



Innovation to Improve Kidney Health Outcomes

July 2025

Vivoryon Therapeutics N.V.

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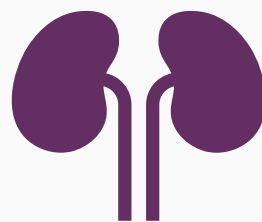
The kidney is the most frequently replaced organ worldwide

3.7 million people on dialysis worldwide¹

Many more would need dialysis but have **no access to therapy**

As context
>1 million hip replacements are conducted each year worldwide²

Over **110,000 kidneys** transplanted annually (2023)³



Average age @ receiving a kidney transplant:
53 years⁴



CKD is a major economic and societal burden in Europe and worldwide

One in every 10

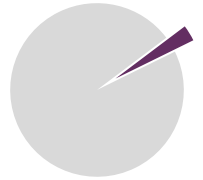
adults in Europe is affected by chronic kidney disease (US 1 in 7)¹



Europe allocates approximately **€140 billion annually** to treat CKD and kidney failure²



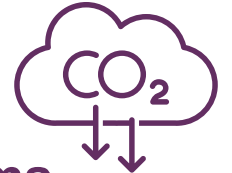
End-stage CKD accounts for **2-3%** of health care budgets



Cost of hemodialysis to health care systems can reach up to **€80,000 per patient per year**³



Driven by dialysis, projections indicate that by 2032, CKD-related environmental burden in Germany alone could generate **approximately 1.24 billion kilograms of carbon emissions** — equivalent to the annual carbon footprint of 737,000 cars⁴



¹ Sundström J, et al., *The Lancet Regional Health – Europe*, 2022; ² van Mil D, et al., *Clin Kidney J*, 2024; ³ EKHA. *European Kidney Alliance*. August 2015;

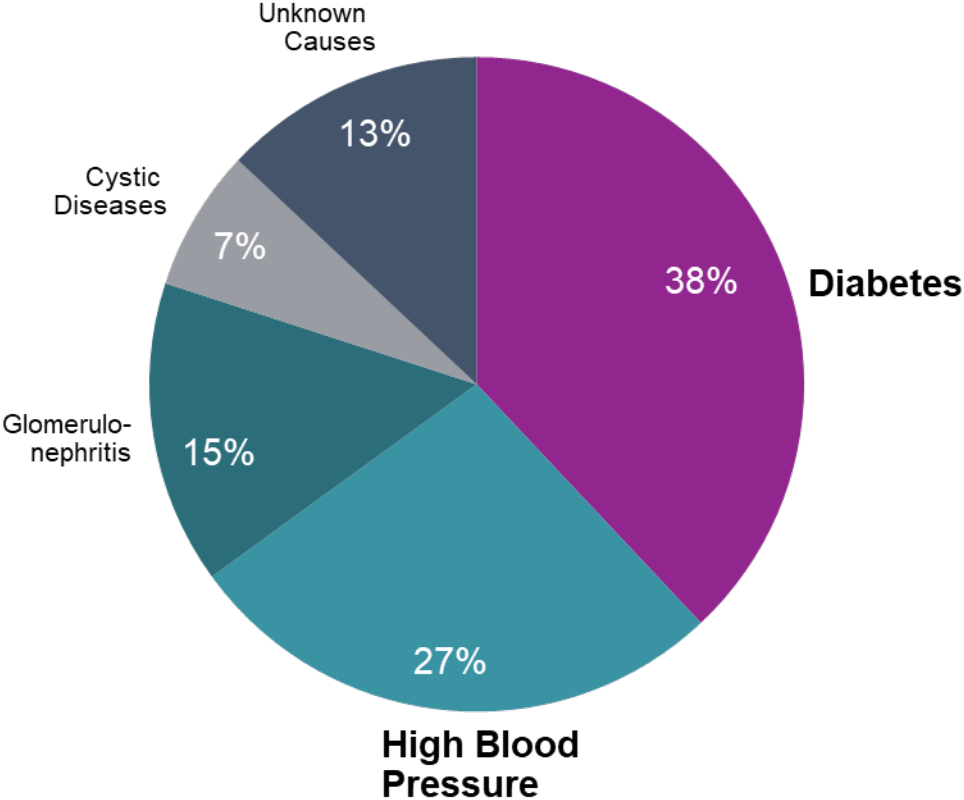
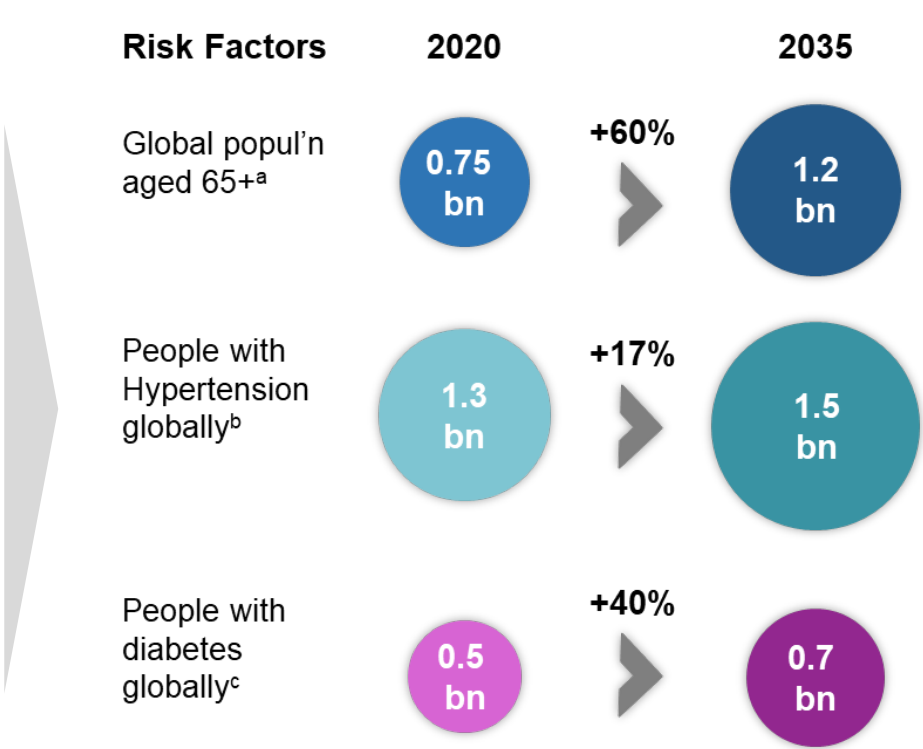
⁴ Rao N, et al. Presented at: WCN 2024,.

Rate of cardio-metabolic risk factors and age are key dynamics in the CKD market

Number of CKD patients and burden of disease expected to increase globally in next decade¹

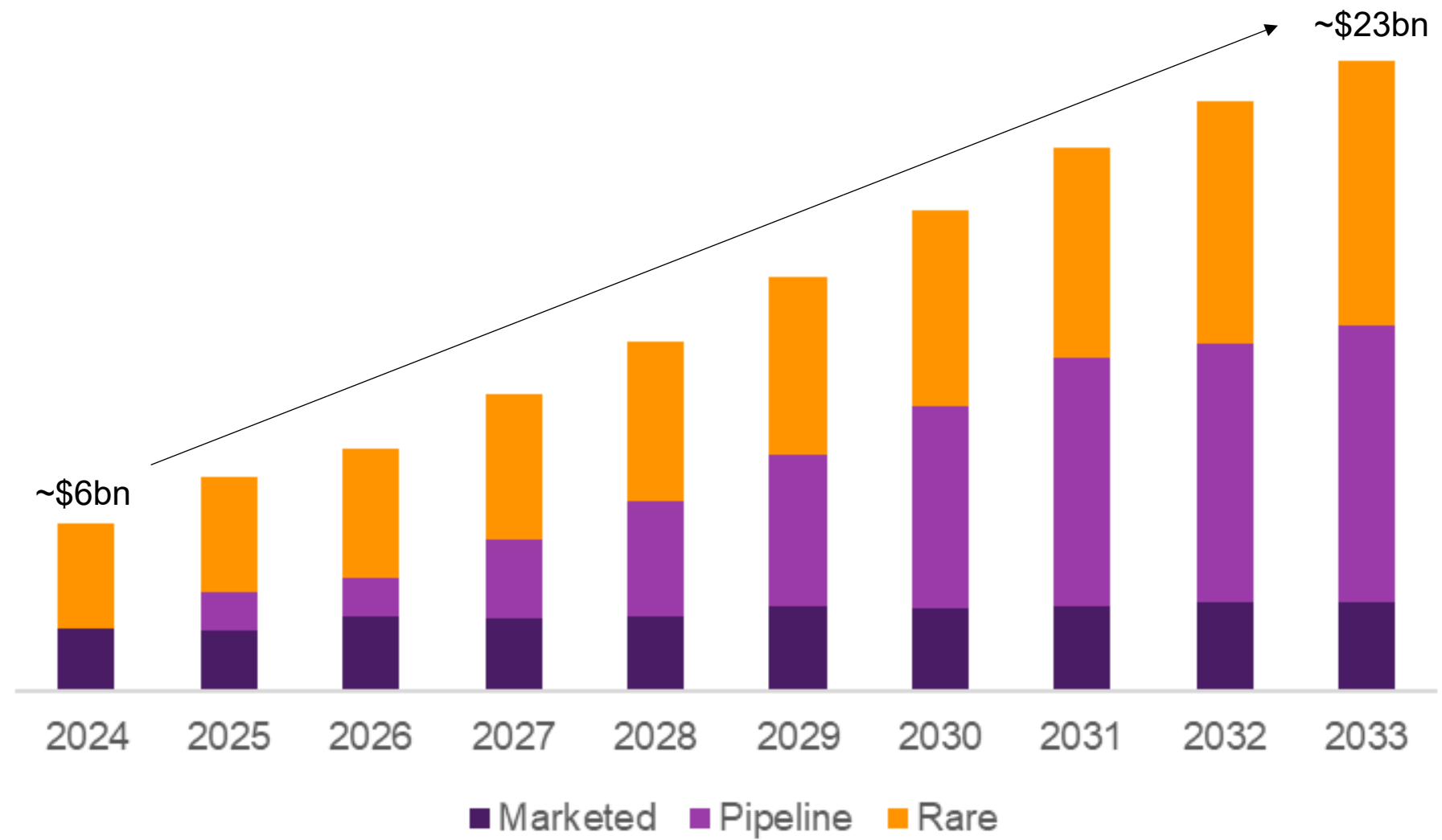
Diabetes and hypertension are leading causes of end-stage kidney disease¹

Global CKD prevalence:
>10% of general population, or
>800mn CKD patients³



¹Adapted from Fresenius Medical Care AG, Investor Presentation Q2 2024, page 5, references include ^aUnited Nations Department of Economic and Social Affairs, Population Division (2022). World Population Prospects 2022: Summary of Results. UN DESA/POP/2022/TR/NO.3. ^bWHO Global Health Observatory (2019), adjusted for population aged >18. ^cIDF Diabetes Atlas 2021 (10th edition); ²US Renal Data System; ³Based on estimates for 2017, Jager et al., Kidney International (2019)

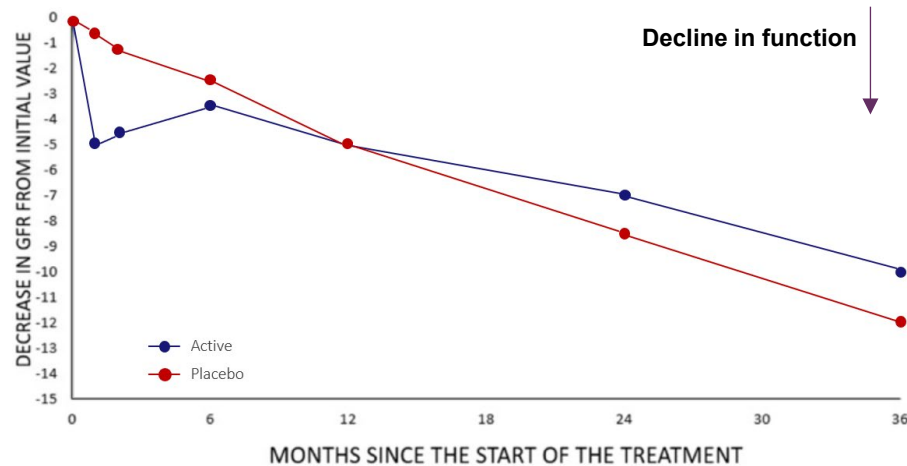
CKD market driven largely by new molecules in development pipeline



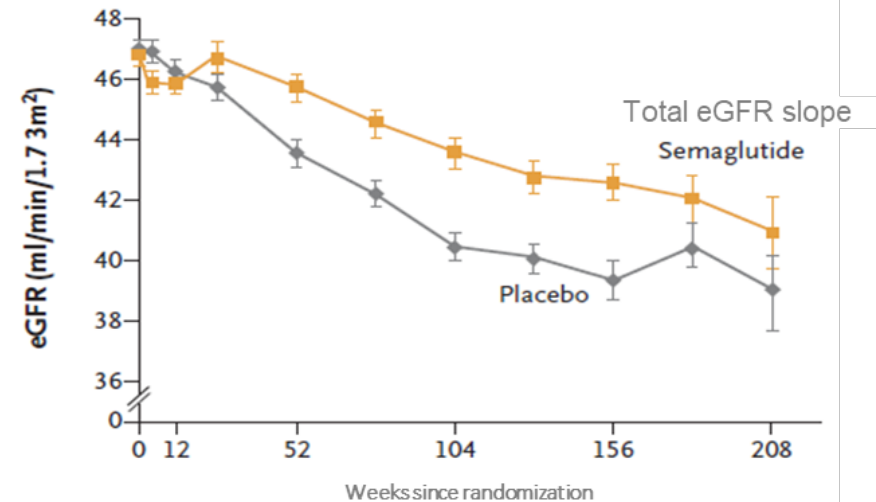
Schematic. Illustrative purposes only. CKD market value forecasts 7 major markets. Based on GlobalData 2024 (Marketed and pipeline CKD), Healthcare Research Reports (rare CKD, differentiation between marketed and pipeline not available). Note Rare CKD includes Lupus, Fabry Disease, aHUS, IgAN, FSGS, GMN, C3 glomerulopathy, Alport, Nephrotic cystinosis, ADPKD, Fabry Disease and e.g. lupus are major drivers of current marketed value.

Novel therapies are needed to address the rising global health challenge of kidney disease

Current therapies do not halt or reverse the progressive decline in kidney function characteristic of chronic kidney disease



SGLT2i effect on kidney function (eGFR; compiled data)¹



Semaglutide effect on kidney function (FLOW trial eGFR)²



Vivoryon: Mid clinical stage biotech company aiming to transform the treatment of kidney disease with its novel drug candidate varoglutamstat



MEDICAL NEED



Therapies that can **stabilize or improve kidney function** with the aim of stopping progression to kidney failure / ESKD



SOLUTION



Target key drivers of kidney inflammation and fibrosis with **varoglutamstat, a first-in-class QPCT/L inhibitor**



EVIDENCE



Varoglutamstat has shown **unique potential to stabilize and partially recover** kidney function in two independent clinical studies¹

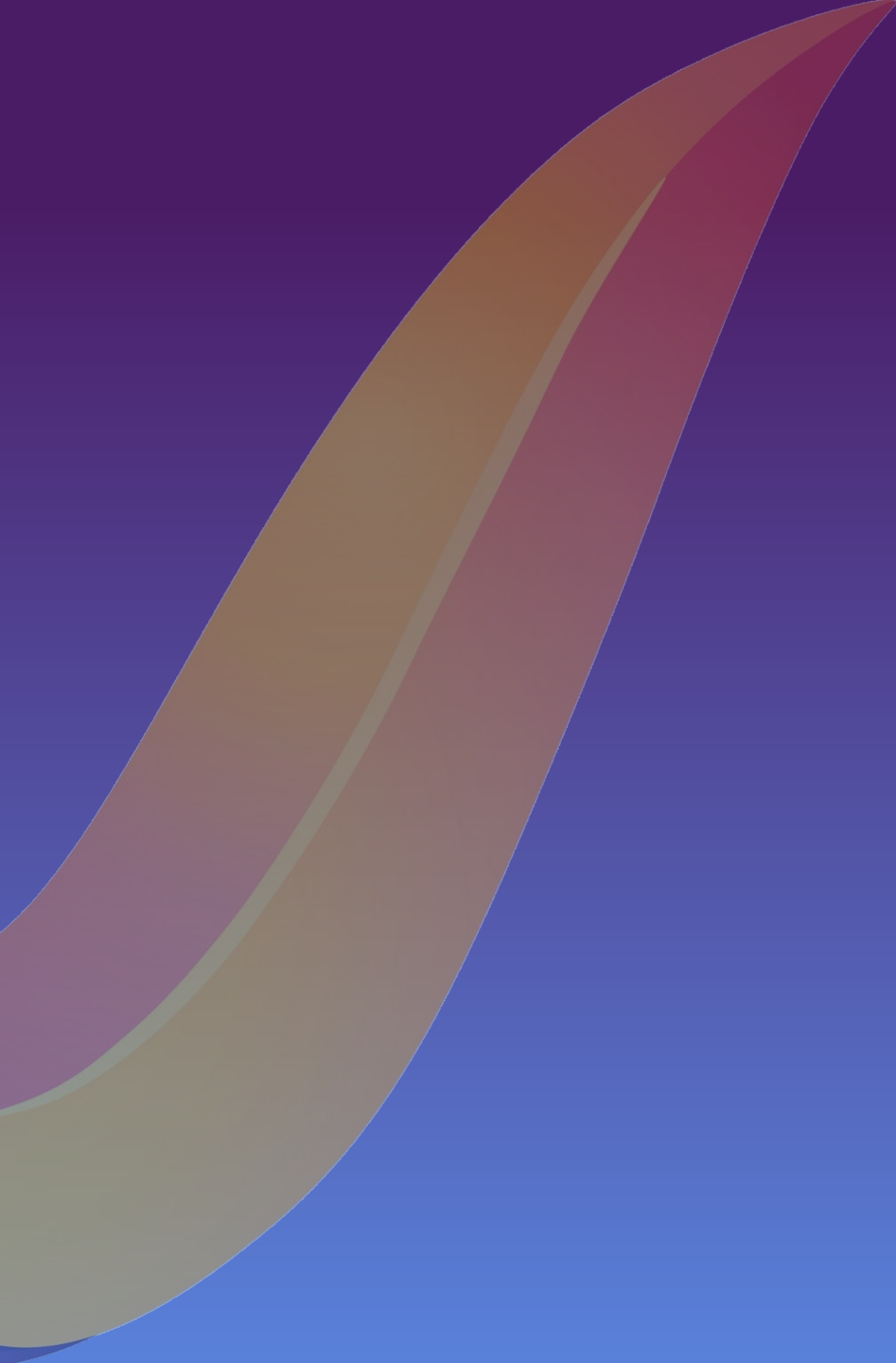


OPPORTUNITY



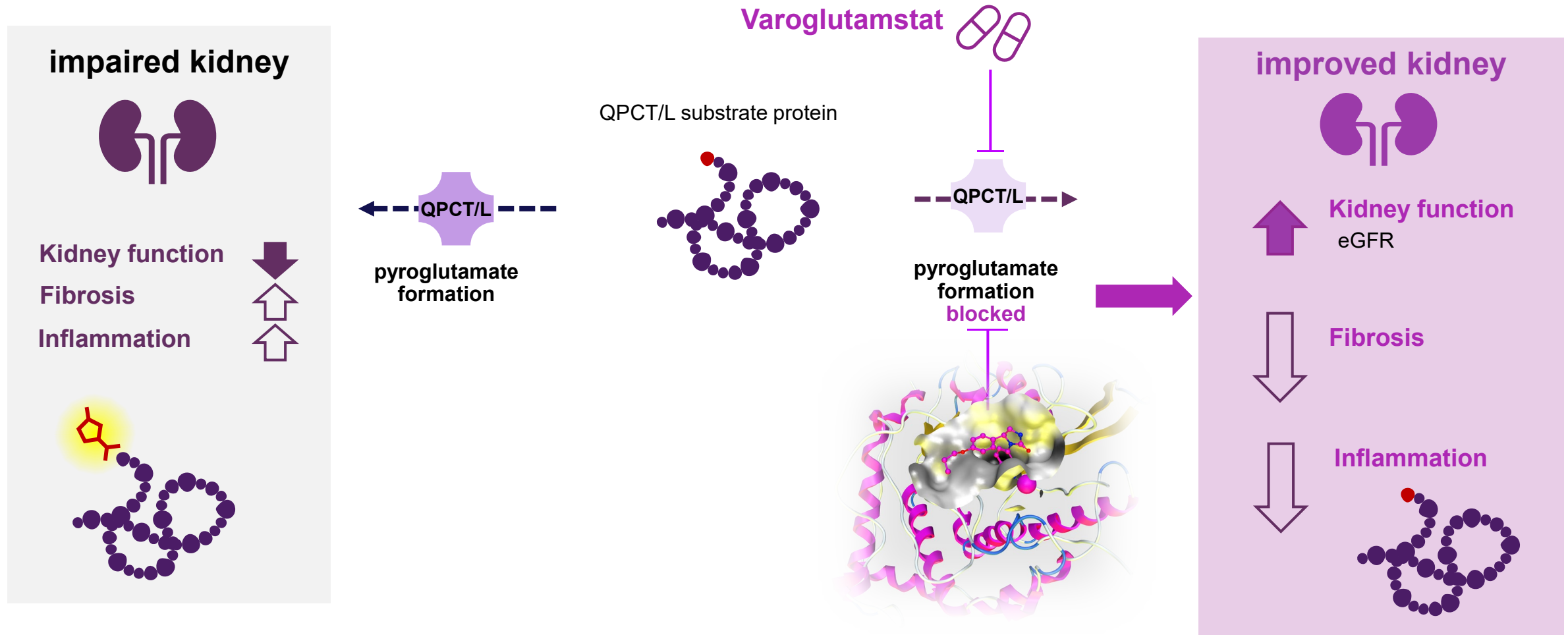
Clear path to market in large and growing global population; initial target market DKD





The Technology: Reducing
inflammation and fibrosis in
the kidney stabilizes and
improves kidney function

Pyroglutamated peptides produced by QPCT/L are a central part of the pro-inflammatory/pro-fibrotic pathways in kidney disease



Varoglutamstat's effect on kidney function has been demonstrated in two independent randomized double-blind placebo-controlled Phase 2 studies

VIVIAD Phase 2b

Europe, n=259
Adults with mild AD 300/600mg BID
Slow up-titration 76 wks tx duration¹

VIVA-MIND Phase 2

USA, n=109
Adults with mild AD 600mg BID
Faster up-titration 46 wks tx duration¹

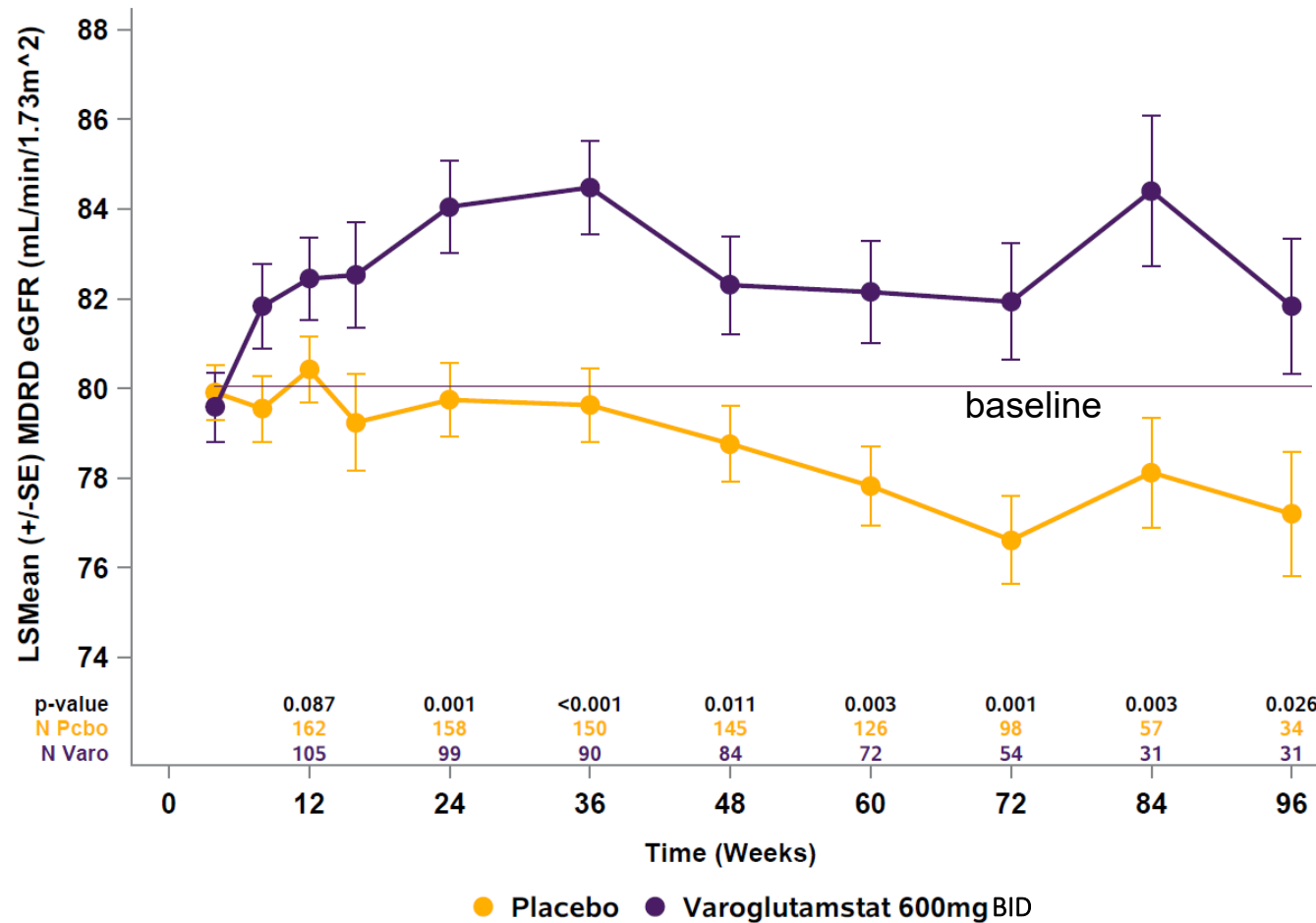
Strong **proof of principle** data in over 360 patients treated for up to 2 years provide basis for development of varoglutamstat in **diabetic kidney disease**

- ◆ Kidney function measured using eGFR, a key regulatory endpoint, prospectively included as a pre-specified safety / exploratory endpoint
- ◆ Statistically significant and clinically meaningful improvement in eGFR in both studies
- ◆ Significant effect first observed at week 24 and sustained until week 96
- ◆ Substantially larger effect size in participants with diabetes vs. without diabetes²
- ◆ Improvement confirmed in a meta-analysis and pooled analysis
- ◆ Varoglutamstat well-tolerated to date in >400 study participants



VIVIAD: [ClinicalTrials.gov IDNCT04498650](https://clinicaltrials.gov/ct2/show/study/NCT04498650); VIVA-MIND: [ClinicalTrials.gov IDNCT03919162](https://clinicaltrials.gov/ct2/show/study/NCT03919162); 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; ¹mean treatment duration; ²Diabetes 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%.

Change in eGFR over time; pooled data from VIVIAD and VIVA-MIND (MMRM); **All subjects**; 600mg BID varoglutamstat



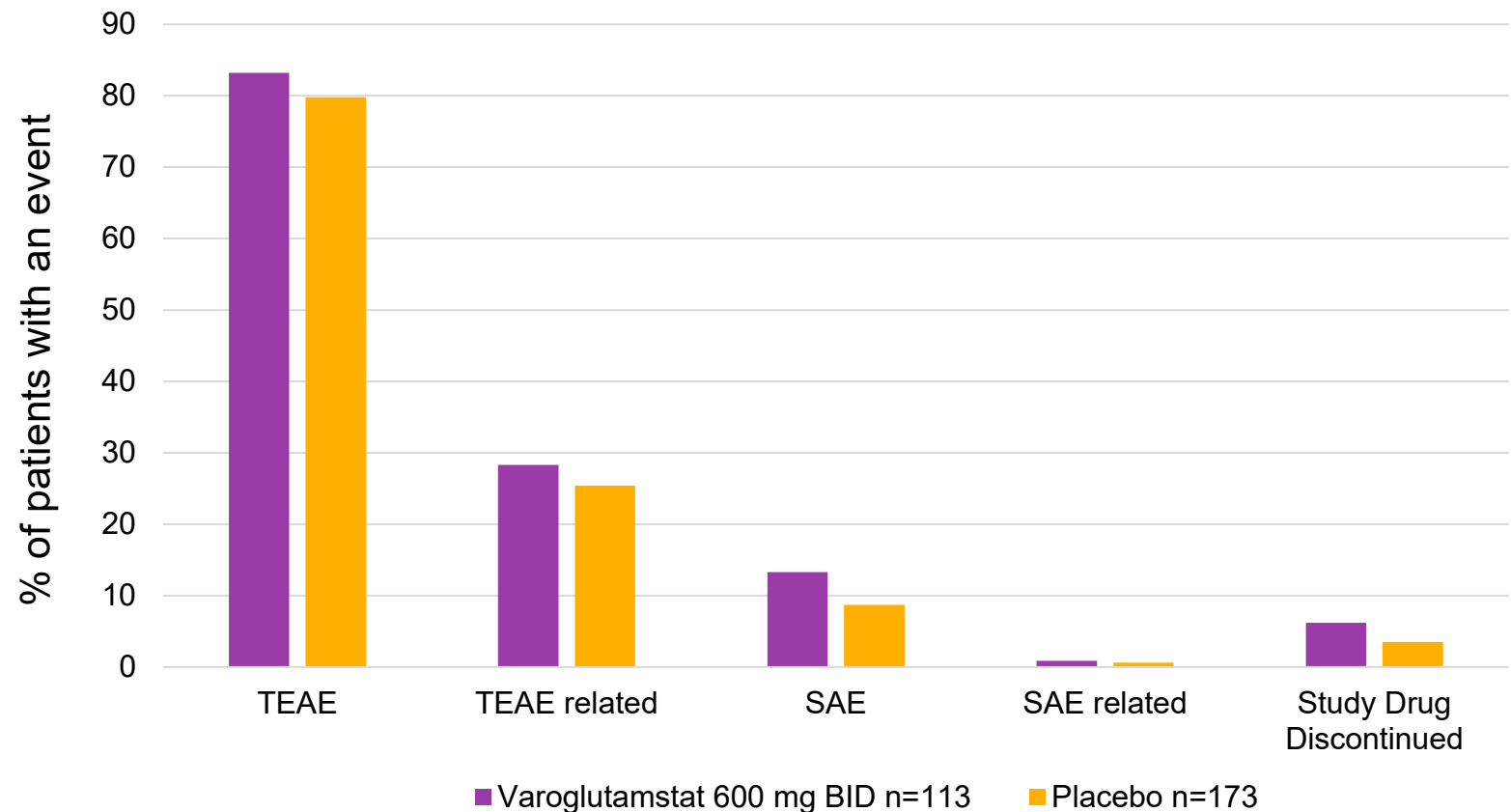
Varoglutamstat

- ◆ Clear and consistent separation after 24 weeks
- ◆ Effect stable and maintained above baseline for 2 years
- ◆ Placebo patients decline mildly



Varoglutamstat shown to be well-tolerated

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

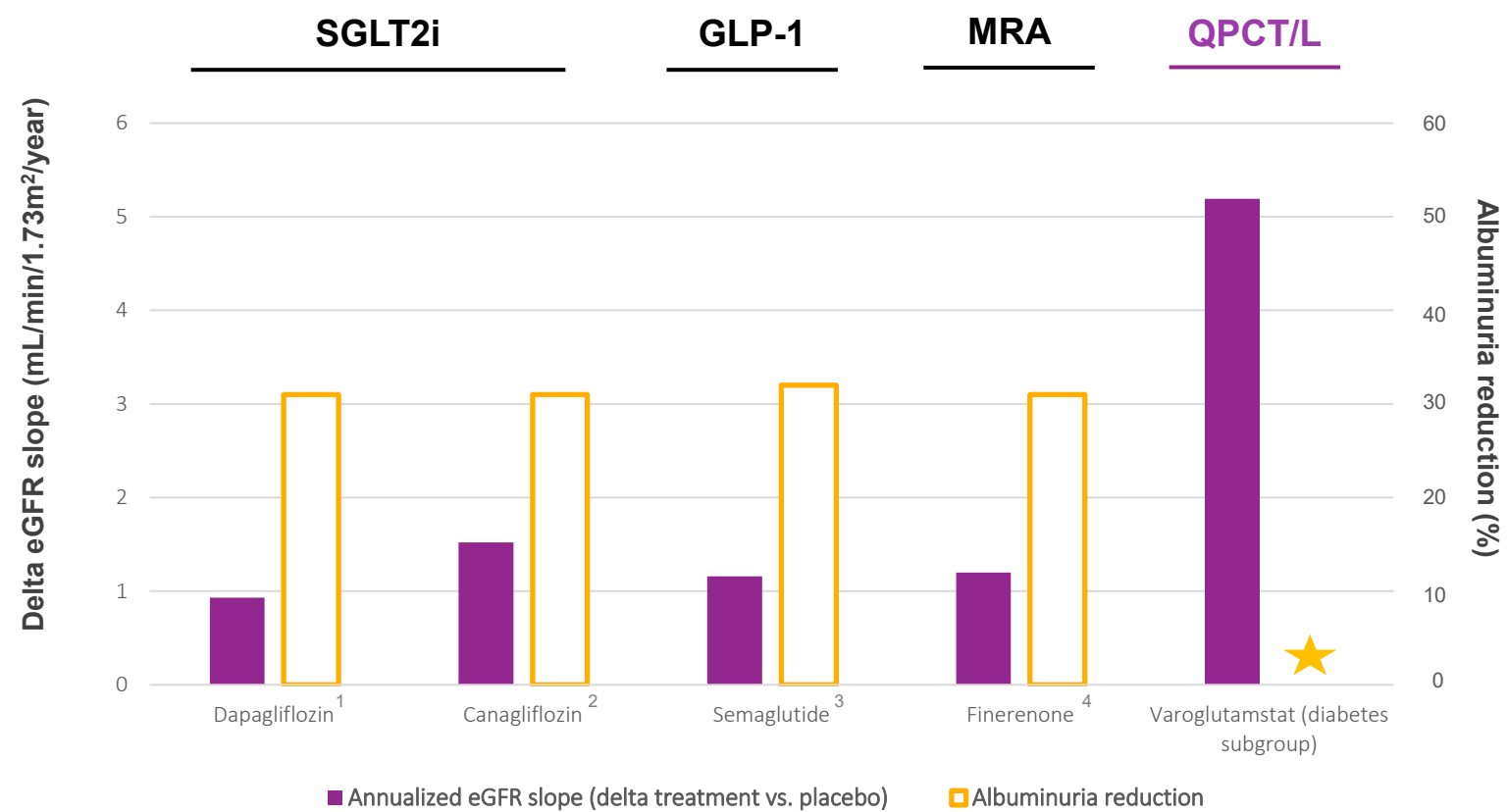
Phase 2 double-blind, placebo-controlled

- ◆ 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



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

Effect size substantially higher than observed with current standard of care (SGLT2i / GLP-1)

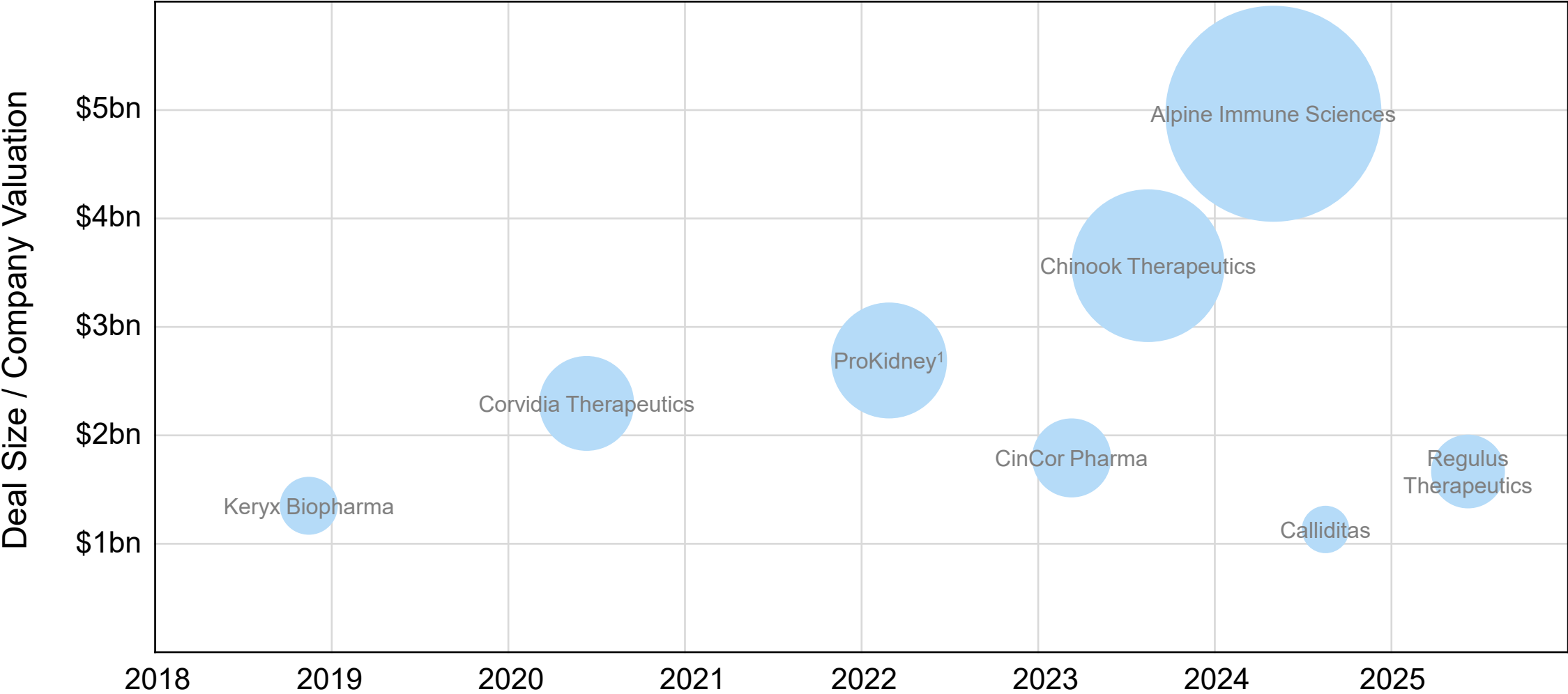


★ Conducted qualitative assessment, no increase in albuminuria observed; analysis of albuminuria planned for next Phase 2b study



Note: data comparisons are for illustrative purposes and not from head-head-studies or comparable patient populations, timelines or methods; Data for varoglutamstat is from pooled slope analysis for VIVIAD / VIVA-MIND Phase 2 study, diabetes subgroup; SGLT2 – sodium glucose cotransporter-2 inhibitor class; GLP-1 Glucagon-like peptide class; MRA: mineralocorticoid receptor antagonist; QPCT/L – varoglutamstat inhibits the glutaminy cyclases QPCT and QPCTL; eGFR: estimated glomerular filtration rate; ¹ Heerspink et al. N Engl J Med, 2020; ² Perkovic et al., N Engl J Med, 2019; ³ Perkovic et al., N Engl J Med, 2024; ⁴ Bakris et al., N Engl J Med, 2020

The kidney space has a strong M&A dynamic

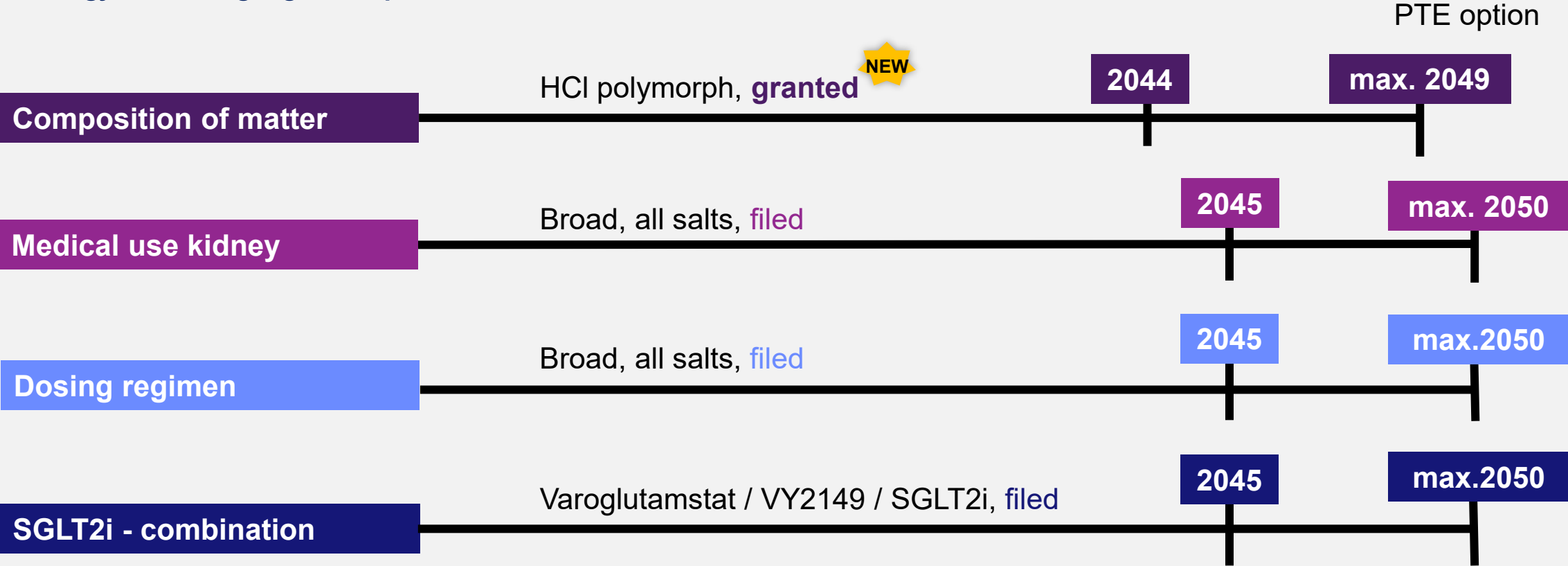


¹Valuation based on equity value after SPAC merger; deal sizes based on publicly available company disclosures



Vivoryon owns a large patent portfolio including a recently granted US patent on composition of matter for varoglutamstat until 2044

IP-strategy: recent highlights & updates



New Study: Efficient study design to confirm the treatment effect in patients with advanced DKD¹

Primary Goal

- ◆ Aiming to confirm the efficacy of varoglutamstat 600mg BID on eGFR in people with advanced diabetic kidney disease in an efficient and timely manner

Key Metrics and Considerations

- ◆ Double-blind randomized placebo-controlled multi-center study
- ◆ Patients with T2DM with stage 3b/4 CKD on top of SoC incl. SGLT2-i
- ◆ Adequately powered for meaningful data readout
- ◆ No. of patients: ~100 – 150
- ◆ Topline data ~24 months; design could include interim analysis at ~15 months to give earlier proof-of-concept²
- ◆ Typical trial cost approx. €12 -18m - dependent on patient number



¹ Draft trial considerations as part of scenario planning; study start and final trial design subject to additional financing / partnership; ² timelines refer to from study start.
BID: twice daily; T2DM: type 2 diabetes mellitus; CKD: Chronic Kidney Disease; SoC: standard of care; SGLT2-i: sodium-glucose cotransporter-2 inhibitor

Why invest?

Market

- ◆ High medical need with no therapies available that stabilize kidney function long-term
- ◆ Sizable population in major markets US, EU and globally
- ◆ Attractive opportunity in kidney space with excellent opportunity to collaborate with big Pharma, particularly with Phase 2b study in DKD



Company/clinical asset



- ◆ Robust clinical evidence in 2 independent studies with a large and unprecedented effect size¹
- ◆ New mechanism of action with excellent pre-clinical pharmacology results
- ◆ Next study with low-risk design and attractive short time to study results within 24 months
- ◆ Experienced management team with proven track record



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;



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