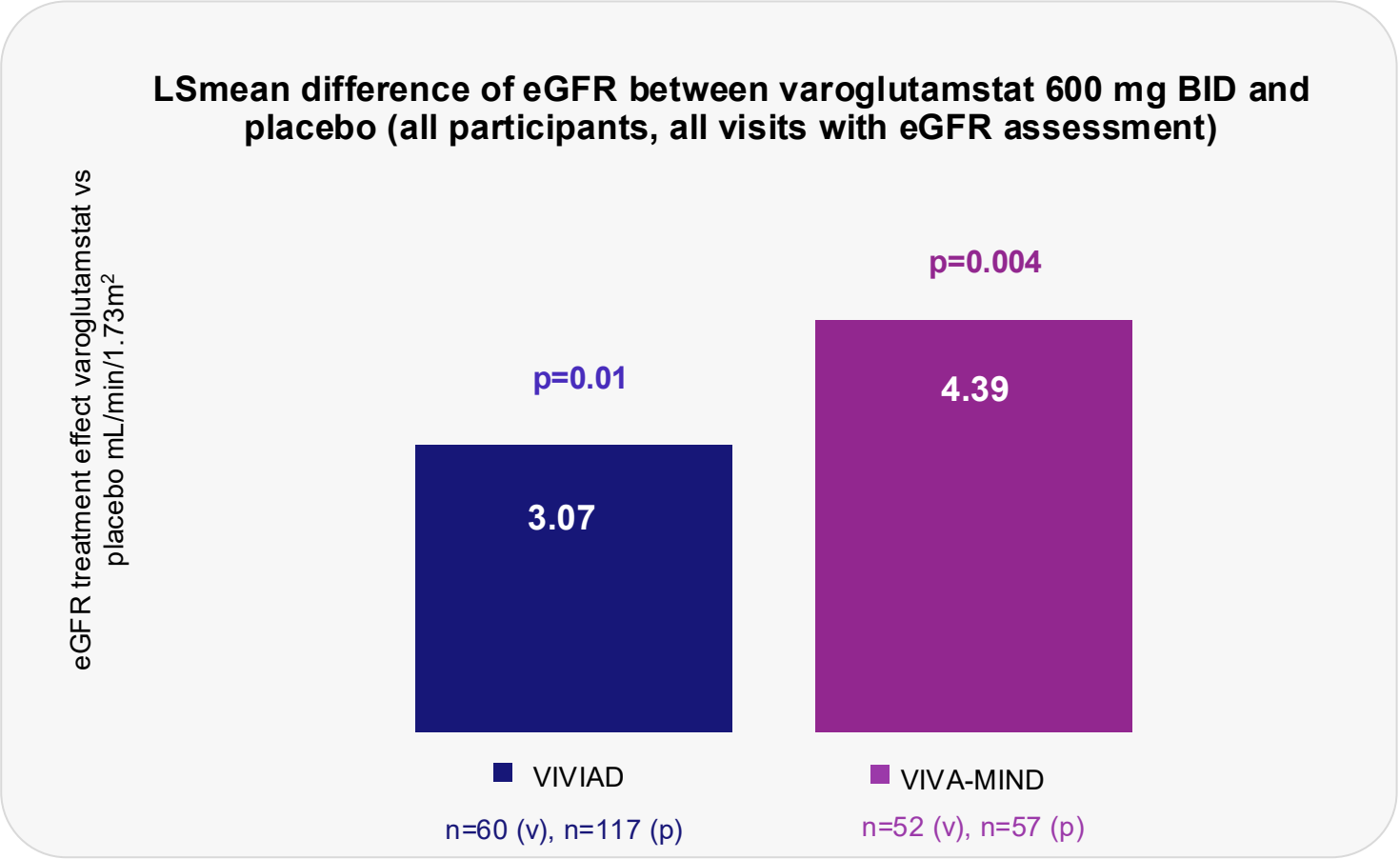
Parameter	VIVIAD (Europe)	VIVA-MIND (U.S.)
Participants selection	Mild AD, mean age 68 yrs	Mild AD, mean age 72 yrs
No. of participants treated	n=259	n=109
Varoglutamstat dose	300 and 600 mg BID	600 mg BID
Dose escalation period	Slow: 600 mg start week 13	Fast: 600 mg start week 9
Treatment duration	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 participants 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 participants 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%

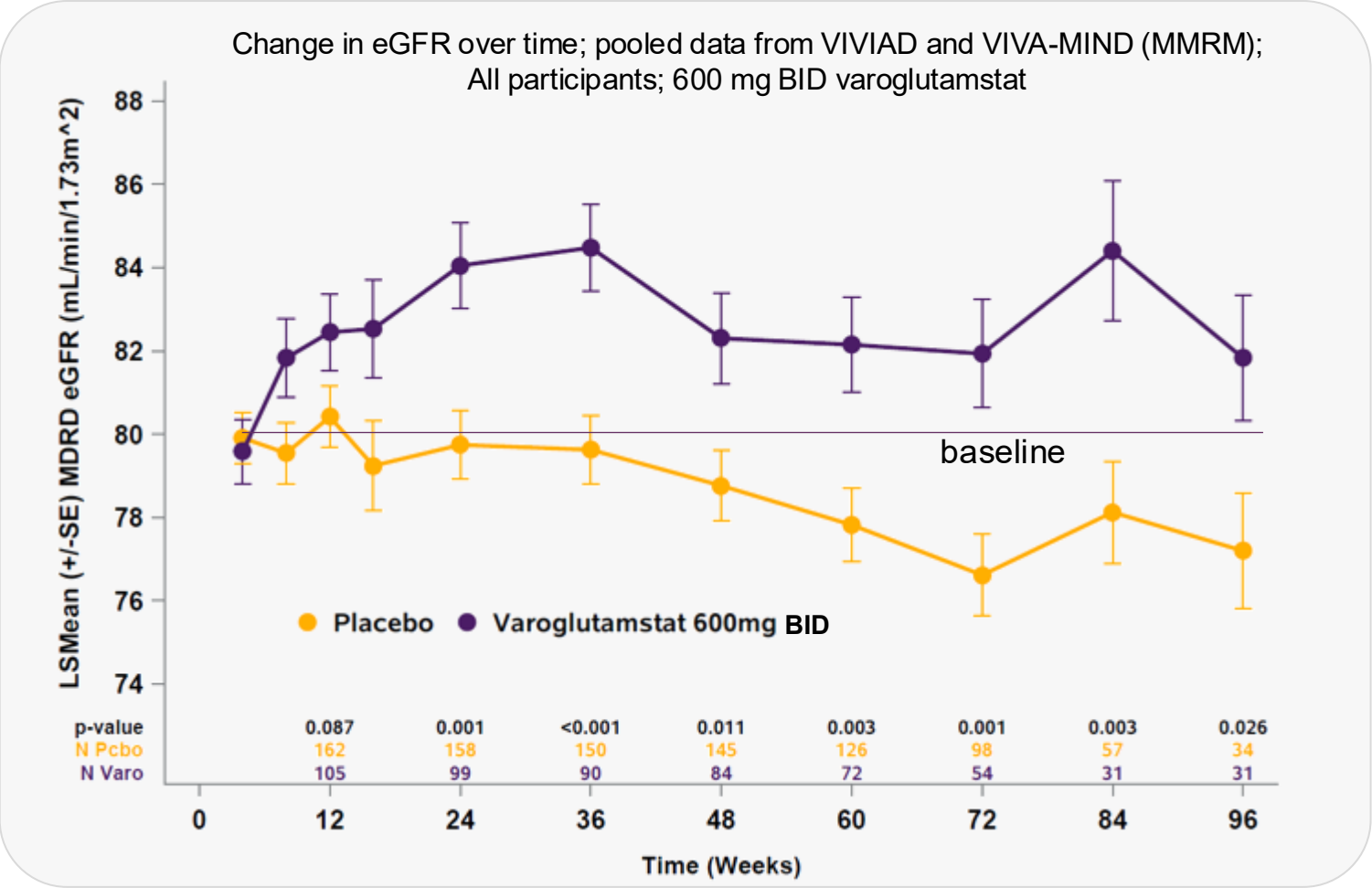
Beneficial kidney function effect consistently observed in VIVIAD and VIVA-MIND

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 study participants treated with varoglutamstat compared to placebo



Varoglutamstat

Clear and consistent separation of curves after 24 weeks

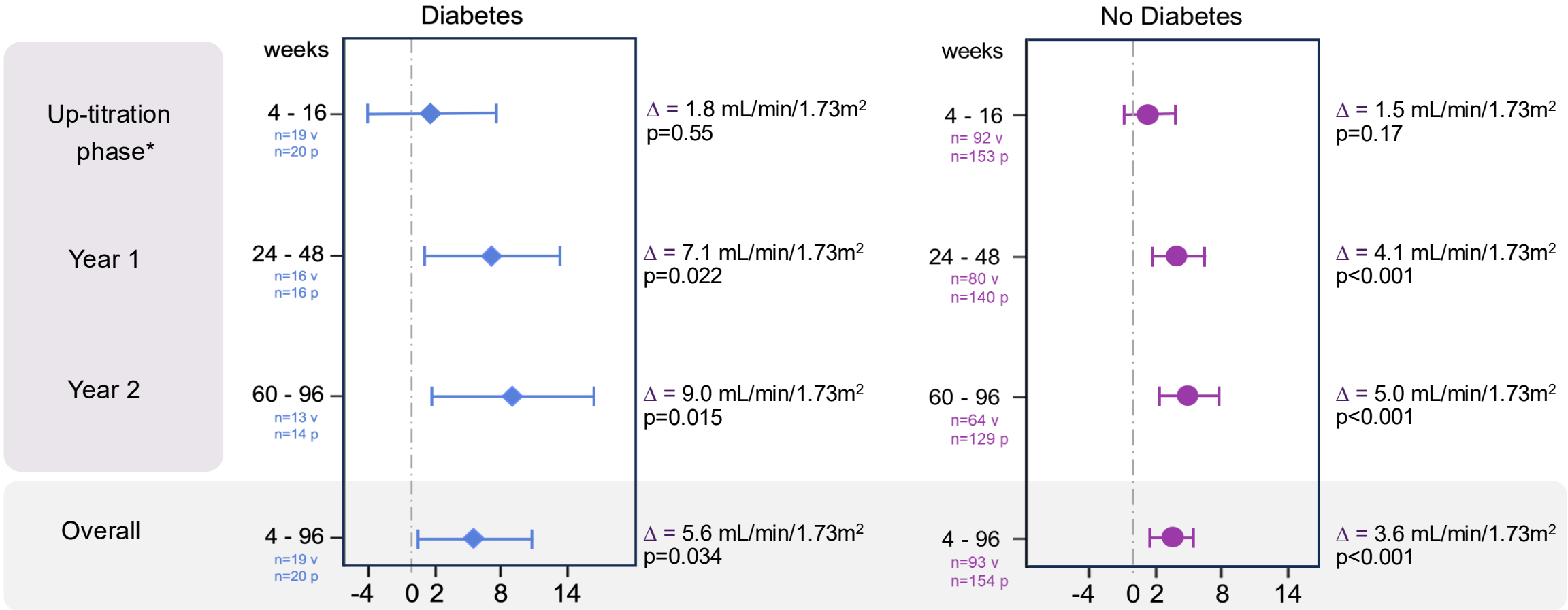
Effect stable and maintained above baseline for 2 years

Participants in placebo group 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)

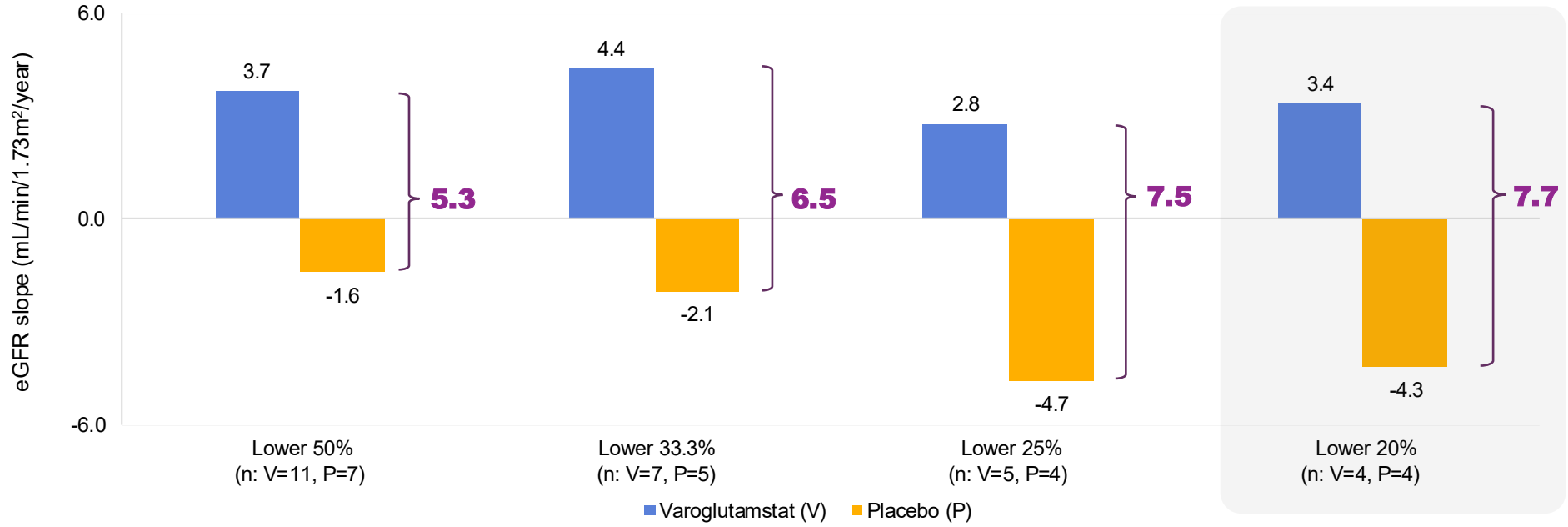
0: No treatment effect; > 0: Improvement of eGFR (MDRD);

n: Number of participants 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 participants 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)



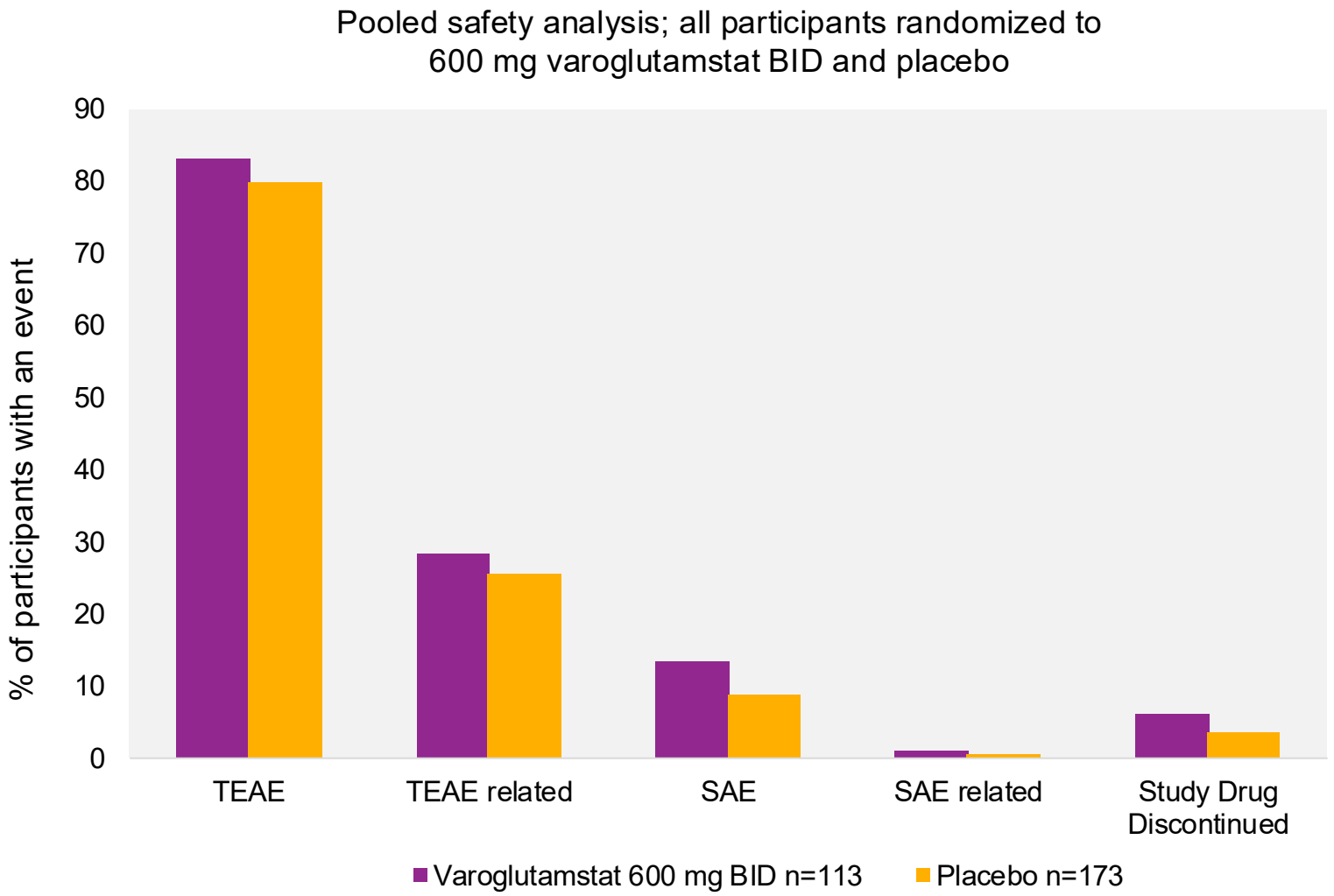
Treatment effect
(mL/min/1.73m²/yr)

Mean baseline eGFR (mL/min/1.73m²)	65.2	60.5	56.6	55.8

more impaired kidney function,
more pronounced treatment effect

*eGFR slope (mL/min/1.73m²/year): random coefficients and MMRM calculations on pooled data from VIVIAD and VIVA-MIND in diabetic patients in the lower percentiles; * Diabetes subgroup defined as patients having at baseline either medical history of diabetes (type 1 or 2, and glucose tolerance impaired, hyperglycaemia) and/or comedication with drugs used in diabetes and/or untreated with a HbA1c > 6.5%; data rounded to one decimal place; number of participants in the varoglutamstat treatment group or the placebo group at week 12*

Varoglutamstat was well tolerated in VIVIAD and VIVA-MIND



Extensive safety package (# / duration)

Pharmacology / Phase 1

Phase 1 study: large trial with 205 participants

Human ADME / mass balance study completed

Phase 2 double-blind, placebo-controlled

Phase 2a study: 120 patients, 12 weeks

VIVIAD Phase 2b study: 259 participants, mean treatment duration 76 weeks

VIVA-MIND Phase 2 study: 109 participants treated, mean treatment duration 46 weeks

TEAE: Treatment Emergent Adverse Event; SAE: Serious Adverse Event

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

Current SoC

Kidney function continues to decline

~30–50% of patients ineligible for SGLT2i and/or GLP-1RA

High discontinuation rates of ~65% for SGLT2i and GLP-1RA

Varoglutamstat

Stabilizes or improves kidney function

Excellent safety profile

Potential to significantly improve outcomes

Shown to improve kidney function

- Data from 2 independent Phase 2 studies
- Prominent effect in participants with diabetes

Well-tolerated convenient oral medicine

- Excellent safety profile in >400 participants over more than two years

Differentiated mechanism of action

- Targets pro-inflammatory & pro-fibrotic pathways
- Complementary to existing therapies
- IP to 2044+ with U.S. composition of matter patent[1]

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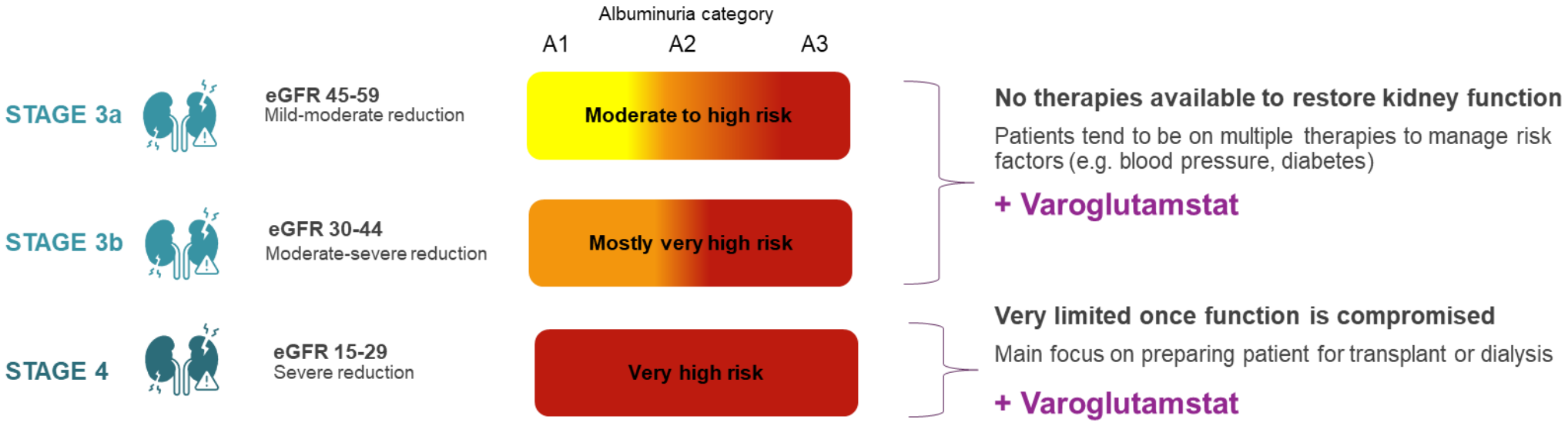
[1] *Potential for Hatch-Waxman extension of up to 5 years*

SGLT2i: sodium-glucose cotransporter-2 inhibitor; GLP-1RA: glucagon-like peptide 1 receptor agonist

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



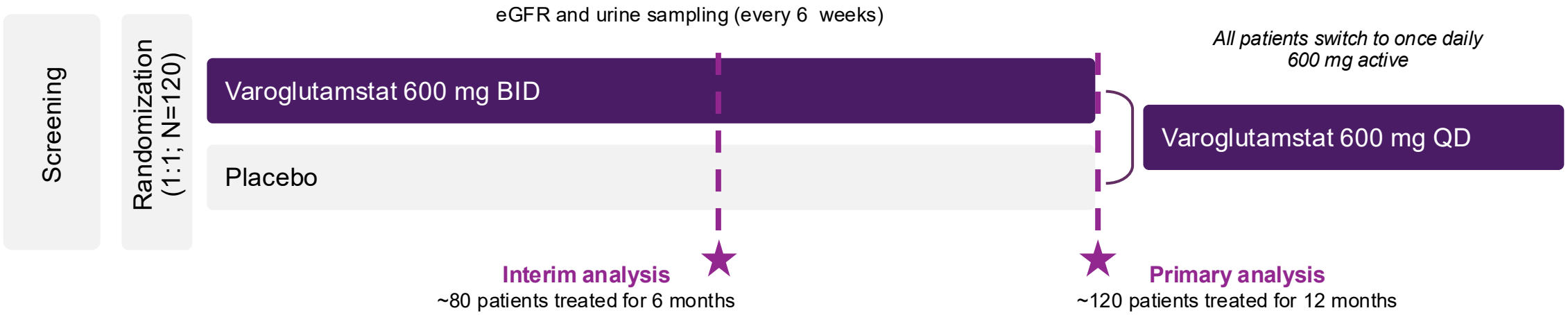
High unmet need in advanced DKD creates unique opportunity for varoglutamstat

- 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

Based on KDIGO-2024 CKD guideline: https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline.pdf; Albuminuria categories defined as A1: Normal to mildly increased <30 mg/g (<3 mg/mmol); A2: Moderately increased 30–300 mg/g (3–30 mg/mmol); A3: Severely increased >300 mg/g (>30 mg/mmol)

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 care[1]



Patient population

- Patients with DKD (stage 3b/4 plus high-risk stage 3a)
  - eGFR 20-60 mL/min/1.73m^2
  - 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 endpoint[2]

[1] *Clinical trial subject to further funding / partnership; Draft design: Trial design based on scenario planning;* [2] *Am J Kidney Dis. 75(1): 84-104;*
SoC: standard of care; SGLT2i: sodium-glucose cotransporter-2 inhibitor; ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin II receptor blocker; DKD: Diabetic kidney disease

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 years[1]

Predictable clinical path: key value inflection points within next 15 - 24 months[2]

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

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[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;*
[2] *Based on draft trial considerations as part of scenario planning; study start and final trial design subject to additional financing / partnership; timelines refer to from study start*

Clear roadmap towards value creation

Required to start Phase 2 in DKD

Current runway into Q4 2026

~EUR 30 M to primary data[2] incl. **~EUR 15 M** to interim data[2]

Study execution

Randomized placebo - controlled trial in stage 3b/4 DKD

First data in stage 3b/4 DKD

Validate efficacy in target population

Comprehensive data set

Data to inform pivotal design and regulatory

Advance to Phase 3

Potential for strategic partnership for Phase 3

[1] Clinical trial subject to further funding / partnership; [2] company estimates; includes funding for study and company operations

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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

[1] Subject to funding / partnership; [2] Cynis et al. 2013; [3] Cynis et al., 2011; [4] unpublished data; [5] Hellvard et al., 2013;
FSGS: Focal segmental glomerulosclerosis; MASH: Metabolic dysfunction-associated steatohepatitis;
MASLD: Metabolic dysfunction-associated steatotic liver disease; IBD: inflammatory bowel disease; MS: multiple sclerosis