Akebia® THERAPEUTICS

Bettering the Lives of People Impacted by Kidney Disease

R&D Day 2026

April 2, 2026

Cautionary note on forward-looking statements

Statements in this presentation regarding Akebia Therapeutics, Inc.'s ("Akebia's") strategy, plans, prospects, expectations, beliefs, intentions and goals are forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, as amended, and include, but are not limited to, statements regarding: Akebia's plans, strategies and prospects for its business; Akebia's plans with respect to its U.S. commercial launch of Vafseo®, including the potential U.S. market opportunity; Akebia's plans for Vafseo to become standard of care for treatment of anemia due to CKD in dialysis, including its ability to build on the body of evidence demonstrating Vafseo's value potential, and progress towards that goal; Akebia's expectations and beliefs about demand for Vafseo, including the number of patients with access to Vafseo and the focus of dialysis organizations; Akebia's beliefs with respect to patient dosing demand for Vafseo in 2026; Akebia's plans and expectations with respect to publication of additional analyses of INNO2VATE data; Akebia's plans and expectations with respect to the VOICE trial, including the timing of top-line data and potential to demonstrate favorable outcomes in the composite of all-cause mortality and hospitalization in patients treated with vadadustat compared to ESA; Akebia's plans and expectations with respect to the VOCAL trial, including timing of top-line data; Akebia's beliefs and expectations regarding the mechanism of action of its technologies' and ability to address the biological need of certain diseases; Akebia's plans and expectations with respect to praliciguat and the Phase 2 trial, including to assess the use of praliciguat in other rare podocytopathies, the number of patients to be enrolled in the trial, its potential for successful development and regulatory path, and expected patient demand and annualized cost of care; Akebia's plans and expectations with respect to AKB-097, including the timing of initiation of, and initial data from, an open label Phase 2 basket study and the indications to be evaluated, other potential indications for consideration, its potential for pipeline in a product, its potential to achieve opportunities to address unmet need and limitations of current complement inhibitors and to become the standard of care in multiple rare kidney diseases alone or in combination with other therapies, and expected patient demand and annualized cost of care; and Akebia's plans and expectations with respect to AKB-9090, including the timing of initiation of, and top-line data from, a Phase 1 trial and the indication to be evaluated, and expected patient demand and annualized cost of care.

The terms "intend," "believe," "plan," "goal," "potential," "anticipate, "estimate," "expect," "future," "will," "continue," "could", derivatives of these words, and similar references are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various risks, uncertainties and other factors, including, but not limited to, risks associated with: the potential therapeutic benefits, safety profile, and effectiveness of Vafseo and Akebia's development candidates; the results of preclinical and clinical research; Akebia's ability to initiate and enroll patients in its clinical trials; decisions made by health authorities, such as the FDA, with respect to regulatory filings and other interactions; the potential demand and market potential and acceptance of, as well as coverage and reimbursement related to Auryxia® and Vafseo®, including estimates regarding the potential market opportunity; the competitive landscape for Auryxia and Vafseo, including generic entrants and the timing thereof; the ability of Akebia to attract and retain qualified personnel; Akebia's ability to achieve and maintain profitability and to maintain operating expenses consistent with its operating plan; manufacturing, supply chain and quality matters and any recalls, write-downs, impairments or other related consequences or potential consequences; early termination of any of Akebia's collaborations; and changes in the geopolitical environment and uncertainty surrounding U.S. trade policy on tariffs. Other risks and uncertainties include those identified under the heading "Risk Factors" in Akebia's Quarterly Report on Form 10-K for the year ended December 31, 2025, and other filings that Akebia may make with the U.S. Securities and Exchange Commission in the future. These forward-looking statements (except as otherwise noted) speak only as of the date of this presentation, and, except as required by law, Akebia does not undertake, and specifically disclaims, any obligation to update any forward-looking statements contained in this presentation.

Akebia® THERAPEUTICS

Agenda

Opening Remarks	**John P. Butler** President and CEO, Akebia Therapeutics
Praliciguat Soluble Guanylate Cyclase (sGC) Stimulator	**Steven Burke, MD** Head of R&D and Chief Medical Officer, Akebia Therapeutics **James A. Tumlin, MD** Chief Executive Officer, NephroNet
AKB-097 Anti-C3d-Factor H Fusion Protein Complement Inhibitor	**Steven Burke, MD** **V. Michael Holers, MD** Professor, Medicine-Rheumatology, University of Colorado **Jonathan Barratt, MD, PhD, FRCP** Mayer Professor of Renal Medicine, University of Leicester
AKB-9090 HIF-PH Inhibitor	**Steven Burke, MD**
Q&A Panel	
Closing Remarks	**John P. Butler**

Akebia® THERAPEUTICS

Corporate strategy

Our purpose is to better the lives of people impacted by kidney disease

Drive Vafseo to be standard of care
for the treatment of anemia due to CKD for patients on dialysis in the U.S

Build on our commitment to those impacted by kidney disease

Create a future for Akebia beyond kidney disease

CKD is chronic kidney disease

Drive Vafseo to be standard of care

Vafseo® (vadadustat) Tablets

Oral treatment for anemia due to CKD in dialysis launched in January 2025

2025 Net Product Revenues

$227.3M

Auryxia® (ferric citrate) tablets

Oral phosphate binder used to treat hyperphosphatemia and anemia in patients with CKD

Vafseo Set Up for Growth in a $1 billion market in 2026 and Beyond

Access expanded and revenue base broadening

- ~290,000 patients now have prescribing access to Vafseo
- Higher percentage of new patient starts from clinics outside of US Renal Care

First refill adherence improving

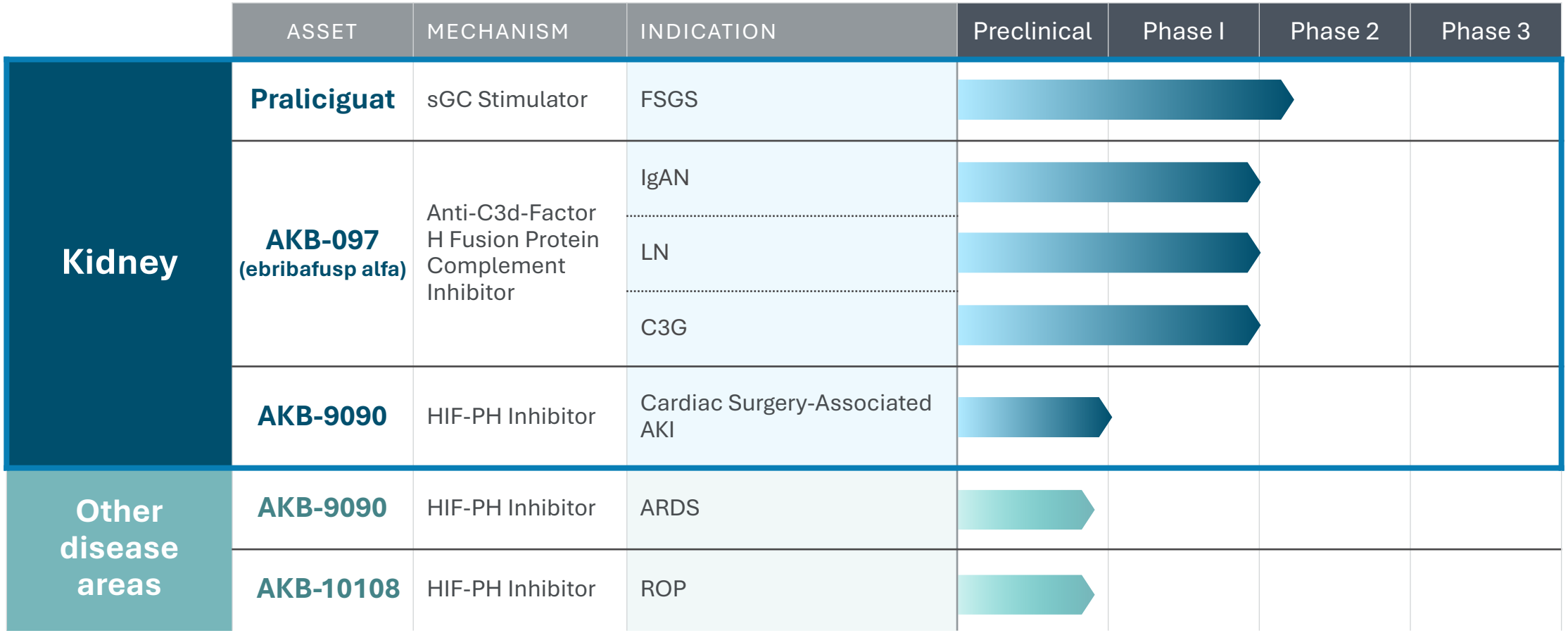
- ~ 87% first refill rates among subset of patients on an observed dosing regimen (up from ~75% in first nine months of 2025)

Building body of clinical evidence

- Win statistics analysis of INNO$_2$VATE data pending publication in *JASN*
- Data from VOCAL trial expected by end of 2026
- Data from VOICE trial expected in early 2027

CKD is chronic kidney disease; JASN is *Journal of American Society of Nephrology*

Leveraging our expertise to develop a robust kidney disease pipeline



FSGS is focal segmental glomerulosclerosis; IgAN is IgA nephropathy; LN is lupus nephritis, C3G is complement 3 glomerulopathy; AKI is acute kidney injury; ARDS is acute respiratory distress syndrome; ROP is retinopathy of prematurity

Akebia® THERAPEUTICS

Targeting severe kidney diseases with high unmet need

PRALICIGUAT

FSGS

- Scarring (sclerosis) in parts (segmental) of some (focal) glomeruli, the kidney's filtering units[1]
- No approved treatment specifically for FSGS
- **Most common primary glomerular disease in patients with ESKD in the U.S.[1]**

AKB-097

IgAN

- Characterized by the accumulation of IgA antibodies in the kidneys[2]
- **Nearly half of patients remain at high risk of progression while receiving supportive care[3]**

LN

- One of the most severe manifestations of SLE and can result in end-stage renal disease[4]
- **6x mortality risk increase vs general population[4]**

C3G

- Caused by C3 protein deposits in the glomeruli[5]
- **Approximately 50% of adult patients progress to kidney failure within 10 years[5]**

AKB-9090

CS-associated AKI

- Results from impact on perfusion, hemolysis, inflammation, and oxygen delivery to kidneys[6]
- **Higher-morbidity and costly complications [6]**

[1]Sprangers et al Biomed Res Int. 2016;2016:4632768 [2]NIDDK; IgA Nephropathy [3]*HCP Live*, « Study Details Characteristics, Risk of Disease Progression in Patients with IgAN," Nov. 16, 2023 [4]Hocaoğlu et al Arthritis Rheumatol. 2023 Apr;75(4):567-573 [5]Java et al Kidney Med. 2024 Nov 13;7(1):100928. [6]Scurt et al Kidney360. 2024 Jun 1;5(6):909-926.

ESKD is end stage kidney disease; SLE is systemic lupus erythematosus; CS is cardiac surgery

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Focus indications are multi-billion-dollar U.S. market opportunities[7]

PRALICIGUAT

FSGS
~40,000 patients[2]
~$120K/yr

AKB-097

IgAN
~126,000 patients[3]
~$120K-$390K/yr

LN
100,000 patients[4,5]
~$65K-$155K/yr

C3G
4,000 patients[6]
~$505K/yr

AKB-9090

CS-associated AKI
~120,000 patients[7]
~$20K/treatment

[1]Market opportunity derived from population and price range based on U.S. WAC reference pricing obtained from analyst research and/or company materials for the following products: FSGS (FILSPARI/sparsentan), IgAN (VOYXACT/sibeprenlimab), LN (LUPKYNIS /voclosporin), C3G (EMPAVELI/pegcetacoplan), AKI pricing is a company estimate due to absence of approved drugs [2]Nephcure Kidney International; FSGS [3]Evercore ISI, Travere Therapeutics, Inc. October 31, 2024 [4]MedScape; Lupus Nephritis [5]CDC; People with Lupus [6]Smith et al Nat Rev Nephrol. 2019 Mar;15(3):129-143. [7]Liu et al Oxid Med Cell Longev. 2021 Mar 9;2021:8873581.

Akebia THERAPEUTICS

Matching our technologies to diseases where MOA is best suited to potentially address the biological need

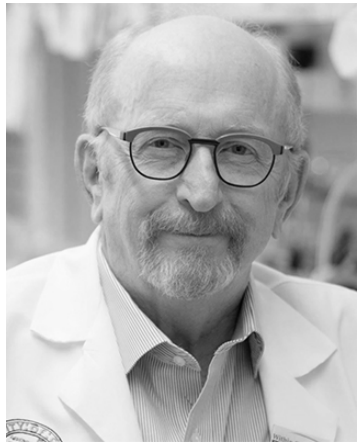
		Differentiated MOAs targeting specific biological activities
FSGS	**PRALICIGUAT** **Soluble Guanylate Cyclase (sGC) Stimulator**	NO pathway is dysregulated in patients with kidney disease – less production, increased inactivation, and impaired downstream signaling.
IgAN, LN, C3G	**AKB-097** **Anti-C3d-Factor H Fusion Protein Complement Inhibitor**	AKB-097 targets complement locally, not systemically. Anti-C3d monoclonal component brings factor H regulatory protein to sites of activation.
CS-AKI	**AKB-9090** **Hypoxia-inducible factor prolyl hydroxylase (HIF-PH) Inhibitor**	HIF activates pathways necessary for cell survival following hypoxic AKI, in addition to pathways that regulate metabolism and reduce oxidative stress and inflammation.

MOA is mechanism of action; NO is nitric oxide

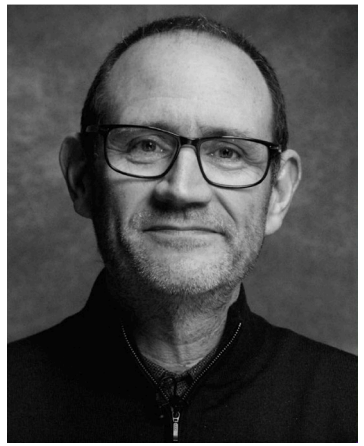
Introduction to presenters

Steven Burke, MD
Chief Medical Officer,
Head of R&D
Akebia Therapeutics

James A. Tumlin, MD
Chief Executive Officer
NephroNet



V. Michael Holers, MD
Professor, Medicine-
Rheumatology
University of Colorado



Jonathan Barratt, MD, PhD, FRCP
Mayer Professor of
Renal Medicine
University of Leicester

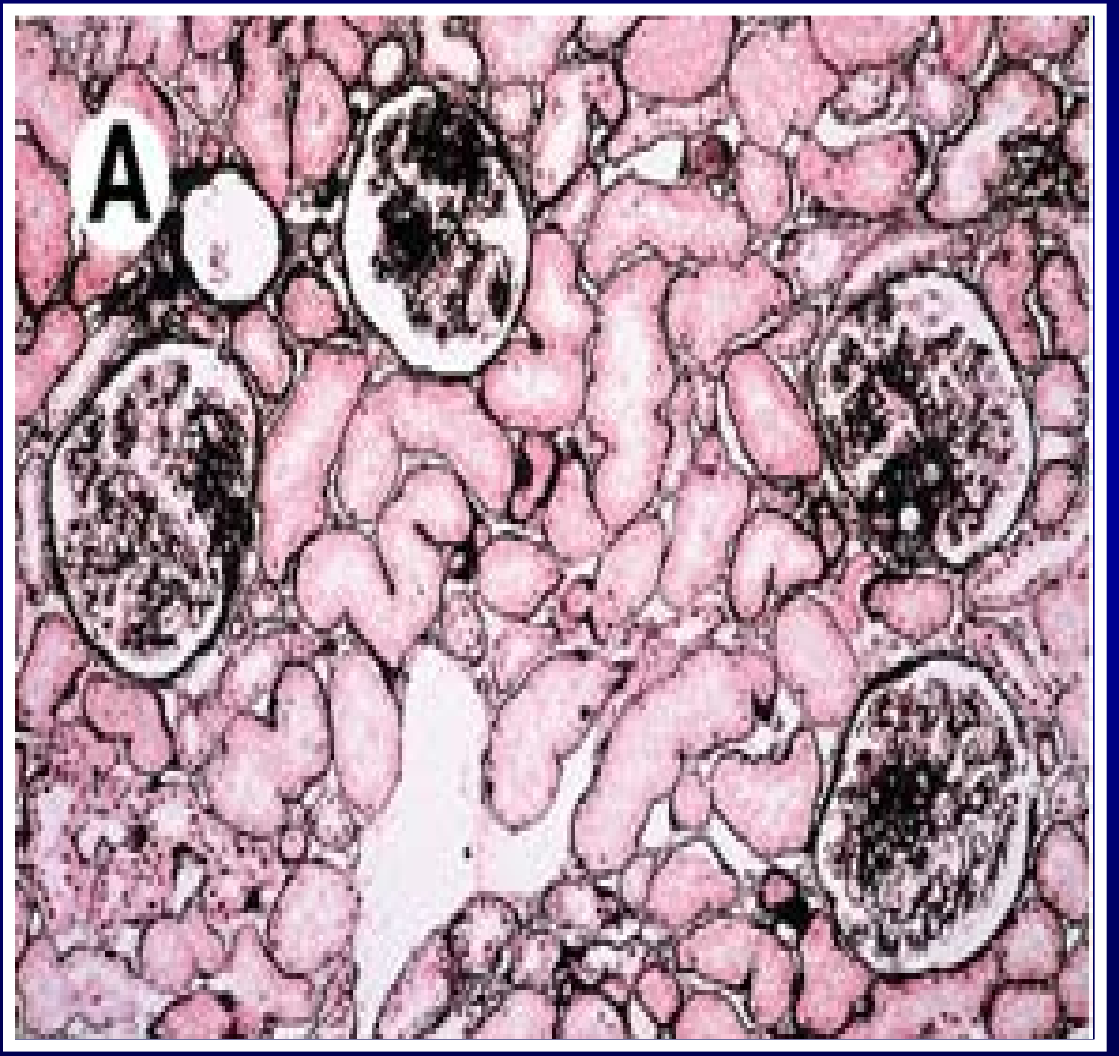
Disclosure: The healthcare professional consultants participating in this presentation are compensated by Akebia for their time and expertise.

Akebia® THERAPEUTICS

Praliciguat

Focal Segmental Glomerulosclerosis (FSGS): Rare Disease with Limited Treatment Options-Significant Unmet Need

- FSGS is a descriptive phenotype of a glomerulopathy that is the product of multiple and varied pathologic mechanisms
- Prevalence of FSGS is growing; highest predilection among patients of African descent
- Identification of APOL-1 and other FSGS-associated genes offer the potential for more directed therapy in approximately 5-10% of FSGS
- Treatments for Non APOL-1 FSGS are limited

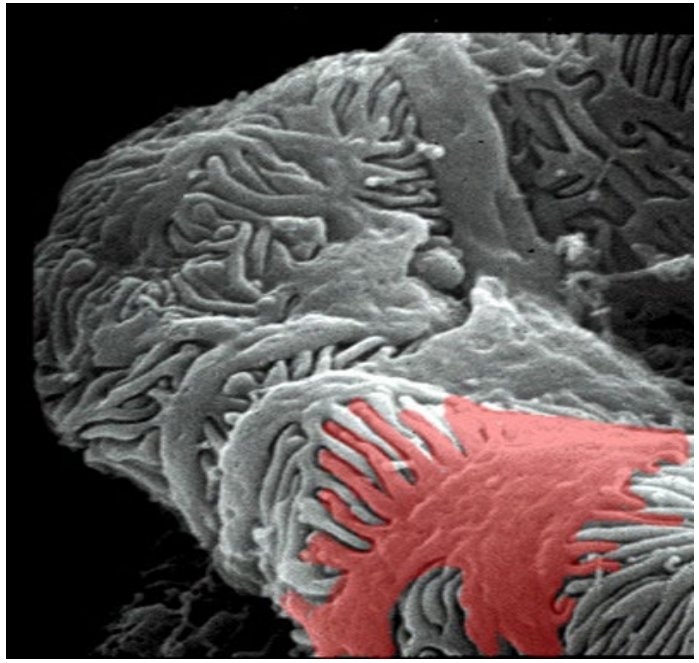


Physiologic Contributors to Podocyte Dysfunction & Apoptosis in FSGS

Cytokines
TGF-α & TGF-β
Type I Interferons

Altered Genetics
Nephrin, Podocin,
α-actinin-4, TRPC6

Endothelin-1
Aldosterone
Ang-II



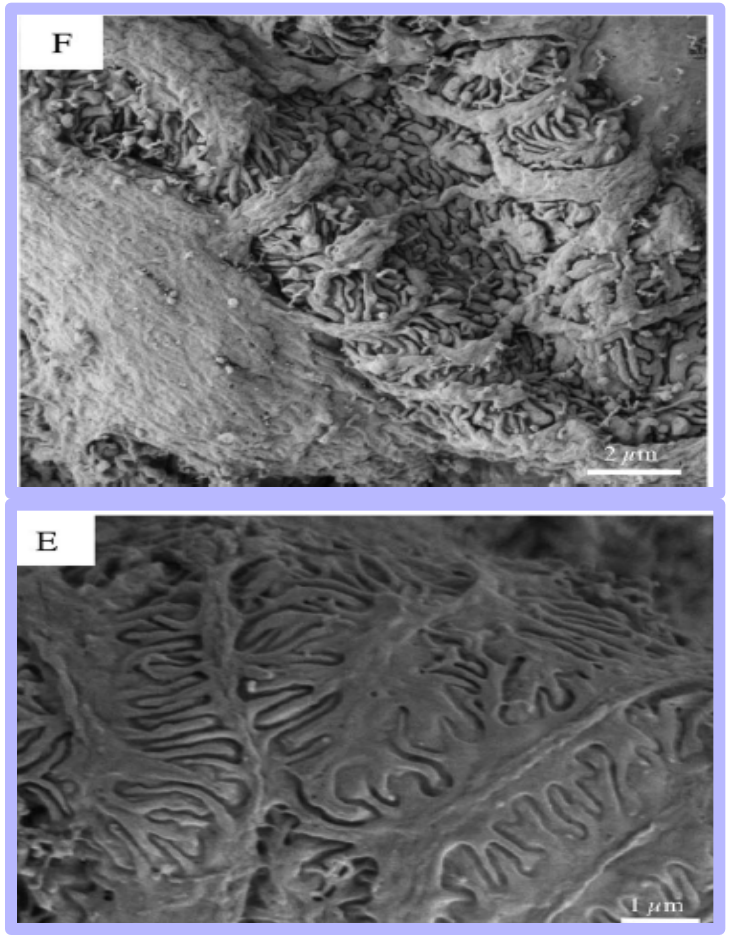
Impaired NO & VEGF Production

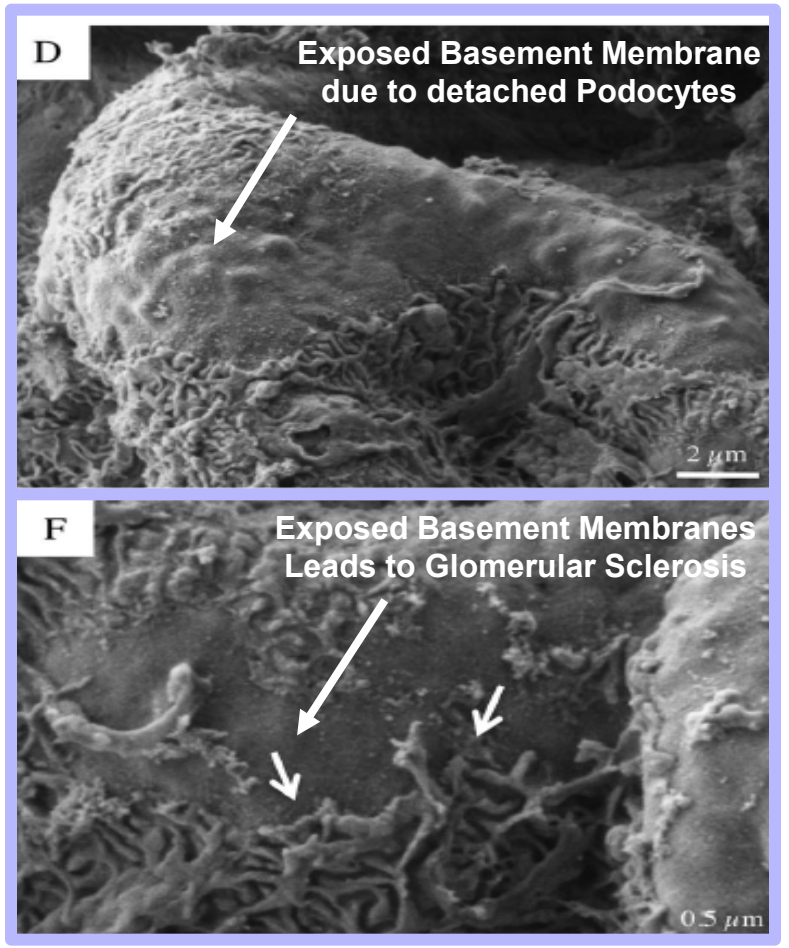
Permeability Factors:
Cardiotrophin-Like Cytokine-1

SuPAR
Soluble Urokinase Plasminogen Activator Receptor

Reactive Oxygen Species (ROS) Oxidant Injury

Podocyte Detachment Leads to Exposed Capillary Basement Membranes: Contribute to Glomerular Sclerosis

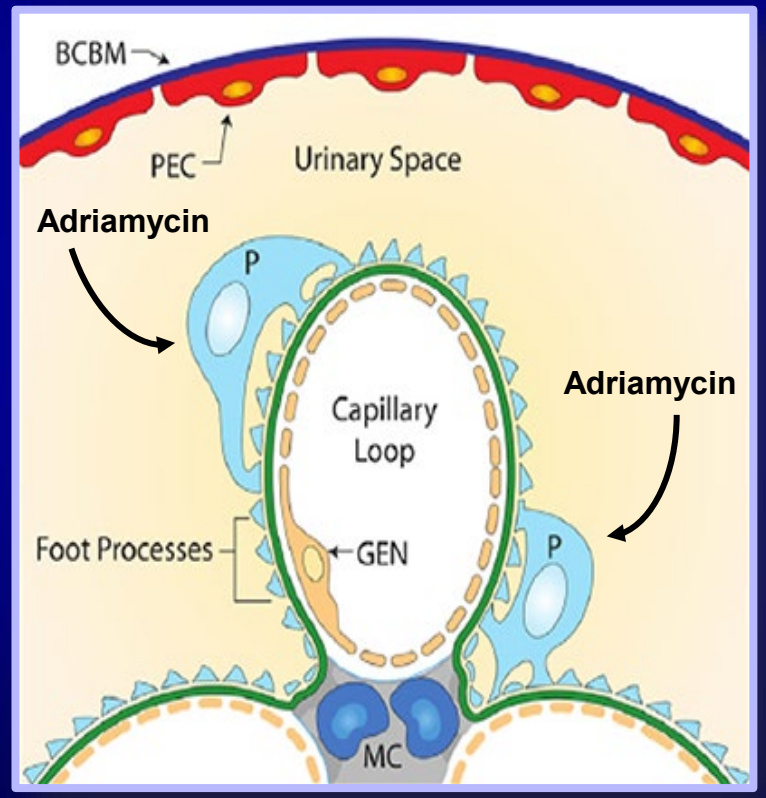




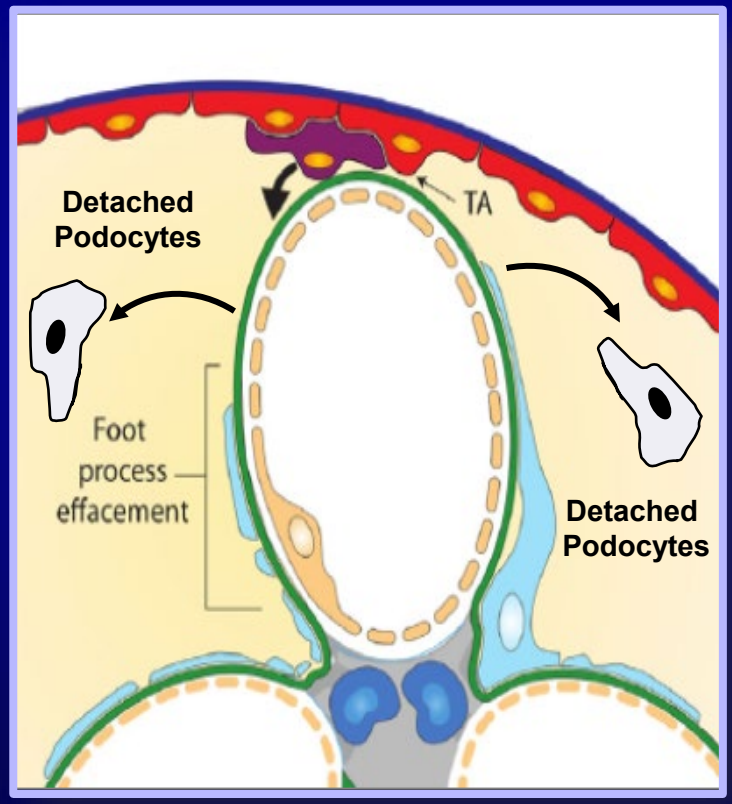
Conti et al Scientific Reports. 2018 March 20;8:4909

Podocyte Injury: Progression from Injury to Detachment to Tuft Adhesion to Glomerulosclerosis

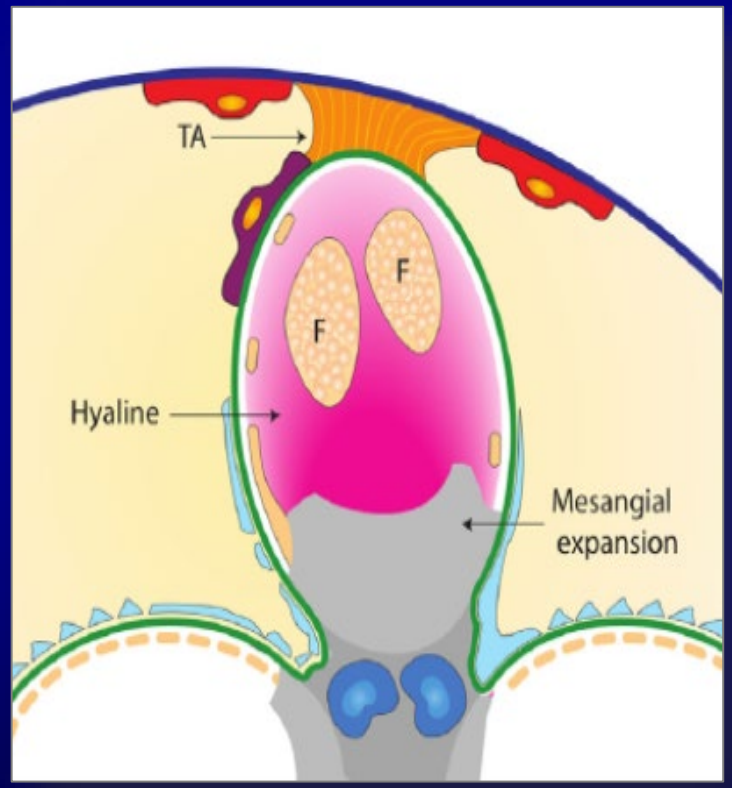
Normal Glomerular Capillary & Pre-Detached Adriamycin Injured Podocytes



Post Injury Podocyte Detachment: Foot Plate Effacement with Exposed Basement Membrane



Glomerular Tuft Adherence to Bowman's Capsule. Initiation Glomerulosclerosis and Expansion Mesangial Matrix

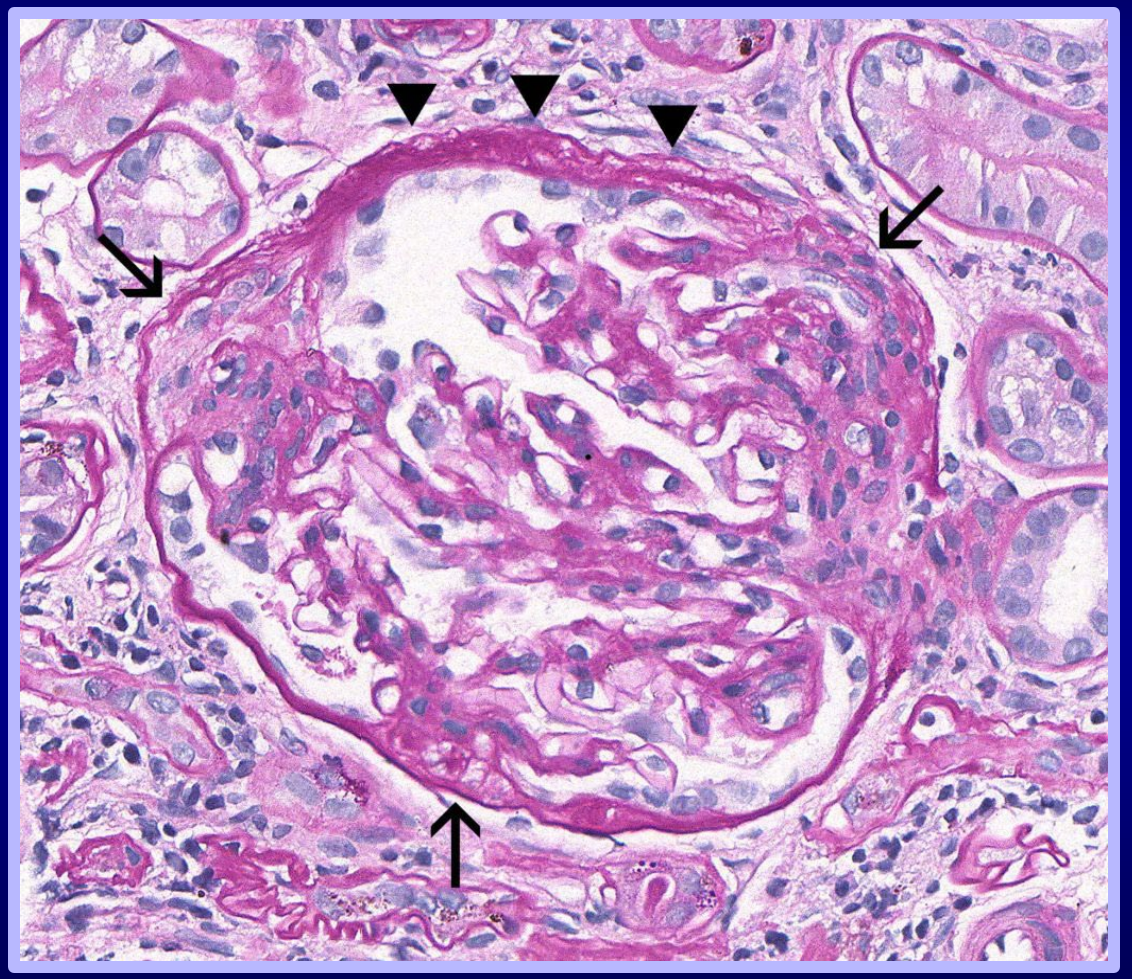


Jefferson and Shankland Adv Chronic Kidney Dis. 2024 September;21(5):408-416

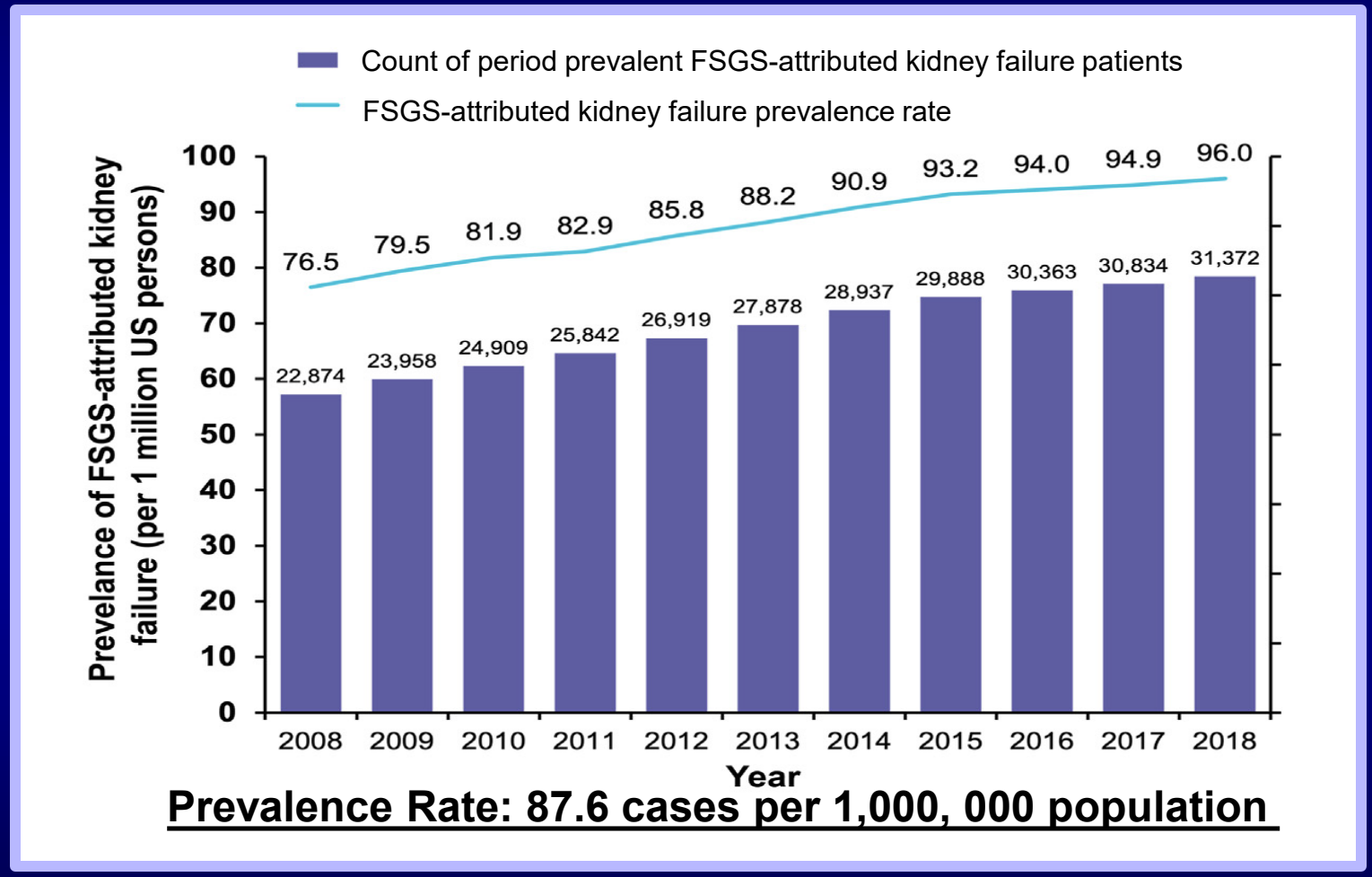
FSGS-NOS Histology: Tuft Adhesions

Pathologic Features

- Segmental occlusion glomerular capillaries by accumulation of extracellular matrix proteins
- <u>Adherence of Glomerular Tuft to Bowman's Capsule</u>
- Hyalinosis: accumulation of eosinophilic, trichrome-red staining amorphous material beneath basement membrane
- Proximal tubular foam cells intracellular protein droplets



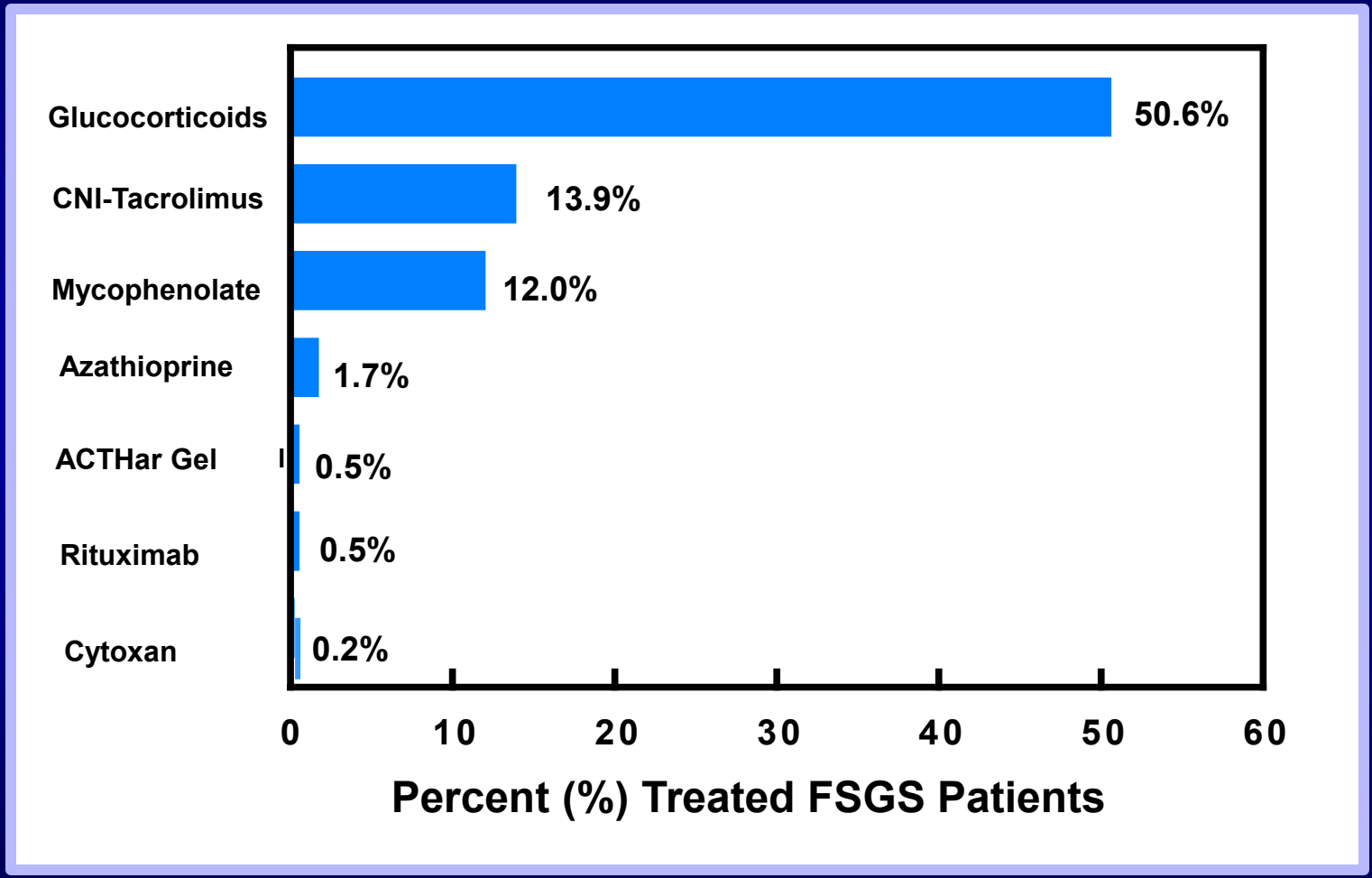
Kidney Failure Attributed to Focal Segmental Glomerulosclerosis (FSGS): A USRDS Epidemiologic Analysis



Prevalence Rate: 87.6 cases per 1,000, 000 population

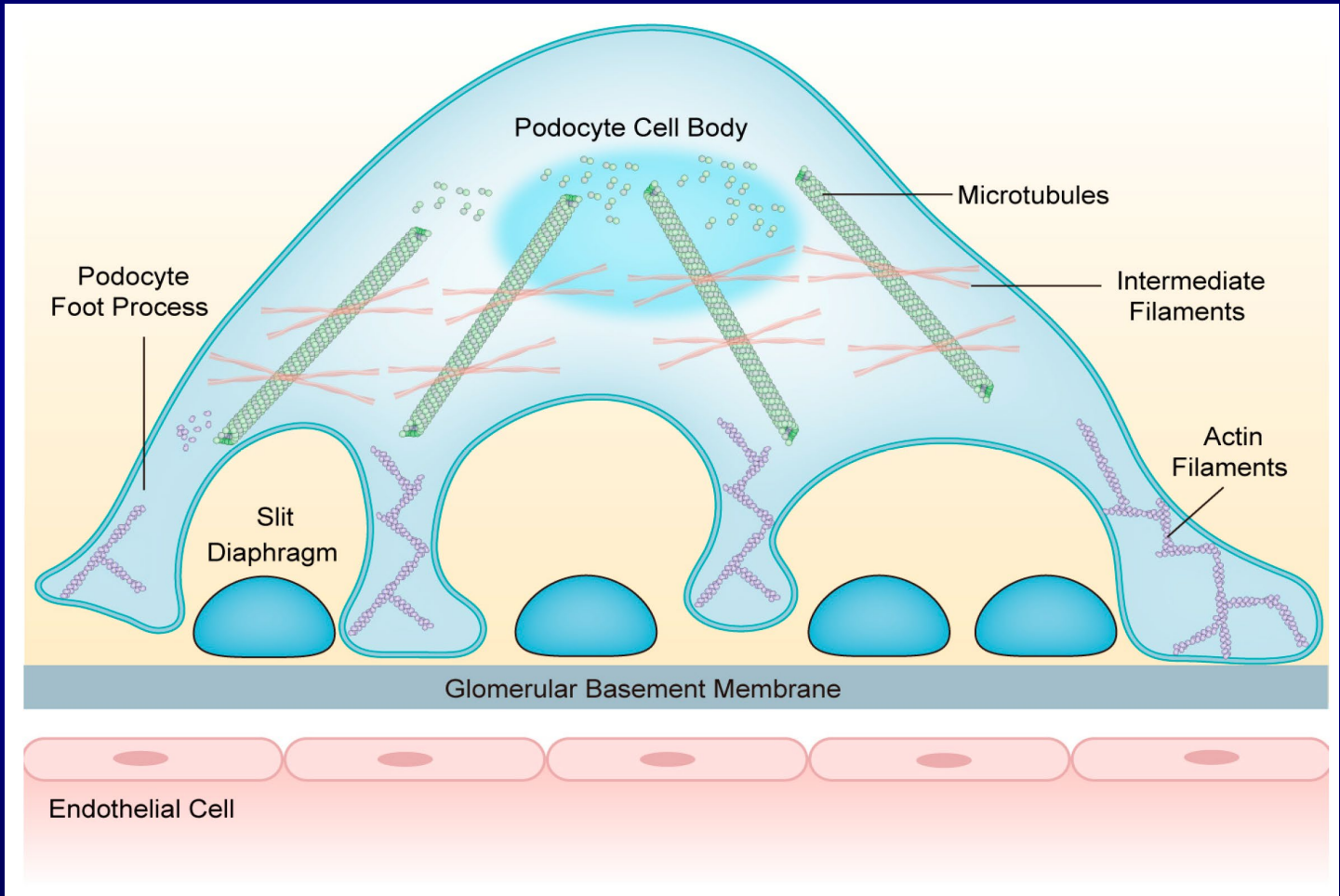
Bensink et al Kidney Med. 2024 February;6(2):100760

Prescription Immunosuppressants Used for FSGS



Redrawn from Kalantar-Zadeh et al Kidney Int Rep. 2021 Aug 9;6:2679–2688

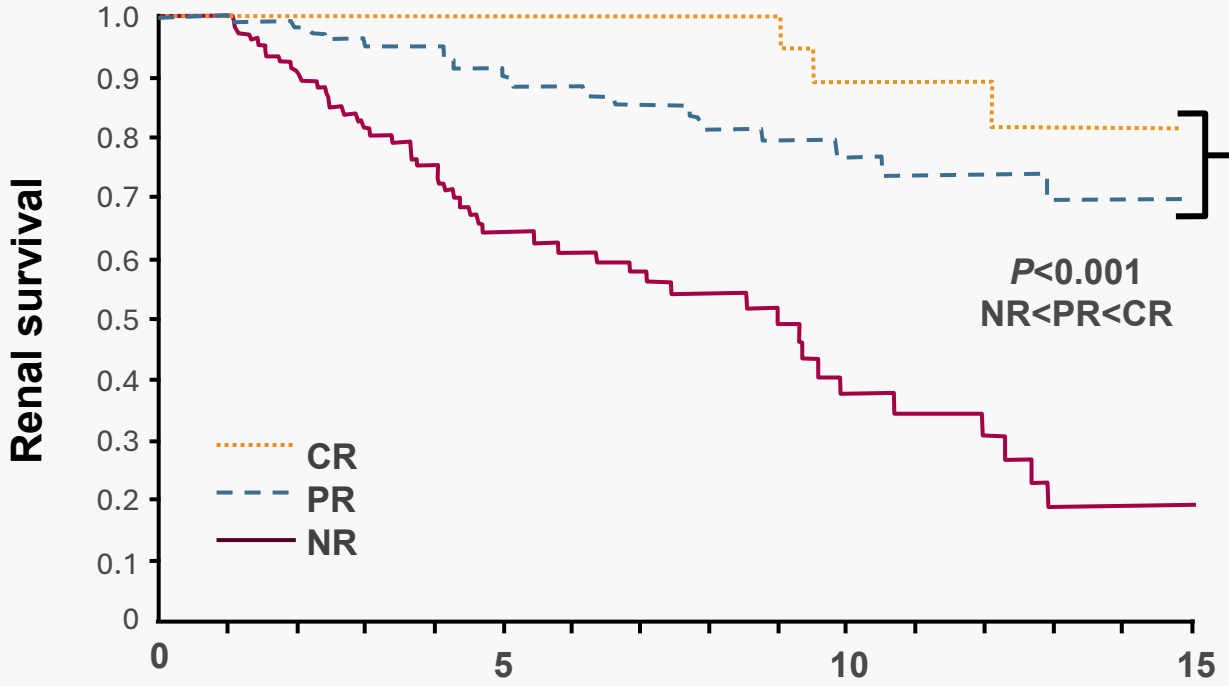
The Structure of Podocytes and the Network of Podocyte Cytoskeletons



Ma et al Internal J Mol Sciences. 2024 Jan 4;25:647

Reduction in Urinary Protein Losses Is Universally Beneficial in FSGS

Achieving Either Complete or Partial Remission of Proteinuria in FSGS Is Important For Improving Kidney Outcomes



Achieving complete or partial remission of proteinuria in patients with primary FSGS is a valid therapeutic goal

Number of patients assessed at follow-up:

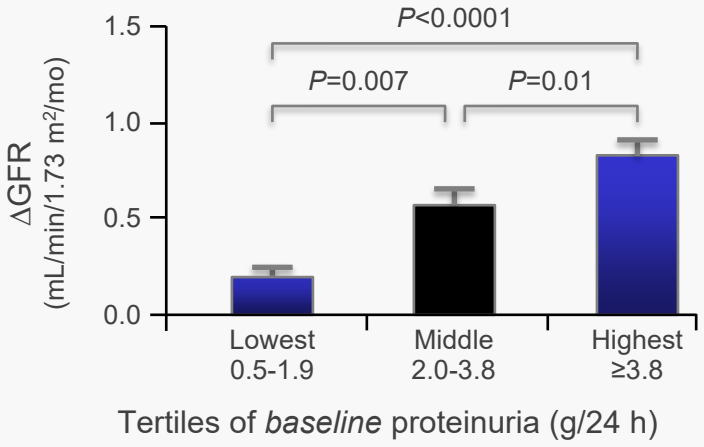
Years	0	5	10	15
CR	102	67	33	12
PR	135	74	32	9
NR	106	34	9	4

Study included 281 patients with primary FSGS from the Toronto Glomerulonephritis Registry. Patients had nephrotic-range proteinuria at some point during follow up; baseline proteinuria of 4.7 g/d; minimum of 12 months of follow up.

CR = complete remission: proteinuria ≤300 mg/d; NR = no remission; PR = partial remission: proteinuria <3500 mg/d plus a 50% reduction from peak value. Adapted with permission from Troyanov et al J Am Soc Nephrol. 2005 April;16(4):1061-1068.

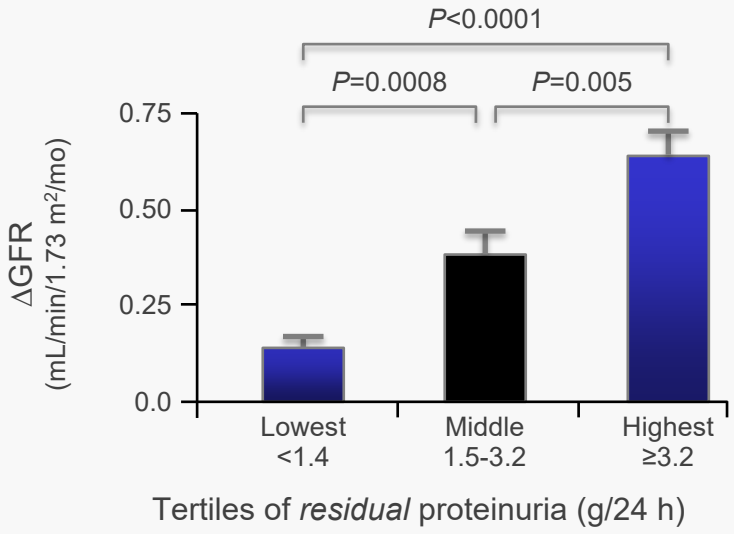
There Is a Strong Association Between Proteinuria and Risk of Progression to ESKD

Proteinuria was the *only* baseline variable that correlated with the rate of GFR decline and progression to ESKD[1,a]



ESKD (%)	**4.3**	**15.3***	**32.5*‡**

Short-term changes and residual proteinuria predicted long-term disease progression regardless of BP control and treatment[1,2,b]



ESKD (%)	**3.3**	**19.8**	**46.2‡§**

A meta-analysis[1,3] of 1860 patients with chronic nephropathies concluded:

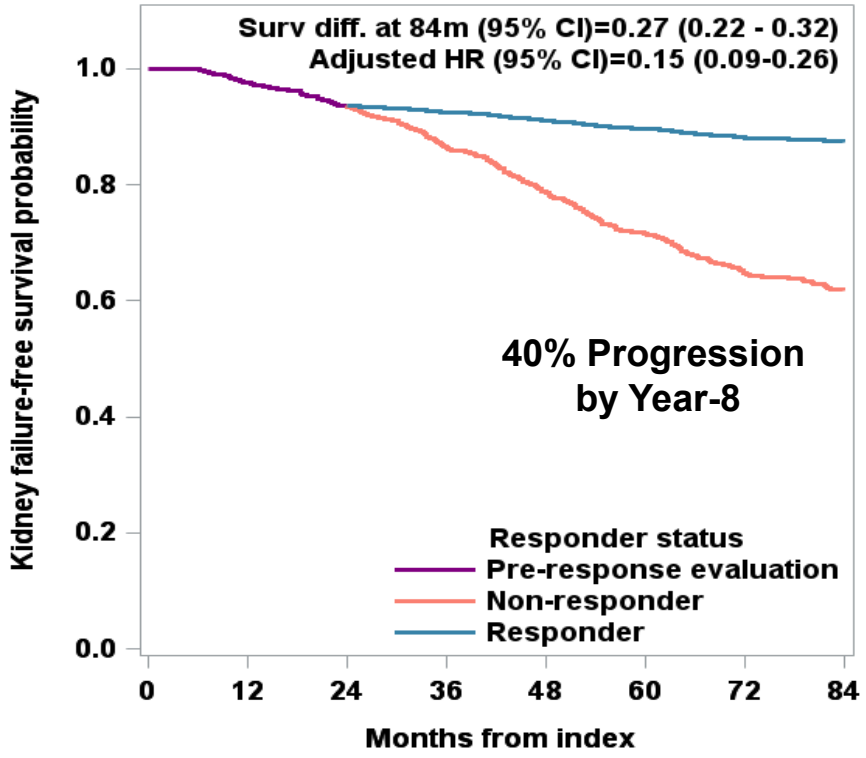
- ***Proteinuria is an important modifiable risk factor* to slow progression of disease**
- **Reduction of urine protein excretion should be the *main goal of treatment***

a. Trial included 274 patients with nondiabetic chronic nephropathies. b. In a post hoc analysis of 273 patients from the Ramipril Efficacy in Nephropathy (REIN) trial.
*P=0.01 vs lowest tertile; ‡P ≤0.0001 vs the middle and lowest tertiles; §P=0.002 vs the middle and lowest tertiles.

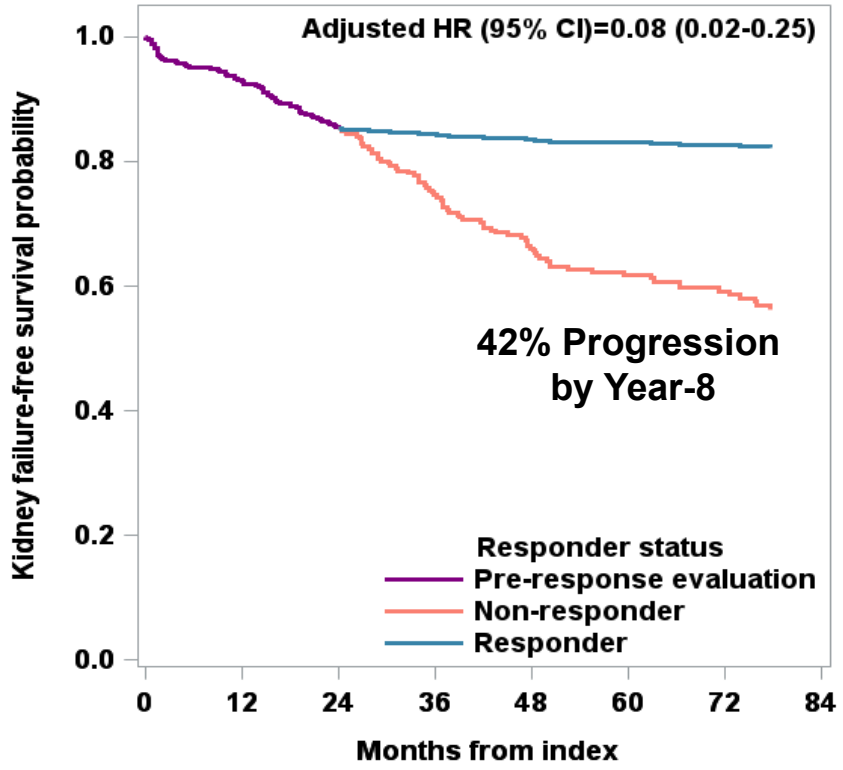
1. Cravedi et al Nat Rev Nephrol. 2012 May;8:301-306. 2. Ruggenenti et al Kidney Int. 2003 Feb 4;63:2254-2261. 3. Jafar et al Kidney Int. 2001 April 16;60:1131-1140. ESKD = end stage kidney disease, BP = blood pressure

Achieving UP/Cr Below 700 mg/gm Reduces Progression to ESKD: Results of the Parasol Study

PARASOL: Renal Survival with UP/Cr < 700 mg/gm-Independent of Treatment



RaDaR: Renal Survival with UP/Cr < 700 mg/gm-Independent of Treatment



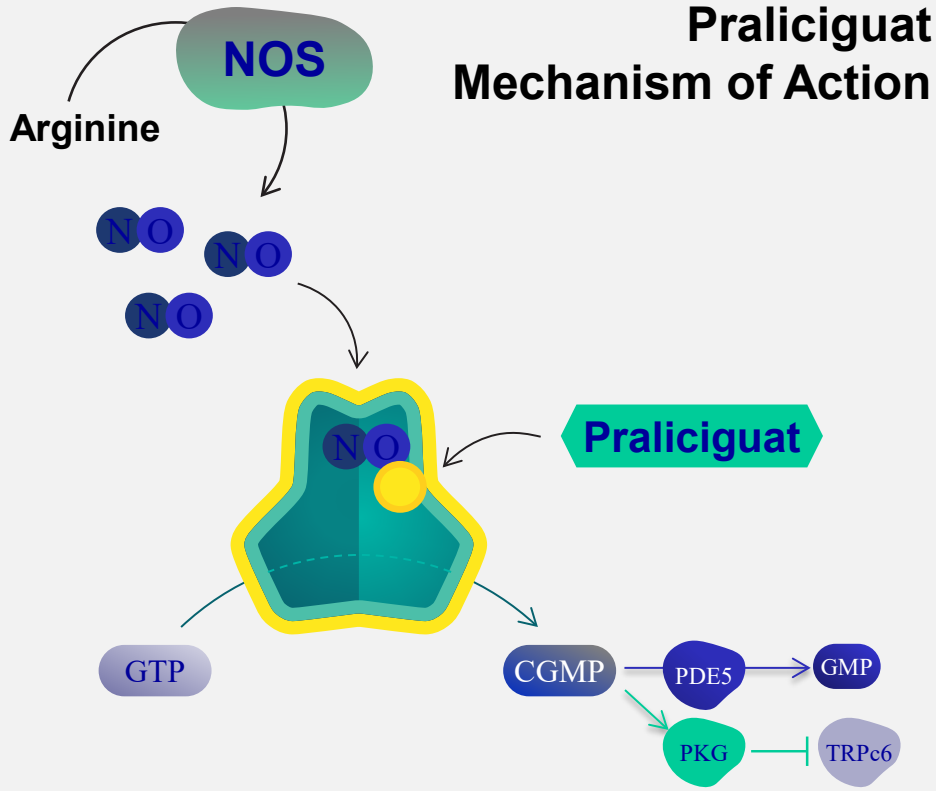
Smith AR, et al. ASN 2024. Translational session. ESKD = end stage kidney disease; UP = urinary protein; CR = creatinine; mg/gm = milligram per gram

Praliciguat Augments Deficient NO-sGC-cGMP Signaling Pathways in Glomerular Podocytes

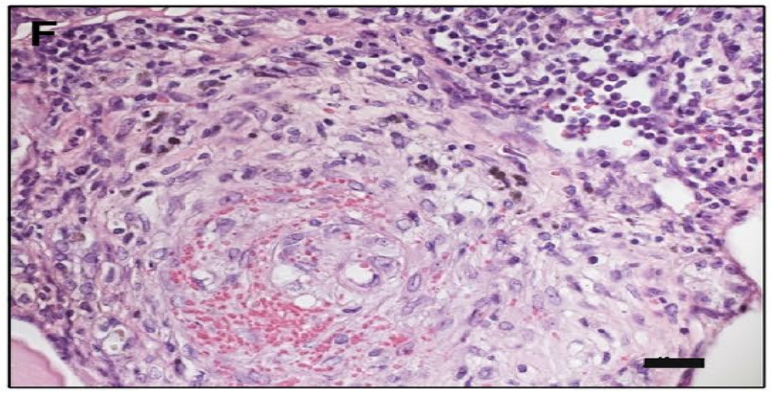
Praliciguat: Preclinical Studies

- Protamine sulfate-induced podocyte injury
- TNFα-induced inflammation and TGF-β fibrosis in human proximal tubule cells ★
- DSS rat model of glomerulosclerosis
- Rat ZSF1 model of diabetic kidney disease
- Rat Unilateral Ureteral Obstruction (UUO) model
- Adriamycin mouse model of FSGS ★
- 5/6 Nephrectomy rat model of CKD ★

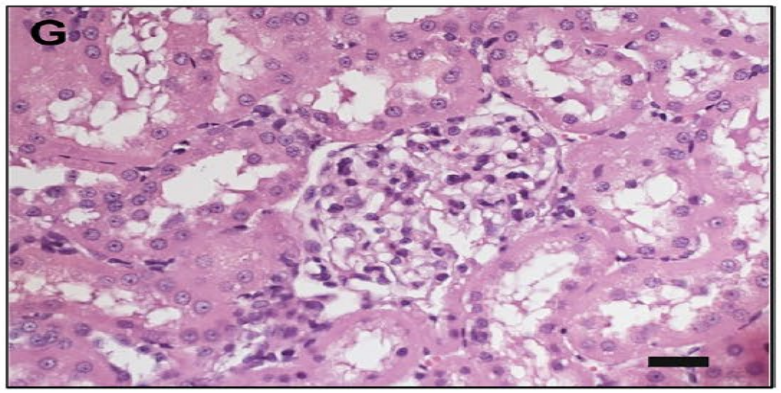
Praliciguat Mechanism of Action



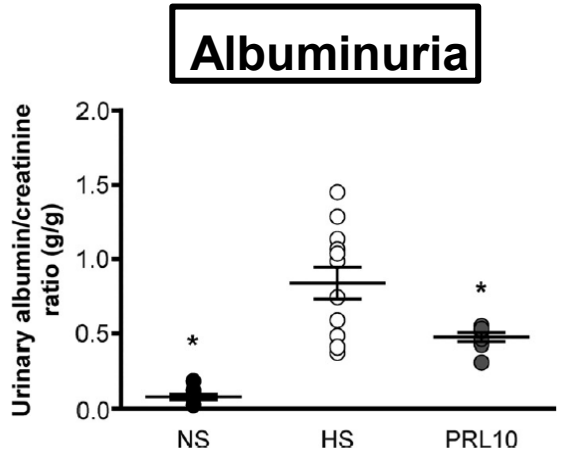
Multi-Faceted Functions of Praliciguat: Reduction in TGF-beta Dependent Glomerulosclerosis and Fibrosis in Hypertensive CKD

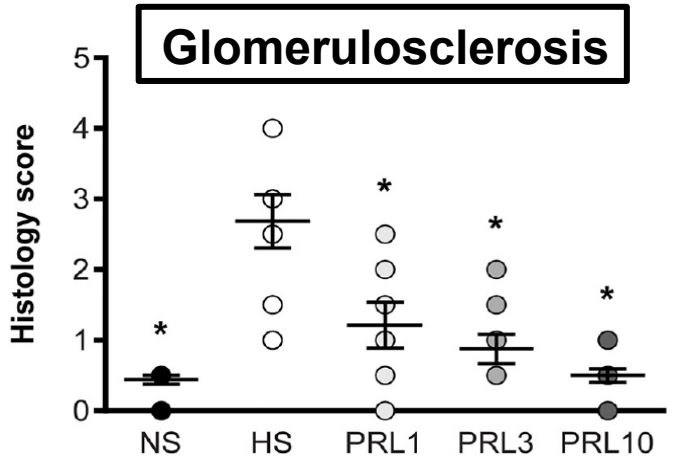


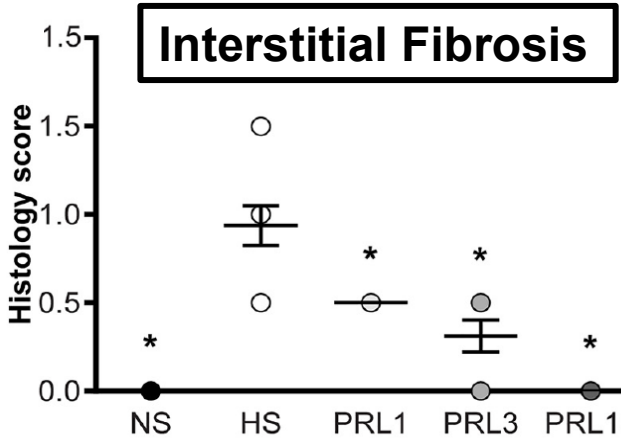
Untreated Animals

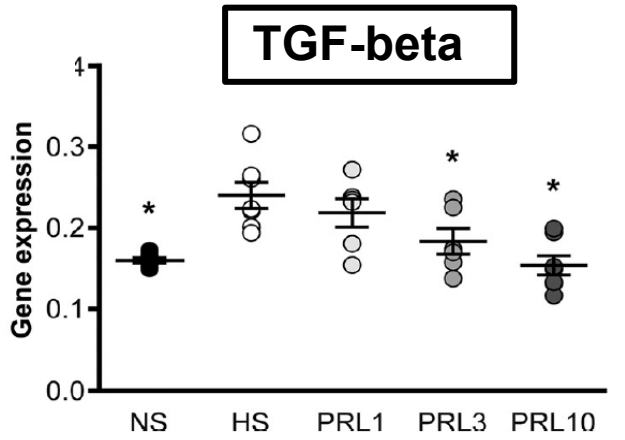


Praliciguat 10 mg/kg/day







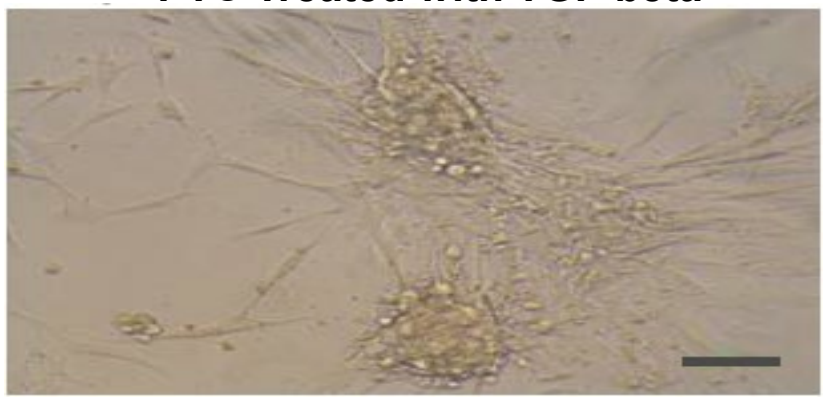


Shea et.al. Am J Physiol Renal Physiol 318: F148–F159, 2020.

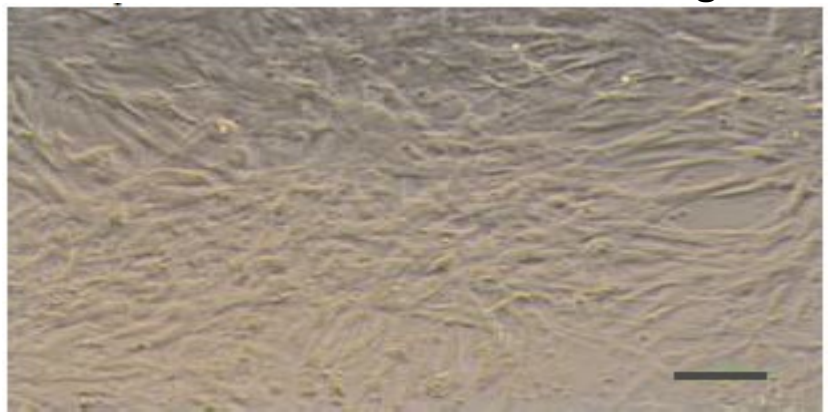
TGF-beta = transforming growth factor beta; CKD = chronic kidney disease; NS = isnormal salt; HS = high salt; PRL1 = Praliciguat 1μM; PRL3 = Praliciguat 3μM; PRL10 = Praliciguat 10μM

Multi-Faceted Functions of Praliciguat: Blocks TGF-beta Induced Apoptosis of Cultured Proximal Tubular Cells

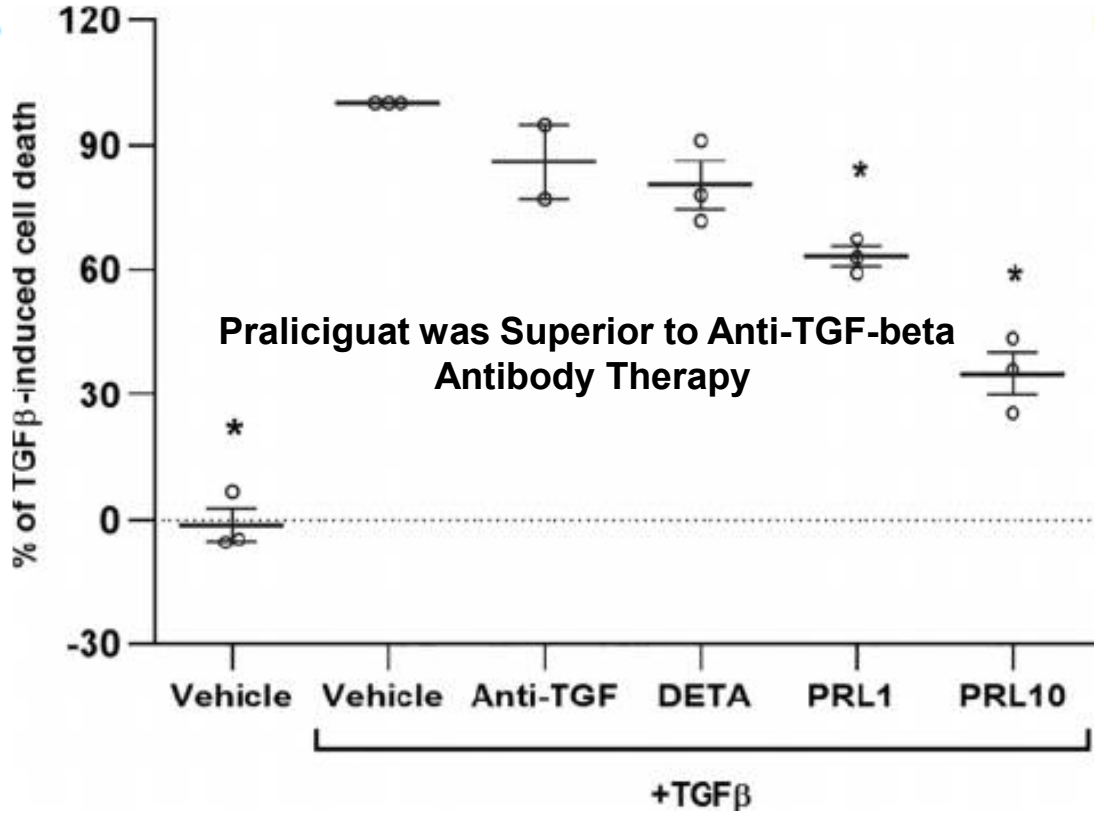
PTC Treated with TGF-beta



PTC Treated withTGF-beta + Praliciguat 1 μM



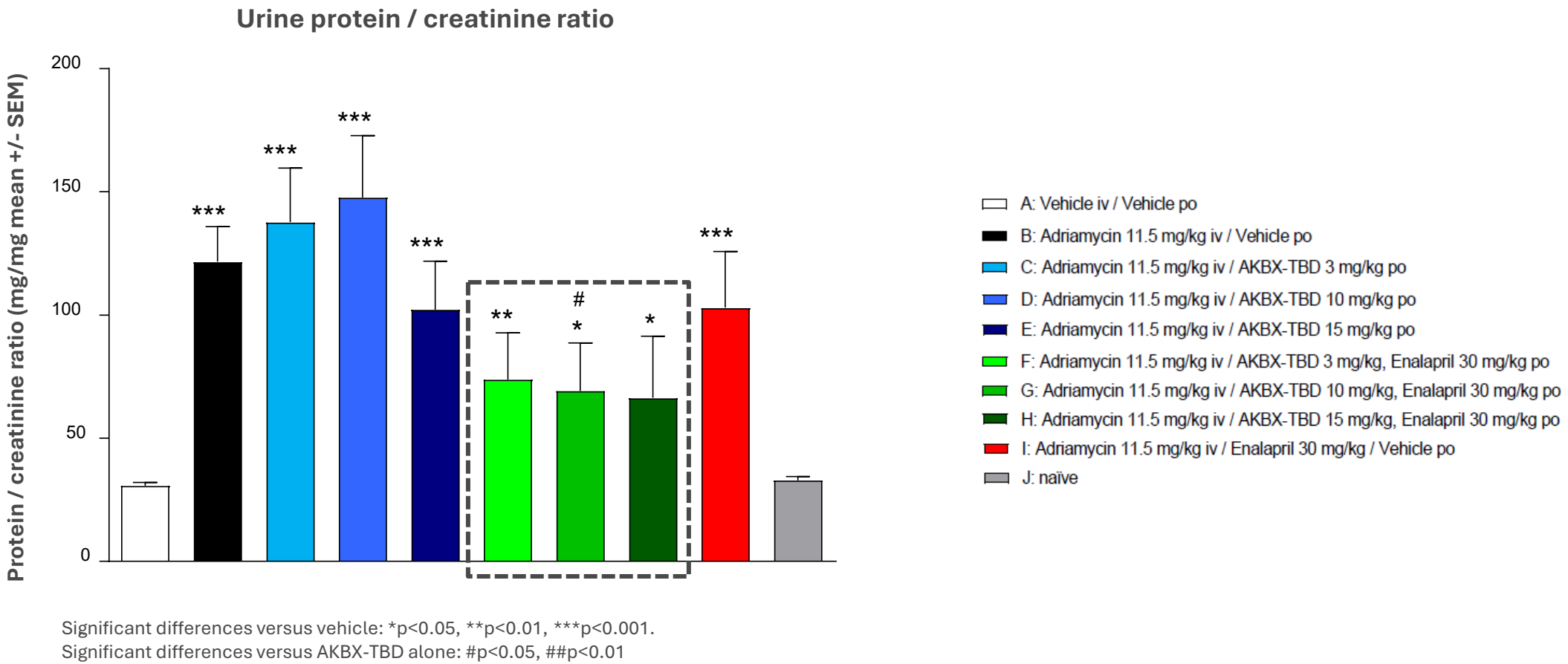
TGF-beta + Praliciguat 1 μM (PRL1) and 10 μM (PRL10)



Liu et.al. Am J Physiol Renal Physiol 319: F697–F711, 2019.

TGF-beta = transforming growth factor beta; PTC = proximal tubular cells; DETA (an NO donor) = Diethylenetriamine-NONOate

Praliciguat treatment on a background of enalapril reduced proteinuria in Adriamycin mouse model of FSGS[1]

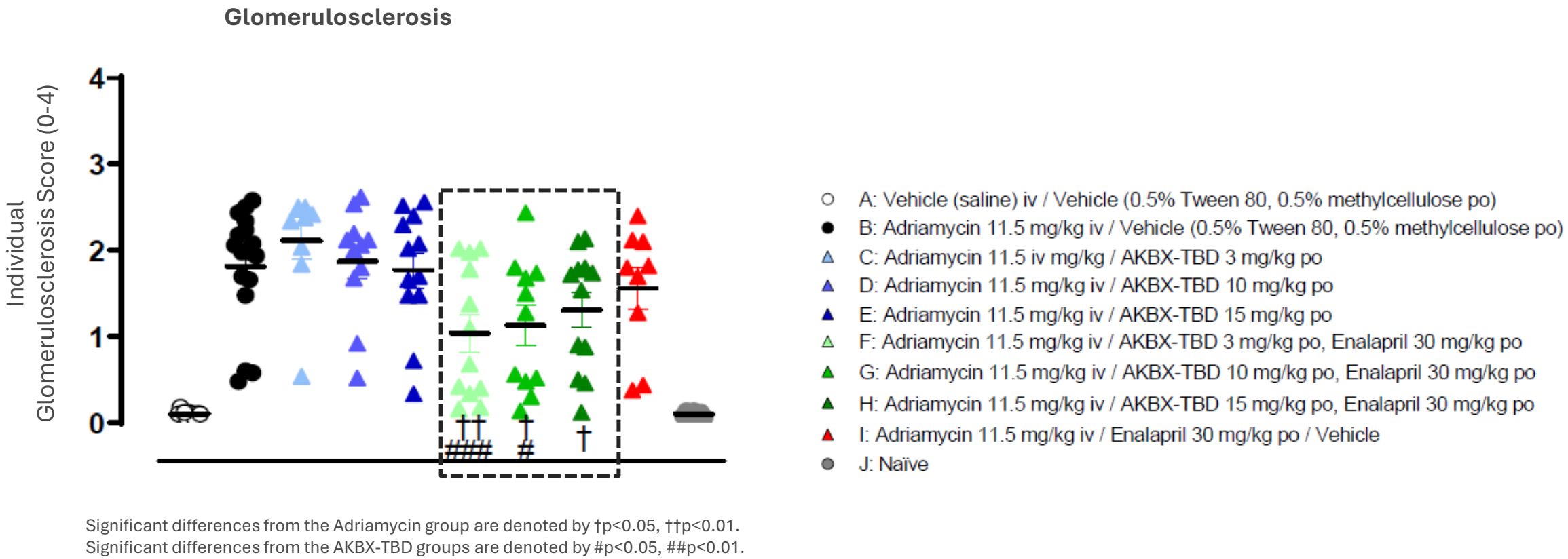


Significant differences versus vehicle: *p<0.05, **p<0.01, ***p<0.001.
Significant differences versus AKBX-TBD alone: #p<0.05, ##p<0.01

IV is intravenous; PO is oral; AKBX-TBD is praliciguat; [1] Data from preclinical study conducted by Akebia: RS2493

Akebia® THERAPEUTICS

Praliciguat treatment on a background of enalapril reduced the glomerulosclerosis score in Adriamycin mouse model of FSGS[1]

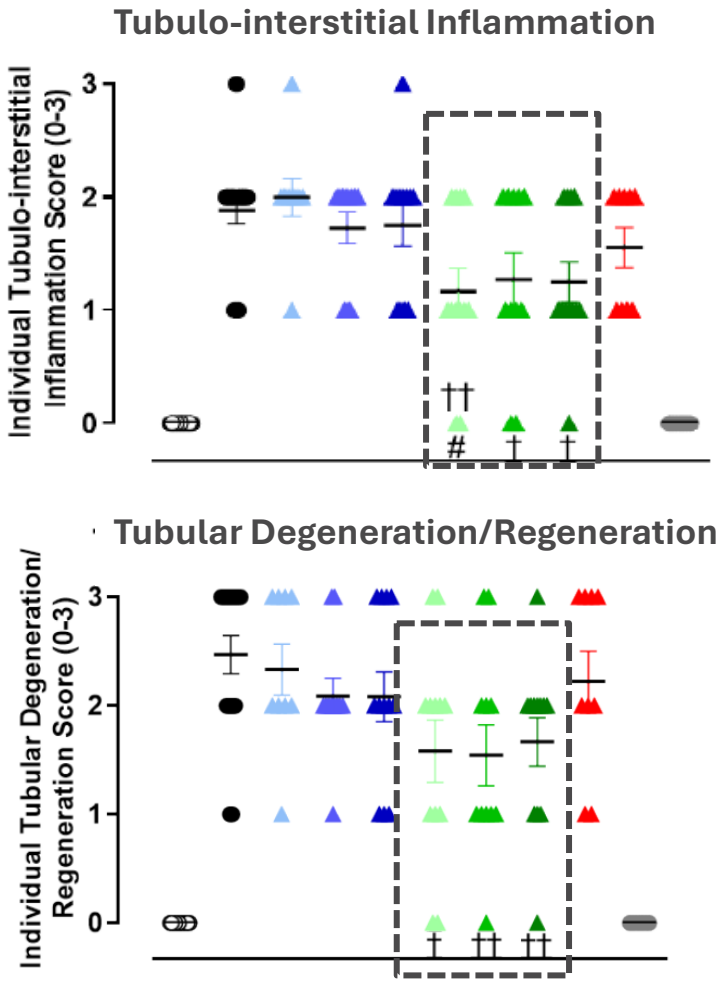


Significant differences from the Adriamycin group are denoted by †p<0.05, ††p<0.01.
Significant differences from the AKBX-TBD groups are denoted by #p<0.05, ##p<0.01.

IV is intravenous; PO is oral; AKBX-TBD is praliciguat [1] Data from preclinical study conducted by Akebia: RS2493

Akebia THERAPEUTICS

Praliciguat treatment on a background of enalapril reduced tubulo-interstitial inflammation and tubular degeneration/regeneration scores in Adriamycin mouse model of FSGS[1]

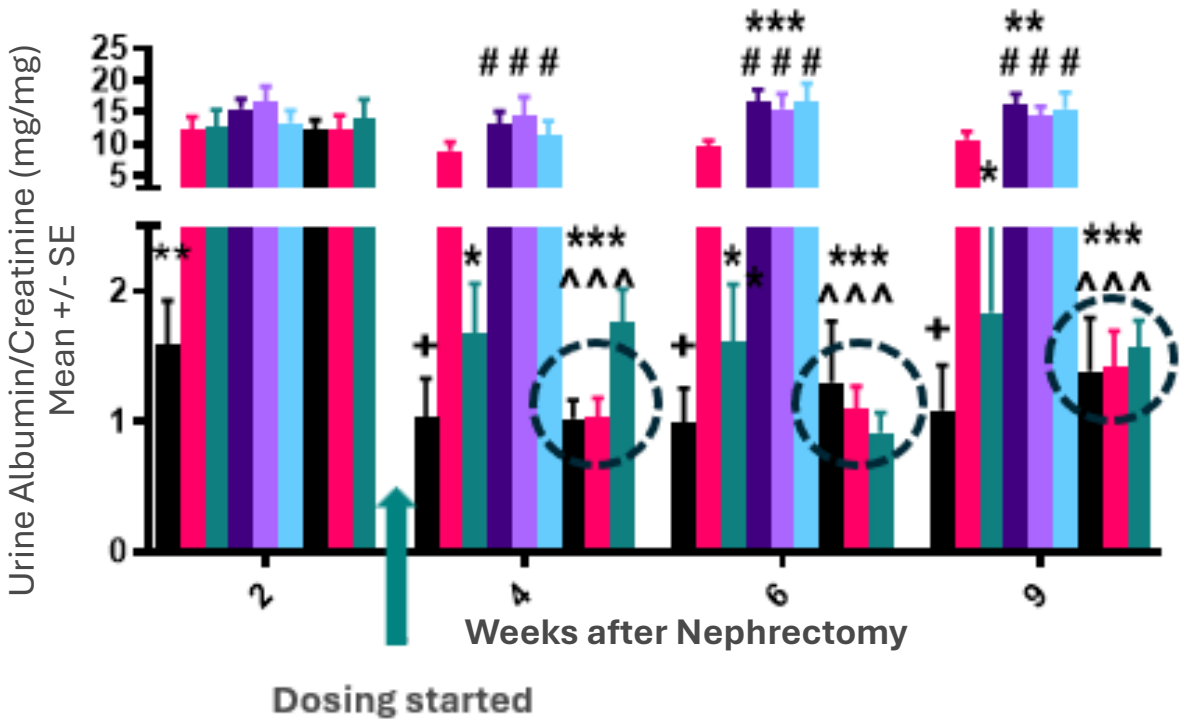


Significant differences from the Adriamycin group are denoted by †p<0.05, ††p<0.01.
Significant differences from the AKBX-TBD groups are denoted by #p<0.05, ##p<0.01.

- A: Vehicle (saline) iv / Vehicle (0.5% Tween 80, 0.5% methylcellulose po)
- B: Adriamycin 11.5 mg/kg iv / Vehicle (0.5% Tween 80, 0.5% methylcellulose po)
- C: Adriamycin 11.5 iv mg/kg / AKBX-TBD 3 mg/kg po
- D: Adriamycin 11.5 mg/kg iv / AKBX-TBD 10 mg/kg po
- E: Adriamycin 11.5 mg/kg iv / AKBX-TBD 15 mg/kg po
- F: Adriamycin 11.5 mg/kg iv / AKBX-TBD 3 mg/kg po, Enalapril 30 mg/kg po
- G: Adriamycin 11.5 mg/kg iv / AKBX-TBD 10 mg/kg po, Enalapril 30 mg/kg po
- H: Adriamycin 11.5 mg/kg iv / AKBX-TBD 15 mg/kg po, Enalapril 30 mg/kg po
- I: Adriamycin 11.5 mg/kg iv / Enalapril 30 mg/kg po / Vehicle
- J: Naïve

IV is intravenous; PO is oral; AKBX-TBD is praliciguat [1] Data from preclinical study: RS2493

Praliciguat treatment on a background of enalapril lowered albuminuria in the 5/6 nephrectomy rat model[1]



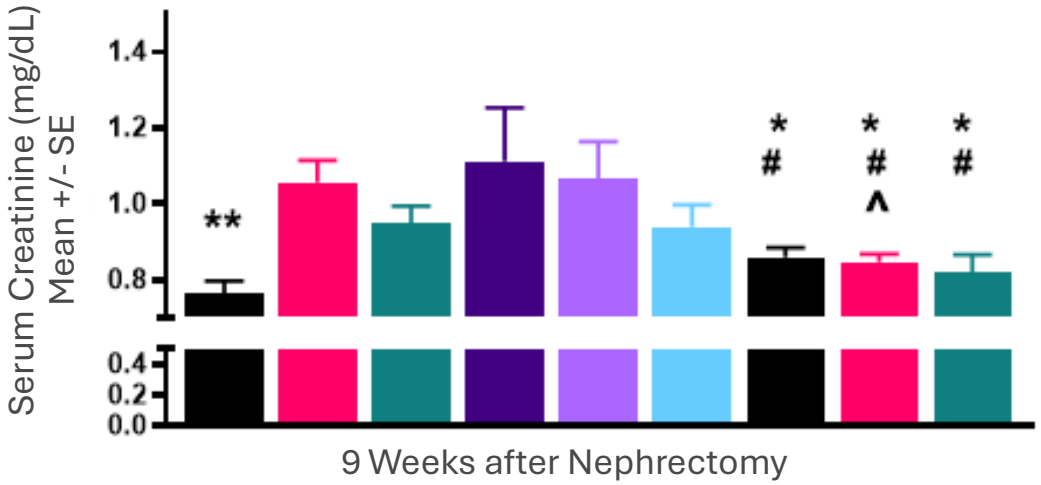
G1: Naive (n=4/timepoint)
G2: 5/6Nx (n=12, 12, 10, 10 per timepoint, respectively)
G3: 5/6Nx + Enalapril 10 mg/kg/day (n=13/timepoint)
G4: 5/6Nx + AKB Cmpd 1.5mg/kg/day (n=15, 14, 14, 13 per timepoint, respectively)
G5: 5/6Nx + AKB Cmpd 3mg/kg/day (n=13, 12, 11, 11 per timepoint, respectively
G6: 5/6Nx + AKB Cmpd 10mg/kg/day (n=13, 12, 12, 11 per timepoint, respectively)
G7: 5/6Nx + AKB Cmpd 1.5mg/kg/day + Enalapril 10mg/kg/day (n=13/timepoint)
G8: 5/6Nx + AKB Cmpd 3mg/kg/day + Enalapril 10mg/kg/day (n=13/timepoint)
G9: 5/6Nx + AKB Cmpd 10mg/kg/day + Enalapril 10mg/kg/day (n=14, 11, 11, 9 per timepoint, respectively)

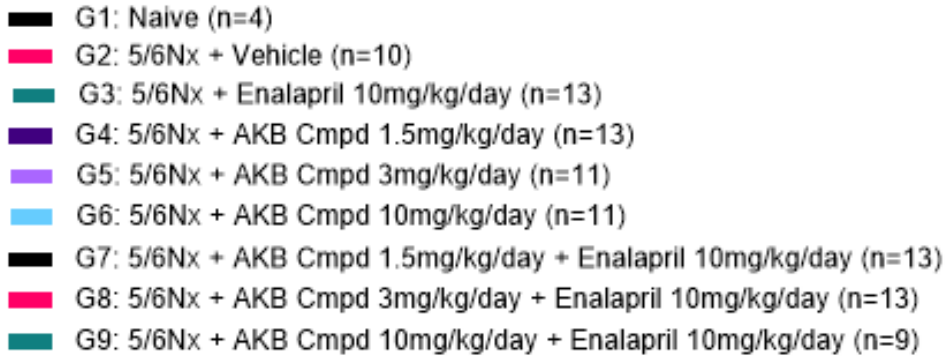
*p < 0.05 vs Vehicle; # p < 0.05 vs Enalapril; ^ p < 0.05 vs respective monotherapy; ** p < 0.05 vs all groups; + p < 0.05 vs Vehicle, monotherapy (all doses).

AKB Cmpd is praliciguat; [1] Data from preclinical study: 1692-211348NI

Akebia THERAPEUTICS

Praliciguat treatment on a background of enalapril reduced serum creatinine in the 5/6 nephrectomy rat model[1]





*p < 0.05 vs Vehicle; # p < 0.05 vs Enalapril; ^ p < 0.05 vs respective monotherapy; ** p < 0.05 vs all groups.

AKB Cmpd is praliciguat; [1] Data from preclinical study: 1692-211348NI

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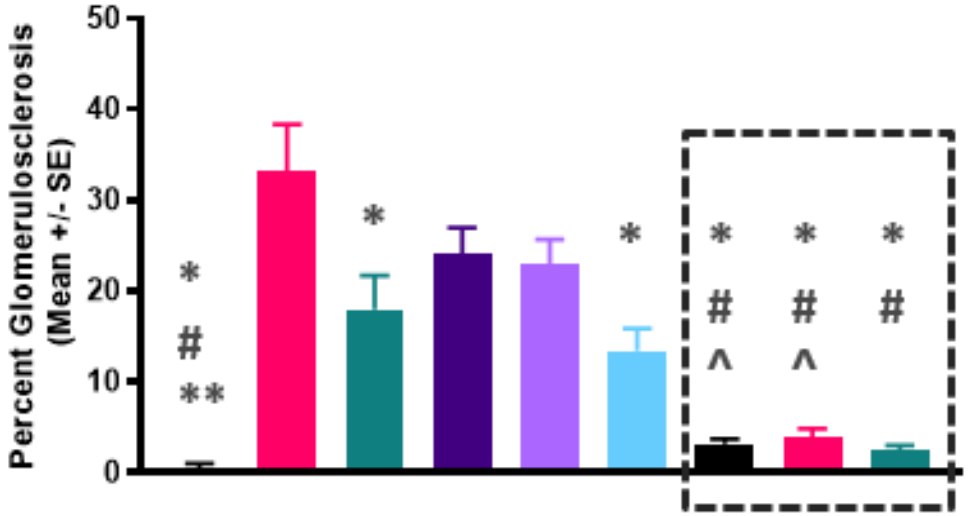
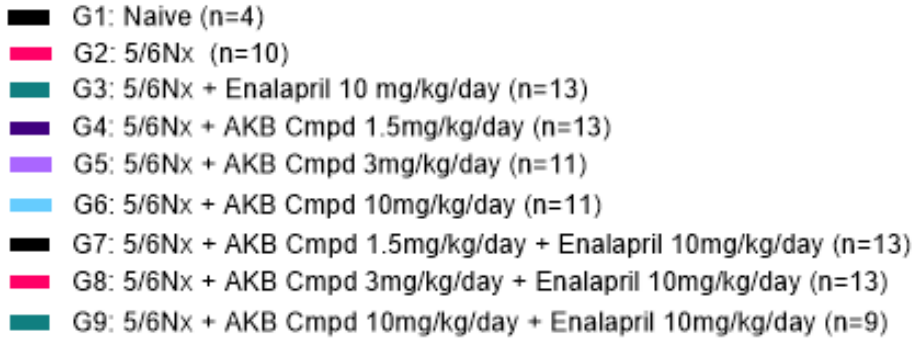
In the 5/6 nephrectomy model, glomerulosclerosis reductions were greatest when praliciguat was administered with enalapril compared to either agent alone[1]





* $p < 0.05$ vs Vehicle; # $p < 0.05$ vs Enalapril; ^ $p < 0.05$ vs respective monotherapy; ** $p < 0.05$ vs monotherapy @ 1.5, 3 mg/kg/day

AKB Cmpd is praliciguat; [1] Data from preclinical study: 1692-211348NI

Akebia THERAPEUTICS

Completed Phase 2 study* in patients with DKD receiving standard of care

Objective: To assess safety and tolerability of praliciguat and its effect on renal function in patients with DKD on RAAS inhibitors

Patients [n=156]

- Type 2 diabetes mellitus
- Diagnosed for ≥6 months
- ≥1 anti-hyperglycemic medication with stable regimen
- Stable ACEi or ARB for ≥4 wk
- Albuminuria (UACR 200-5000mg/g)
- eGFR 30-75 mL/min/1.73 m2
- SBP 110-160 mmHg

Double-Blind Period [12 weeks]

1:1:1 Randomization

- **Placebo [N=52]**
- **20 mg Praliciguat [N=50]**
- **40 mg Praliciguat [N=54]**

Assessments

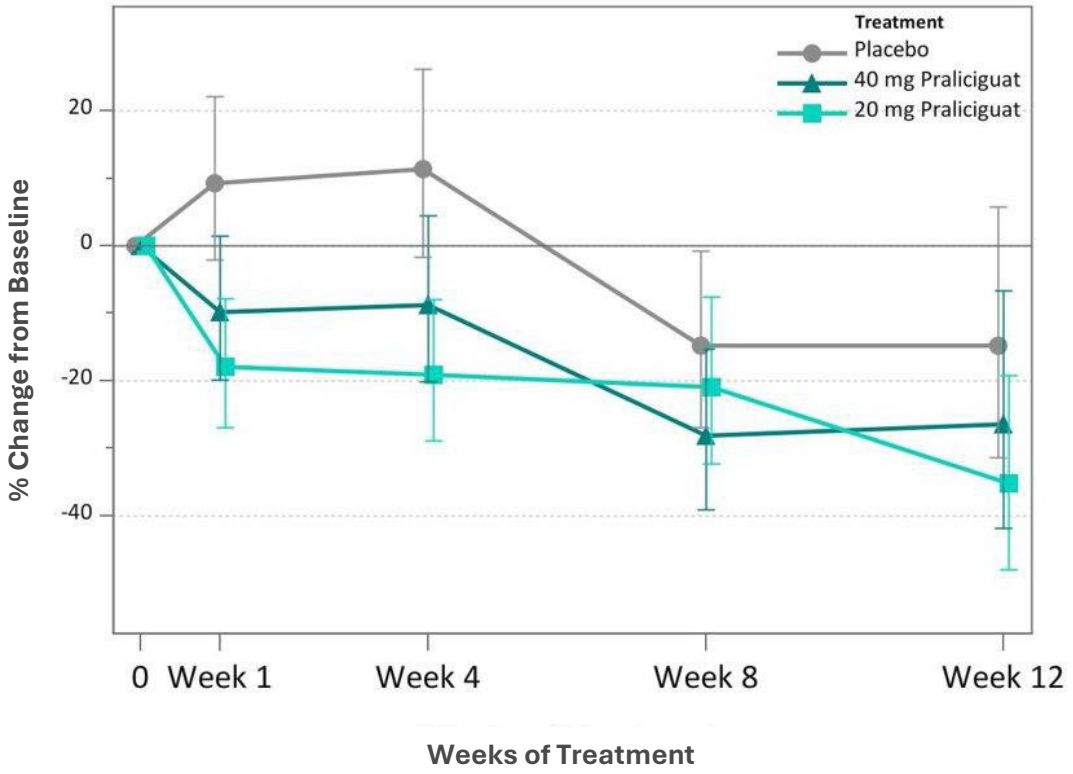
- **Primary endpoints: Urine albumin creatinine ratio (ΔUACR) and TEAEs**
- eGFR
- Hemodynamics (including ambulatory BPs and HR)
- Metabolic: fasting glucose, HOMA-IR, HbA1c, lipids
- Pharmacokinetics
- Exploratory plasma biomarkers

*Study completed by Cyclerion, Inc. Hanrahan et al. CJASN 2021; DKD is diabetic kidney disease; RAAS is renin-angiotensin-aldosterone system; ACE is angiotensin-converting enzyme; ARB is angiotensin II receptor blockers; UACR is urine albumin-to-creatinine ratio; eGFR is estimated glomerular filtration rate; SBP is systolic blood pressure; DBP is diastolic blood pressure; MAP is mean arterial pressure; HR is heart rate; TEAEs is treatment emergent adverse events; HOMA-IR is homeostatic model assessment of insulin resistance; HbA1C is hemoglobin A1C

Phase 2 study* showed praliciguat treatment associated with rapid and sustained reduction in UACR in ITT and post-hoc mITT population

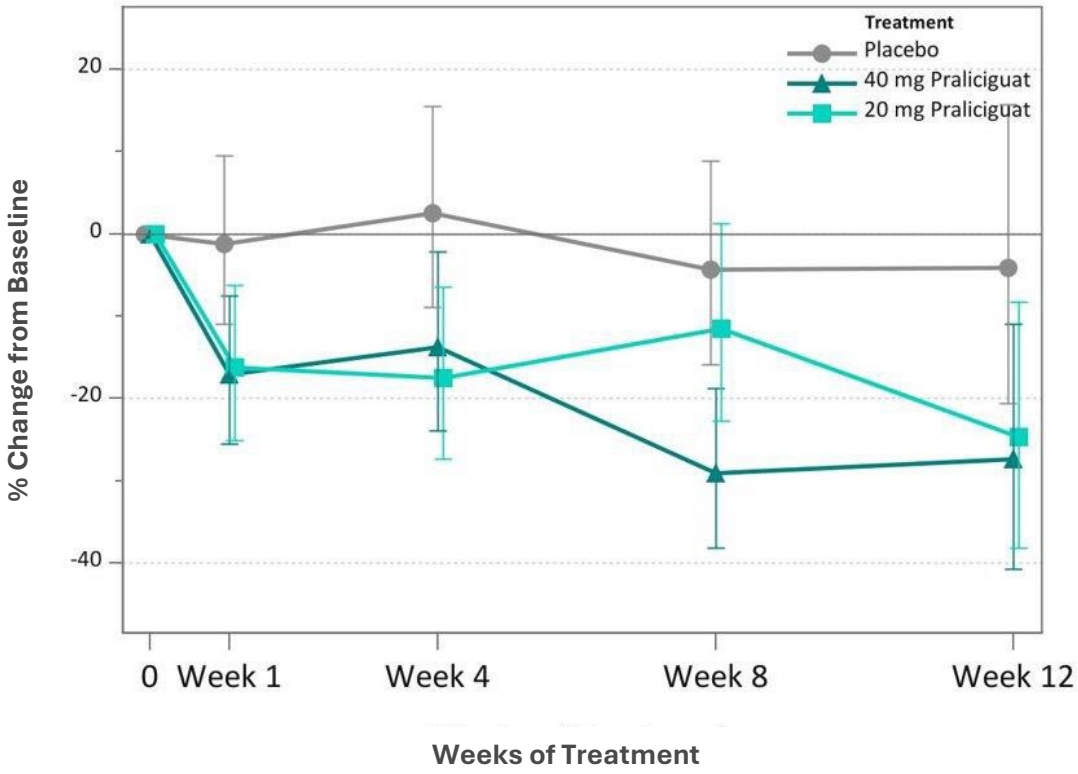
ITT Population
(N=156)

DKD Study: LS Mean (90% CI) Change in Baseline in UARC (mg/g) ITT



mITT (without site 36)
(N=133)

DKD Study: LS Mean (90% CI) Change in Baseline in UARC (mg/g) ITT



*Phase 2 Study (Hanrahan et al. CJASN 2021) evaluating praliciguat versus placebo in patients with diabetic kidney disease completed by Cyclerion, Inc.
DKD is diabetic kidney disease; ITT is intent to treat; mITT is modified intent to treat; UACR is urine albumin-to-creatinine ratio

Akebia THERAPEUTICS

Post hoc analysis of Phase 2 trial* in patients with DN showed increased UACR responses

UACR Cut-point	Praliciguat n/N (%)	Placebo n/N (%)	Difference %	Relative Risk (RR)	95% CI
Any time in 12 weeks					
0.3 g/g	24/84 (28.6)	8/46 (17.4)	+11.2	1.64	0.804, 3.358
0.5 g/g	**43/84 (51.2)**	**16/46 (34.8)**	**+16.4**	**1.47**	**0.941, 2.302**
0.7 g/g	53/84 (63.1)	23/46 (50.0)	+13.1	1.26	0.905, 7.759

UACR of 0.5 g/g approximates a urine protein to creatinine ratio (UPCR) of 0.7 g/g.

*Study completed by Cyclerion, Inc. (Hanrahan et al. CJASN 2021); Calculations completed by Akebia Therapeutics
DN is diabetic nephropathy; UARC is urine albumin-to-creatinine ratio; CI is confidence interval

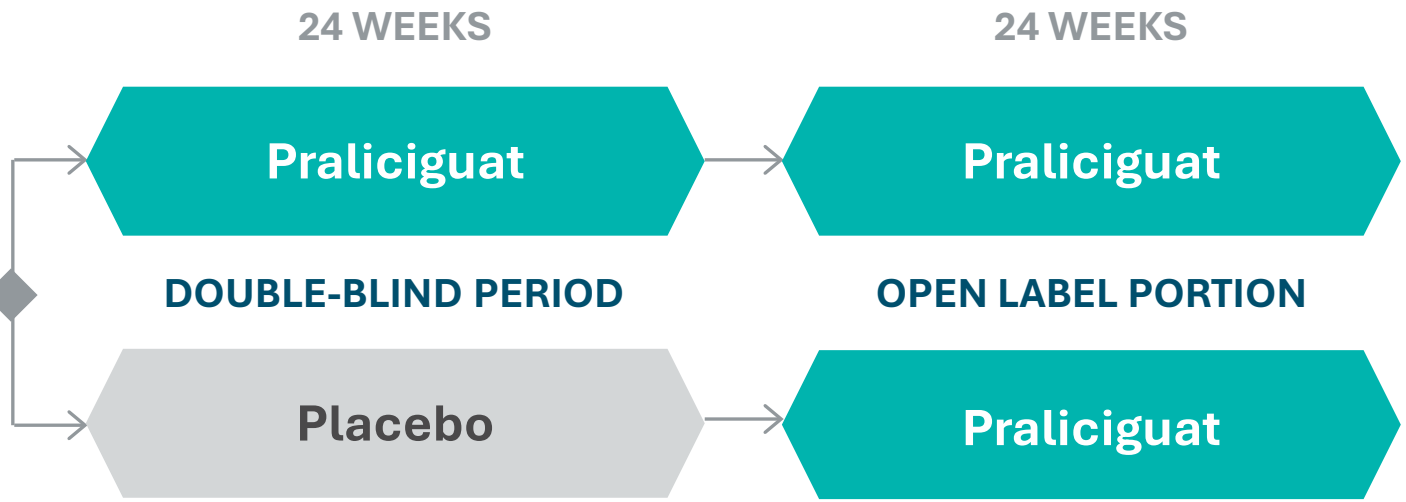
Praliciguat Phase 2 clinical trial in FSGS

Randomized, double-blind, placebo-controlled, dose-titration study to evaluate the efficacy and safety of praliciguat in adults with biopsy-confirmed FSGS.

Phase 2 Study

- Targeting up to 60 patients
- First patient enrolled in December 2025

Randomization 1:1



Primary Outcome

Change from baseline in UPCR at 24 weeks

Secondary Outcome

Percentage of participants with partial remission defined as a 40% UPCR reduction and UPCR<1.5 g/g at 24 weeks

MTD is maximum tolerated dose, UPRC is urine protein-to-creatinine ratio

Akebia THERAPEUTICS

AKB-097
Ebribafusp alfa

The complement system and complement-mediated disease

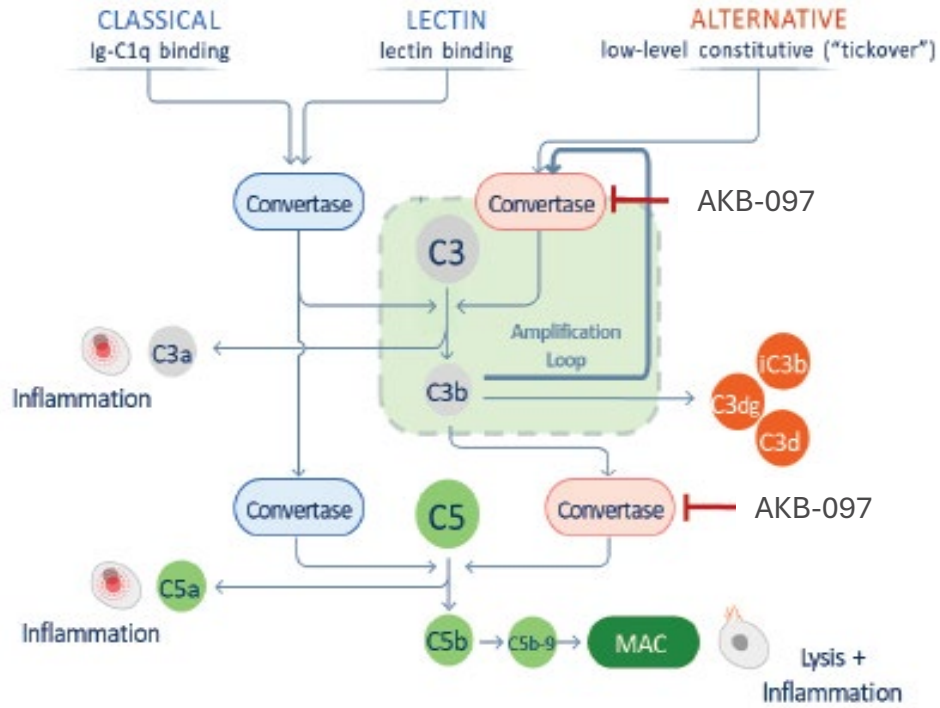
The body's complement system is comprised of ~30 proteins produced by the liver and immune cells that work together as part of the innate immune system. Most of these proteins are found in blood or on cell surfaces.[1]

Main effects of complement[1]

1. Lysis of bacteria and damaged cells
2. Enhancement of pathogen clearance
3. Recruitment of inflammatory cells

The complement system can become dysregulated resulting in numerous inflammatory and autoimmune conditions including multiple diseases of the kidney.[1]

Complement inhibitors work by binding to and preventing the activation of specific complement proteins, halting the cascade and reducing inflammation and the destruction of cells.[2]



[1]Sarma JV. The complement system [2]Thurman JM. . Targeting the complement cascade Image adapted from: Fahnoe KC, Liu F, Morgan JG, Ryan ST, Storek M, Stark EG, Taylor FR, Holers VM, Thurman JM, Wawersik S, Kalled SL, Violette SM. Development and Optimization of Bifunctional Fusion Proteins to Locally Modulate Complement Activation in Diseased Tissue

Akebia THERAPEUTICS

Complement inhibitors approved for kidney diseases

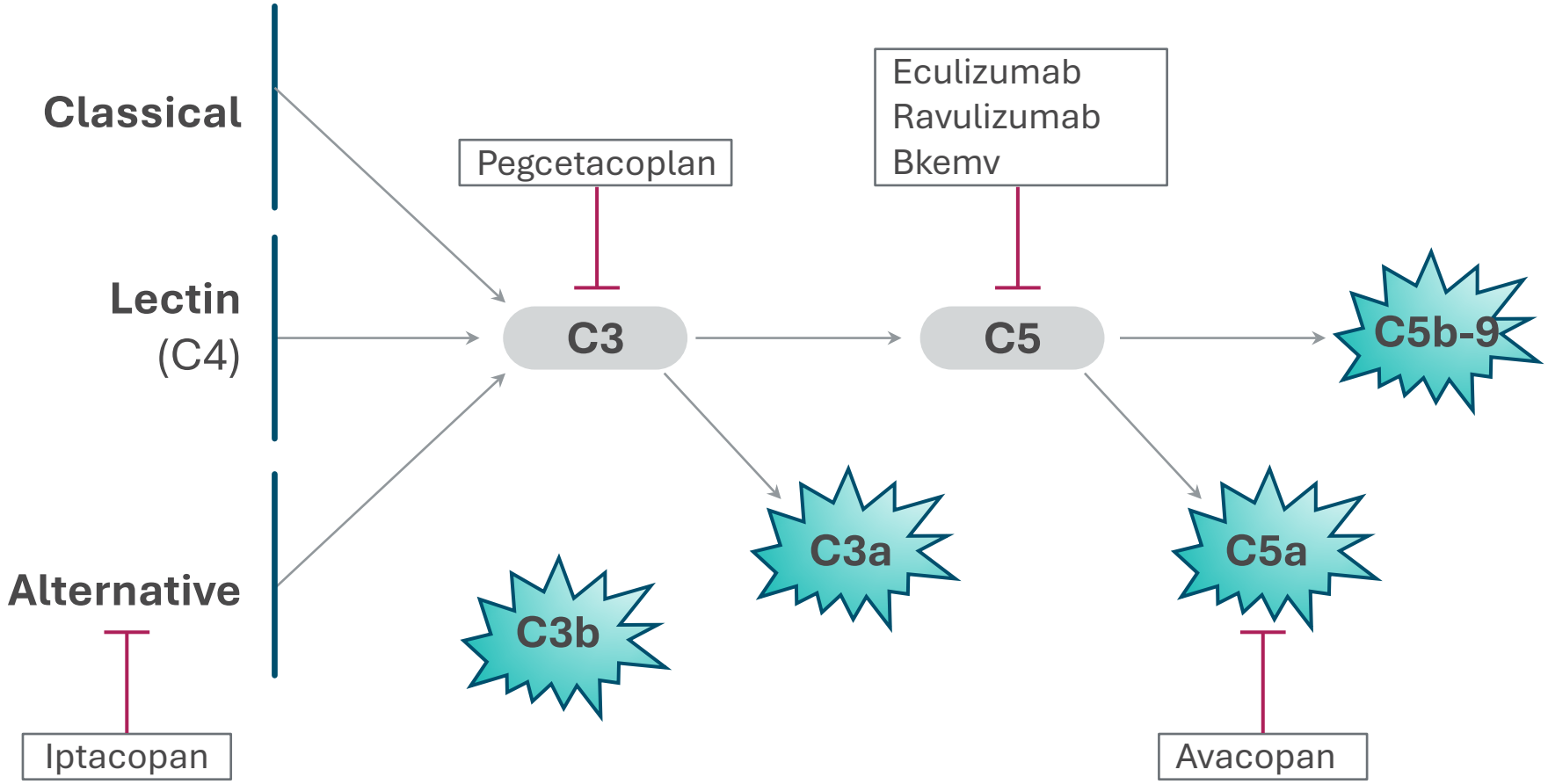


Image adapted from: Thurman JM. . Targeting the complement cascade

Akebia THERAPEUTICS

AKB-097 aims to address limitations of current complement inhibitors

PROBLEM:

- **Limited activity:** Reliant on systemic blockade to impact affected organ
- **High doses, frequent administration required:** High abundance, rapid turnover of most target complement proteins
- **Systemic risk:** Complement plays critical role in combatting infection; systemic complement inhibition carries long-term unknowns

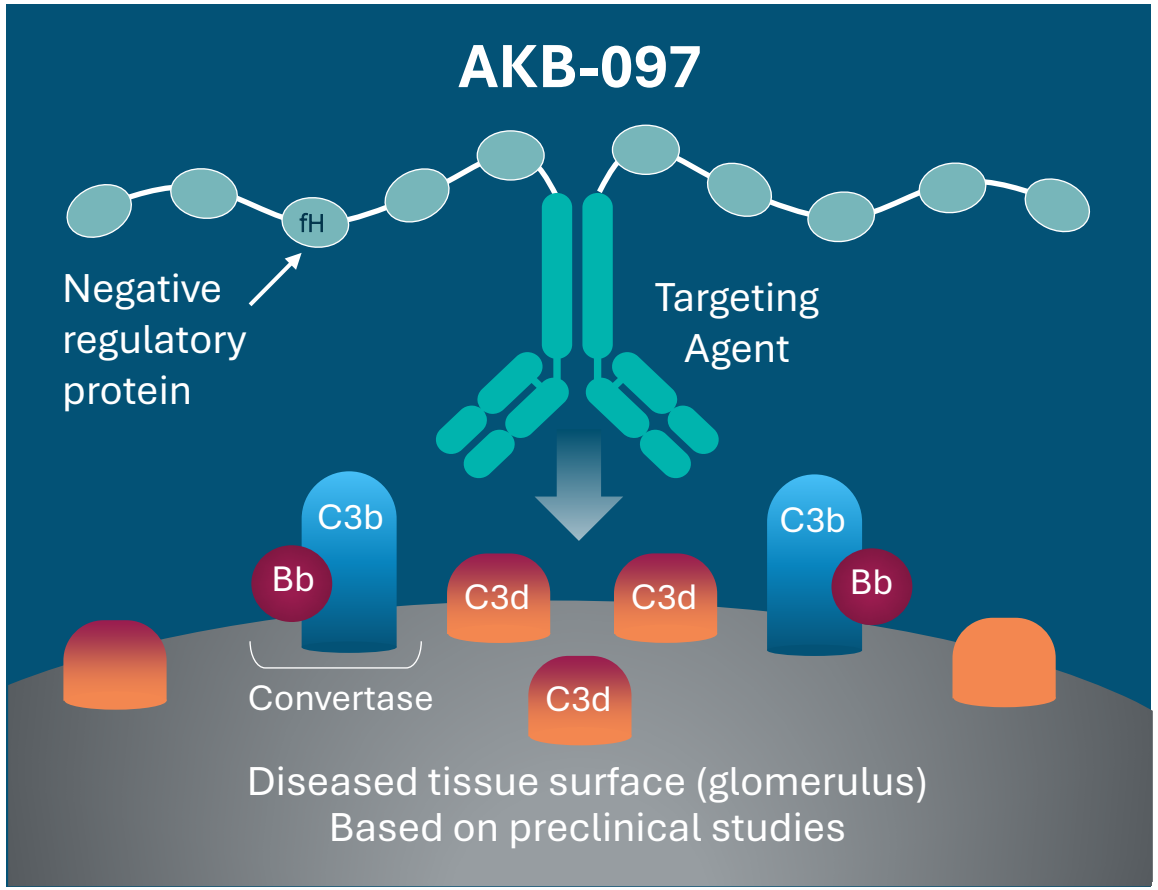
POTENTIAL SOLUTION:

- **Enhanced activity through tissue targeting:** Differentiated approach to driving efficacy by inactivating convertases directly at site of activation
- **Reduced treatment burden:** Subcutaneous route with once weekly dosing; potential for once every two weeks dosing
- **Improved risk/benefit profile:** Designed to maximize therapeutic index while maintaining intact immune surveillance

AKB-097 is a novel, tissue-targeted complement inhibitor

Designed to target complement activity in tissues to degrade alternative pathway convertases

Targeting control of the amplification loop of all 3 complement pathways (alternative, classical, and lectin)



- AKB-097 binds with high affinity to C3d, a long-lived fragment of C3
- Factor H (fH) binds to C3b in alternative pathway C3 and C5 convertases
- fH promotes AP convertase dissociation
- fH with Factor I induces AP convertase degradation

AP is alternative pathway

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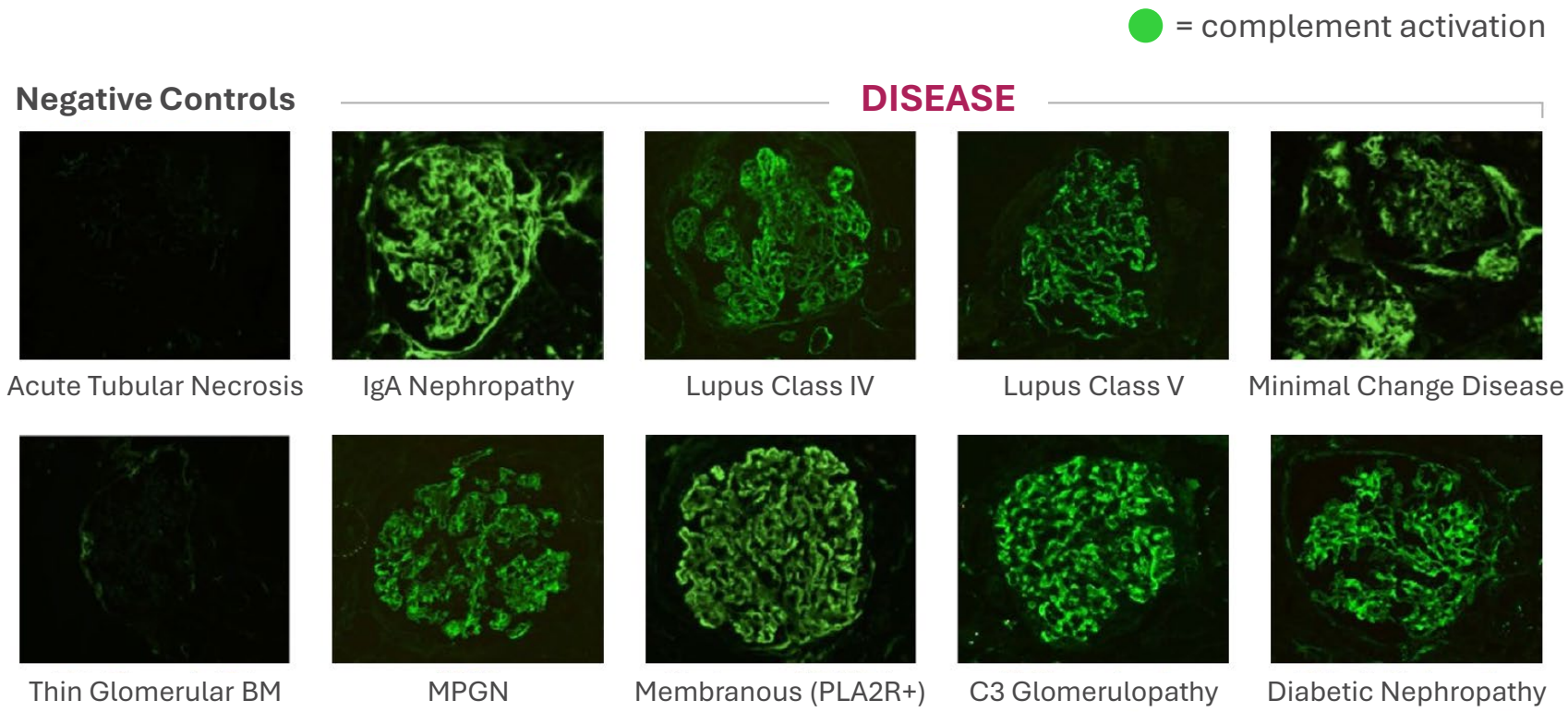
Presence of C3d in human glomeruli is a hallmark of numerous kidney diseases

Immunostaining of C3d in human glomeruli



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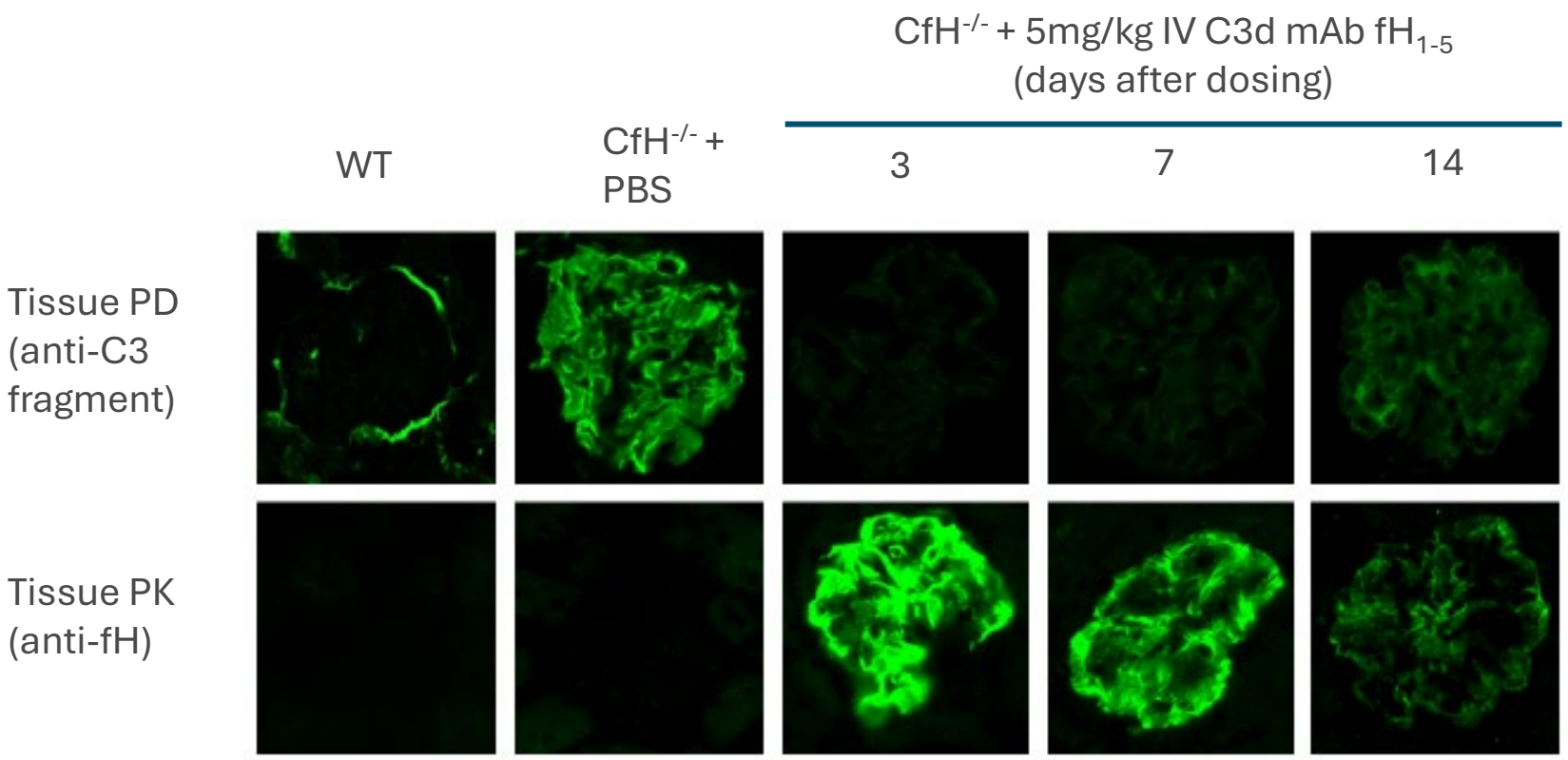
In the fH -/- mouse model of human C3G, AKB-097 had long term, durable kidney PK and PD



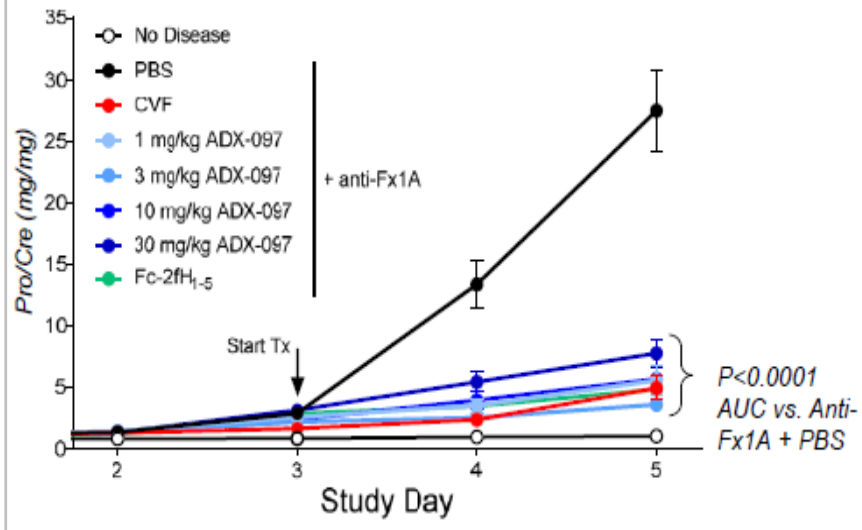
The fH-/- mouse model had uncontrolled complement activation

AKB-097 showed robust inhibition of C3 activity with both SC or IV dosing

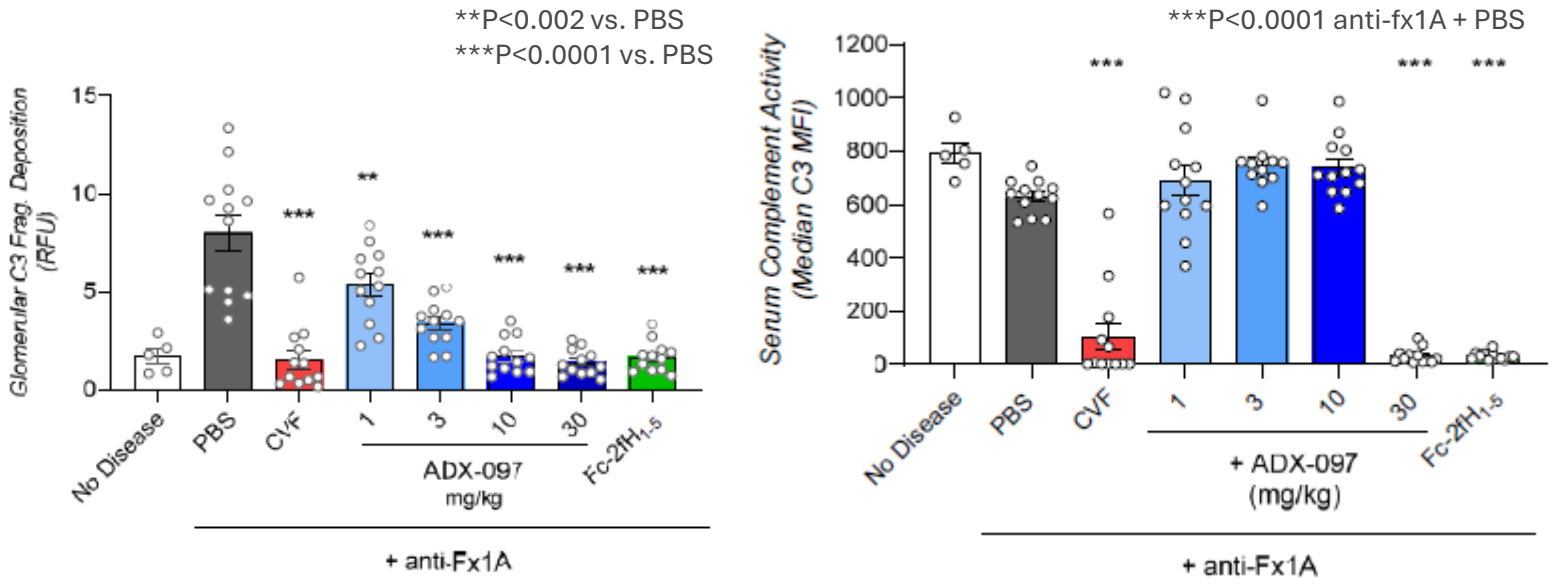
Tissue PK/PD supports SC dosing every 1 to 2 weeks

PK is pharmacokinetics; PD is pharmacodynamics; SC is Subcutaneous; IV is intravenous

AKB-097 IV reduced glomerular complement activation and proteinuria in the rat model of membranous nephropathy



AKB-097, dosed IV, inhibited proteinuria at levels comparable to complement depletion with CVF

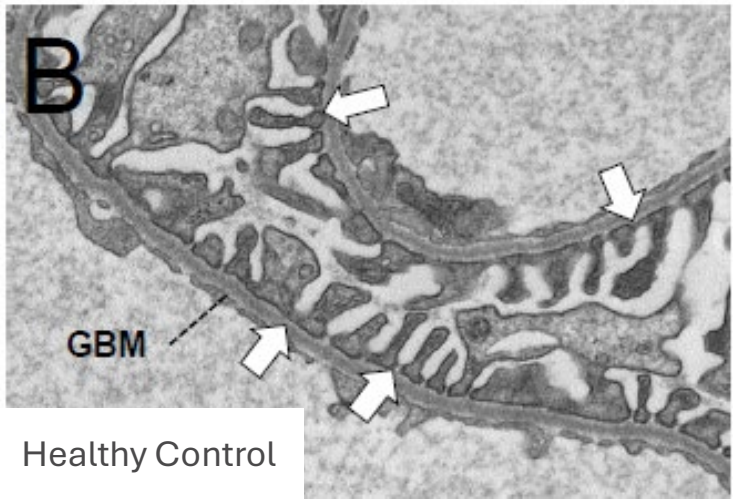


AKB-097 dose-dependently decreased glomerular complement activation without reducing serum complement activity, except at the highest dose

Data source: Liu et al 2024 Mol Therapy 32(4):1061-1079; IV is intravenous; CVF is cobra venom factor; Anti-Fx1A is a sheep antibody to rat proximal tubular epithelial cell brush border antigen; PBS is phosphate buffered saline

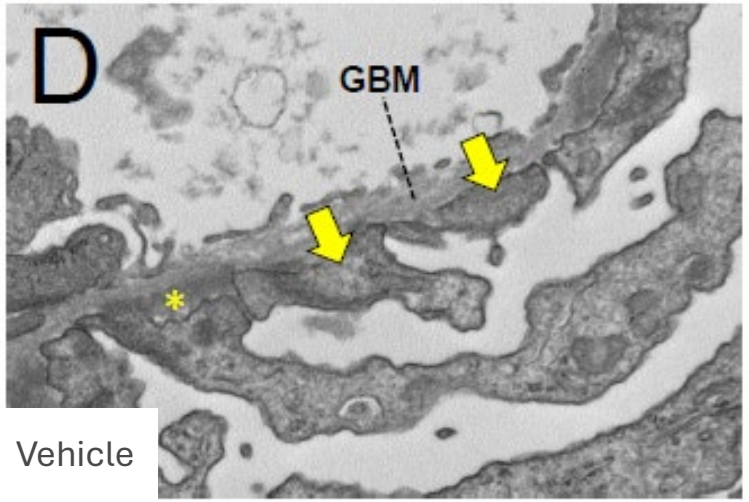
Akebia THERAPEUTICS

AKB-097 protects podocytes from foot process effacement in the membranous nephritis model[1]



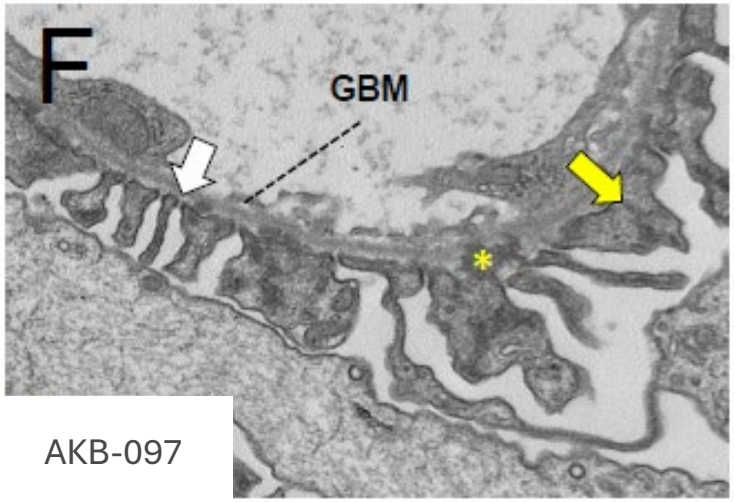
Healthy Control

Transmission electron microscopy Shows well-differentiated podocyte foot processes (white arrows)



Vehicle

In the rat model, there is extensive foot process effacement (yellow arrows) and electron dense regions (yellow asterisk), consistent with immune complex deposition



AKB-097

Treatment with AKB-097 shows substantial preservation of podocyte foot processes (white arrow), though occasional examples of podocyte foot process effacement (yellow arrow) and electron dense regions (yellow asterisk) can be found

GBM is glomerular basement membrane [1]Liu et al 2024. C3d-Targeted factor H inhibits tissue complement in disease models and reduces glomerular injury without affecting circulating complement, Molecular Therapy 32(4):1061-1079.

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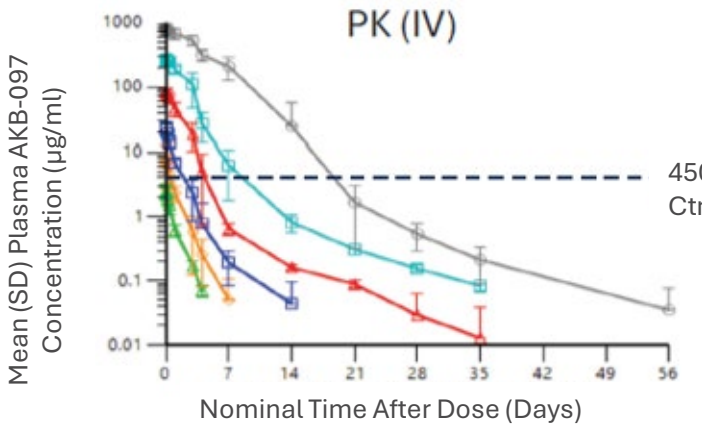
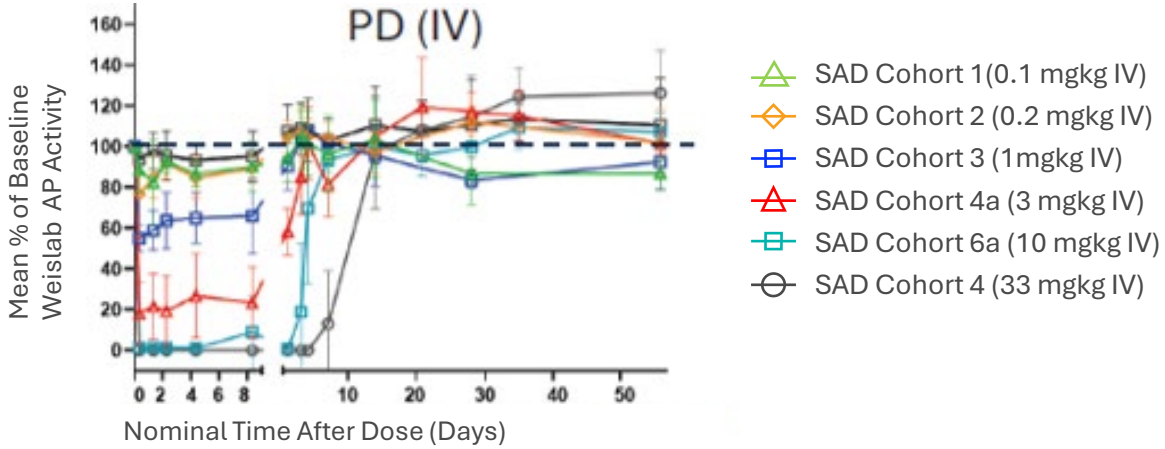
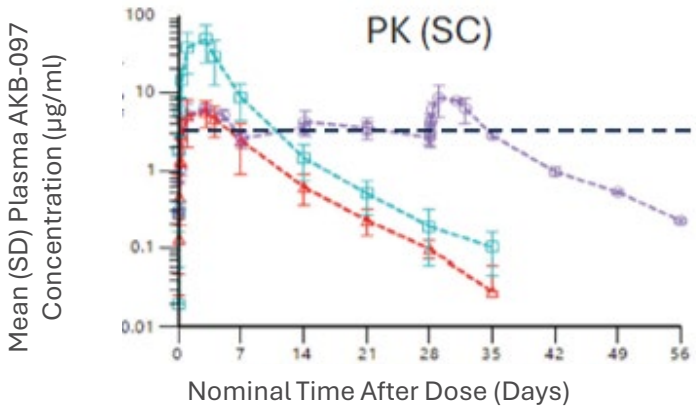
In a Phase 1 study*, weekly SC dosing met desired exposures for predicted complement tissue inhibition without systemic AP pathway inhibition

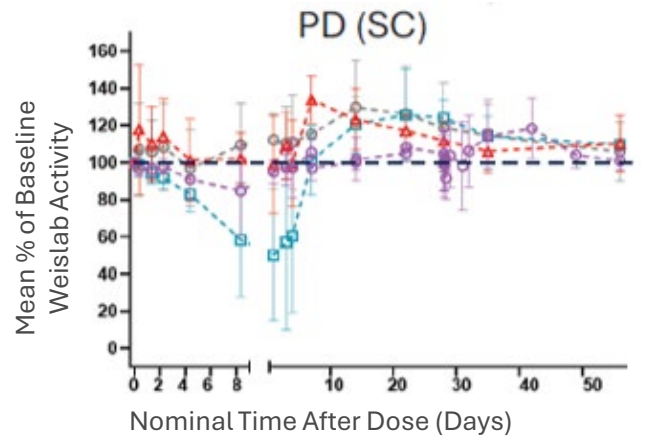


450 mg SC weekly with Ctrough > 3.2 µg/ml





450 mg SC weekly with Ctrough > 3.2 µg/ml



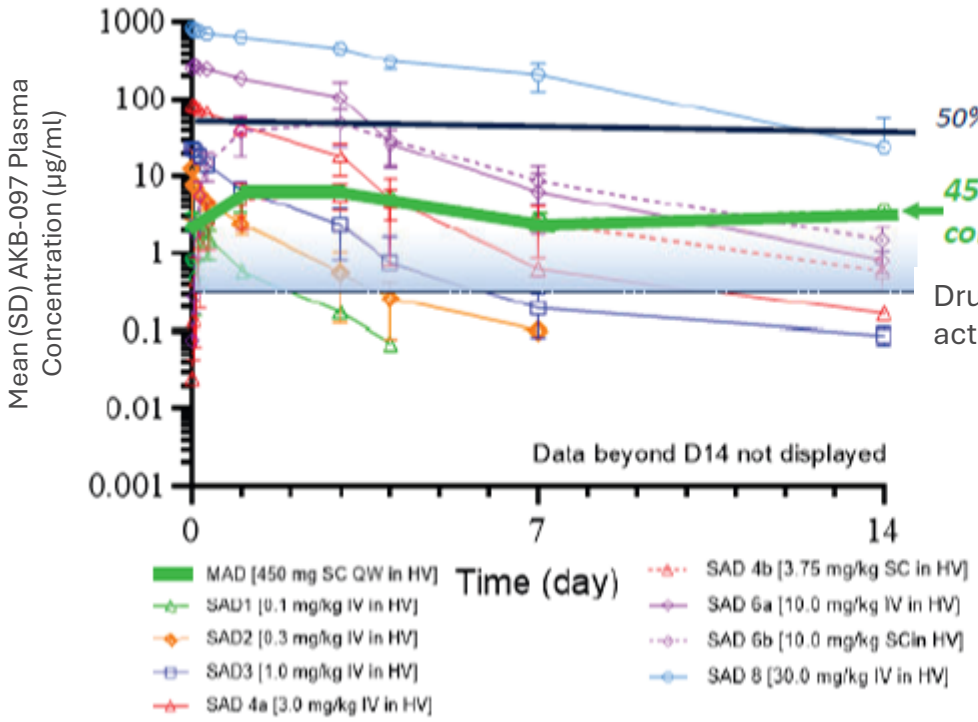
450 mg SC weekly; no inhibition of complement

MAD Cohort 1(450 mg QW SC)
SAD Cohort 4b (3.75 mgkg SC)
SAD Cohort 6b (10.0 mgkg SC)
SAD placebo pool

Phase 1 study of AKB-097 completed by Q32 Bio. AP is alternative pathway, IV is intravenous, SC is subcutaneous

Akebia THERAPEUTICS

Phase 2 dose identified: 450 mg SC met desired exposure goals in Phase 1 study[1]



50% systemic complement inhibition

450mg SC achieved exposures below systemic inhibition and above conservative end of predicted range for clinical activity

Drug levels predicted to provide maximal tissue complement inhibition and activity based on mouse, rat and NHP preclinical data

No serious or severe adverse events (AEs), no discontinuations due to AEs, no AEs related to immunogenicity, and minimal anti-drug antibodies detected with low-level titers only.[1]

[1]Results from Phase 1 SAD/MAD study of AKB-097 completed by Q32 Bio. SC is subcutaneous

Akebia THERAPEUTICS

AKB-097 could become the SOC in multiple rare kidney diseases alone or in combination with other therapies

	IgAN	LN	C3G
Role of complement system in disease	Drives inflammation and kidney injury[1]	Lack of complement inhibitors in SLE, accelerates the development of LN[3]	Overactivation of the complement cascade leads to kidney damage[5]
Shortcomings of SOC or therapies in development	~50% refractory rate for APRIL±BAFF inhibitors[2]	>50% refractory rate for approved treatments[4]	~30% refractory rate for leading, approved complement inhibitor[6]
Potential commercial opportunity	Expect role for multiple therapies as IgAN has highly heterogeneous treatment response, genetics, immunology, and pathology	Expect role for multiple therapies as LN encompasses multiple biological subtypes	Expect role for next-generation complement inhibitors that offer improved convenience, dosing and/or safety profile with equal or better efficacy

SOC is standard of care; SLE is systemic lupus erythematosus; Refractory rate is non-response to treatment [1]Daha MR. Role of complement in IgA nephropathy [2]Vertex Press Release, March 9, 2026 [3]Bao L. Complement in Lupus Nephritis [4]Roche Press Release, October 19, 2025 [5]Willows J. The role of complement in kidney disease [6]Apellis Press Release, July 28, 2025

Ebribafusp alfa Phase 2 open-label rare kidney disease basket trial

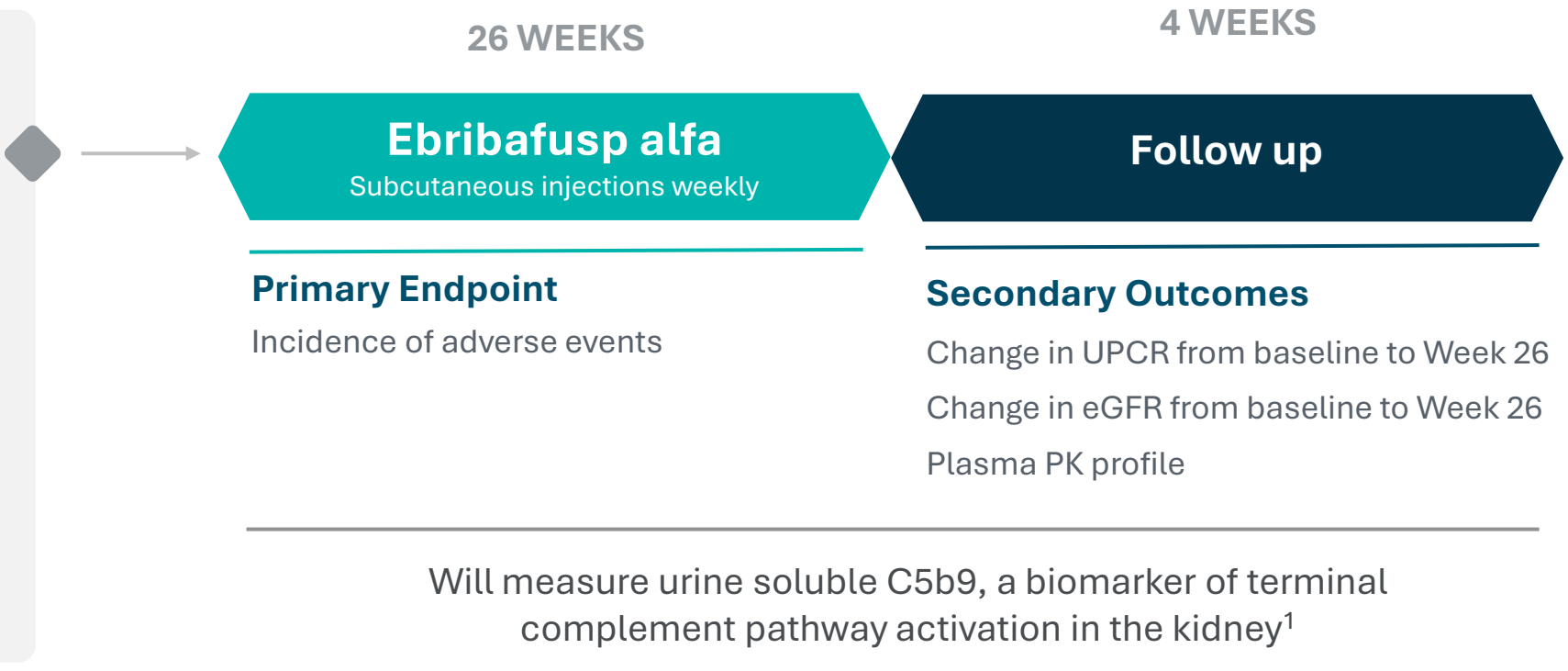
The trial is designed to evaluate the safety, PK/PD, and clinical activity of ebribafusp alfa in patients with IgAN, LN, and C3G.

Phase 2 study

Targeting ~30 patients across 3 indications:

IgAN, LN, C3G

Initial data release expected in 2027



Will measure urine soluble C5b9, a biomarker of terminal complement pathway activation in the kidney[1]

PK is pharmacokinetics; PD is pharmacodynamics; UPCR is urine protein-to-creatinine ratio; eGFR is estimated glomerular filtration rate [1]Yu BC. Urinary C5b-9 as a Prognostic Marker in IgA Nephropathy.

Akebia THERAPEUTICS

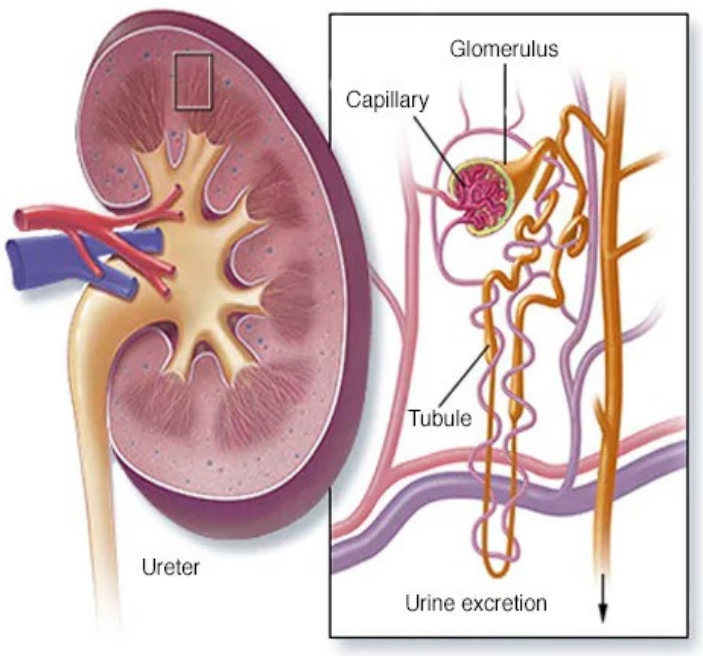
AKB-9090

CS-AKI affects a significant number of patients and there is unmet need for treatment

AKI is a sudden decrease in kidney function measured within a week and often associated with another serious illness or condition.[1]

Can arise from cardiac surgery-related procedures that cause hypoperfusion, hemolysis, inflammation, and reduced oxygen delivery to the kidney.[2]

AKI occurs in up to 30% of the ~400,000 annual cardiac surgical procedures.[2]



3

No approved therapies specifically for CS-AKI

CS-AKI is cardiac surgery related-acute kidney injury [1]National Kidney Foundation – AKI [2]Liu D. et al. Oxid Med Cell Longev. 2021 Mar 9;2021:8873581 [3]Mayo Clinic: AKI

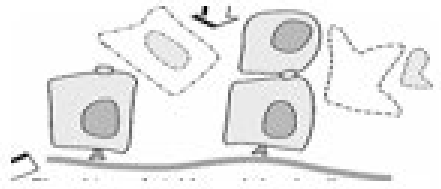
AKB-9090 is a novel HIF-PH inhibitor being evaluated in CS-AKI

The case for HIF-stabilization in AKI

Stabilization of HIF, a transcription factor, by prolyl hydroxylase inhibition leads to coordinated changes in gene expression which activate cell survival pathways, shift cellular metabolism from aerobic to anaerobic, decrease reactive oxygen species (ROS) and reduce inflammation, lessening kidney tubule epithelial and microvascular injury.

Injury to the tubular epithelium and microvascular endothelium underlie the pathophysiology of AKI[1]

Tubular Epithelia



Cell Death/Detachment

Microvasculature

Impaired vasodilation, obstruction and damage/loss

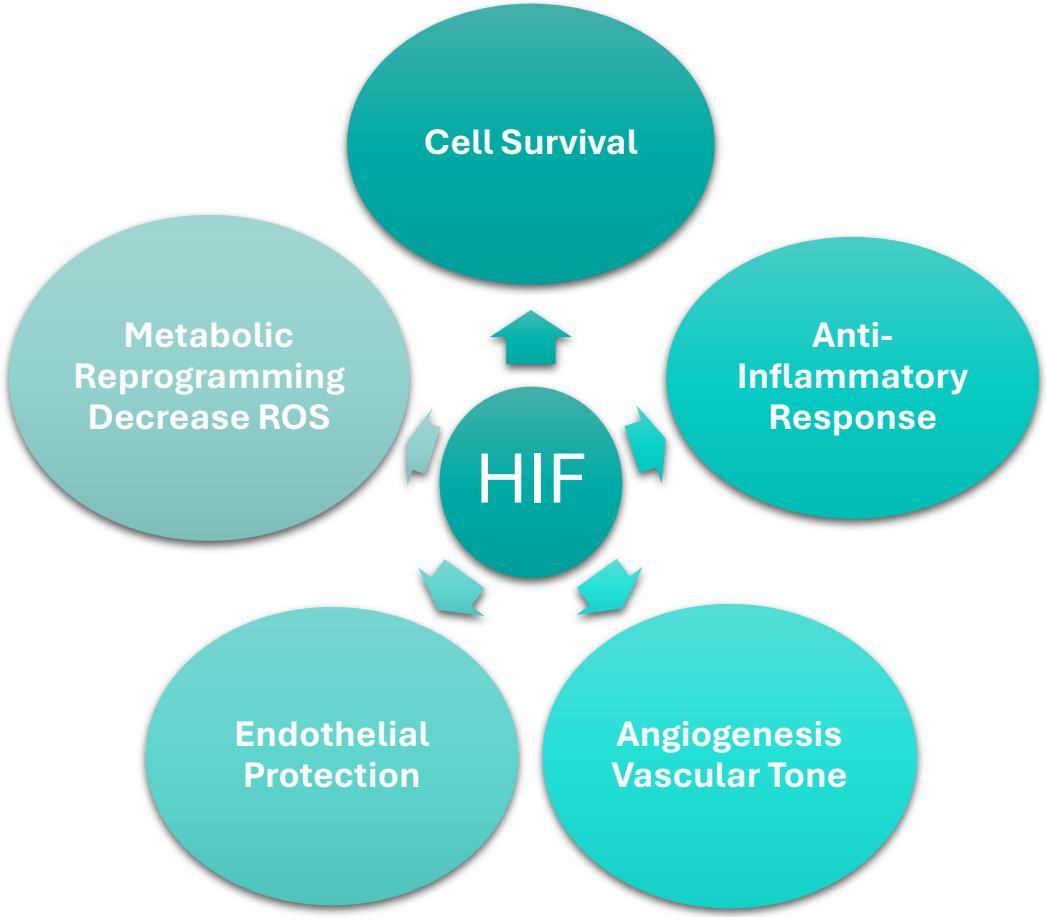
HIF-PH is hypoxia-inducible factor-prolyl hydroxylase. ARDS is acute respiratory distress syndrome. [1]Baker P. Adding insult to injury: the spectrum of tubulointerstitial responses in acute kidney injury

AKB-9090 mechanism of kidney protection[1]

Investigational agents for AKI targeting a single pathway have not worked, including recombinant alkaline phosphatase, p53 inhibitor, HGF mimetic, BMP peptide or α-MSH inhibitor.

Unlike these agents, AKB-9090 activates HIF[2], a transcription factor present in all tissues and cells, which activates the many pathways responsible for adaptation to hypoxia.[3]

AKB-9090 may have utility in other types of AKI, such as sepsis-associated and chemotherapy-associated AKI, and ARDS.



[1,3]Semenza 2012 Cell 148(3):399-408; [1]Maxwell and Eckardt 2016 Nat Rev Nephrol 12(3):157-168, Sanghani and Haase 2019 Adv Chronic Kid Dis 26(4): 253-266, IU-AKB-0010, AKB-10, Addendum to AKB-10, IU-AKB-0011, IU-AKB-0017, 1520-2302890, Addendum to 1520-2302890, AKBA-295-3, Addendum to AKBA-295-3, XD05/XLB443, Addendum to XD05/XLB443, AKB-RR-009, AKB-RR-010; [2]AKB-RR-007

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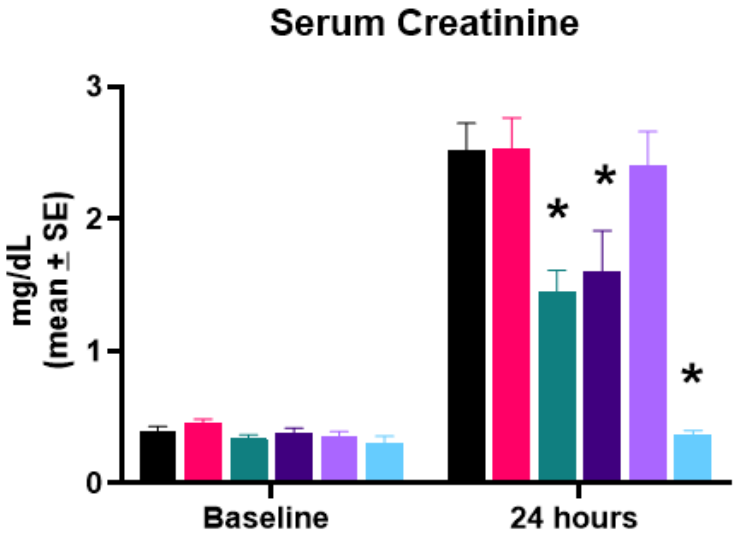
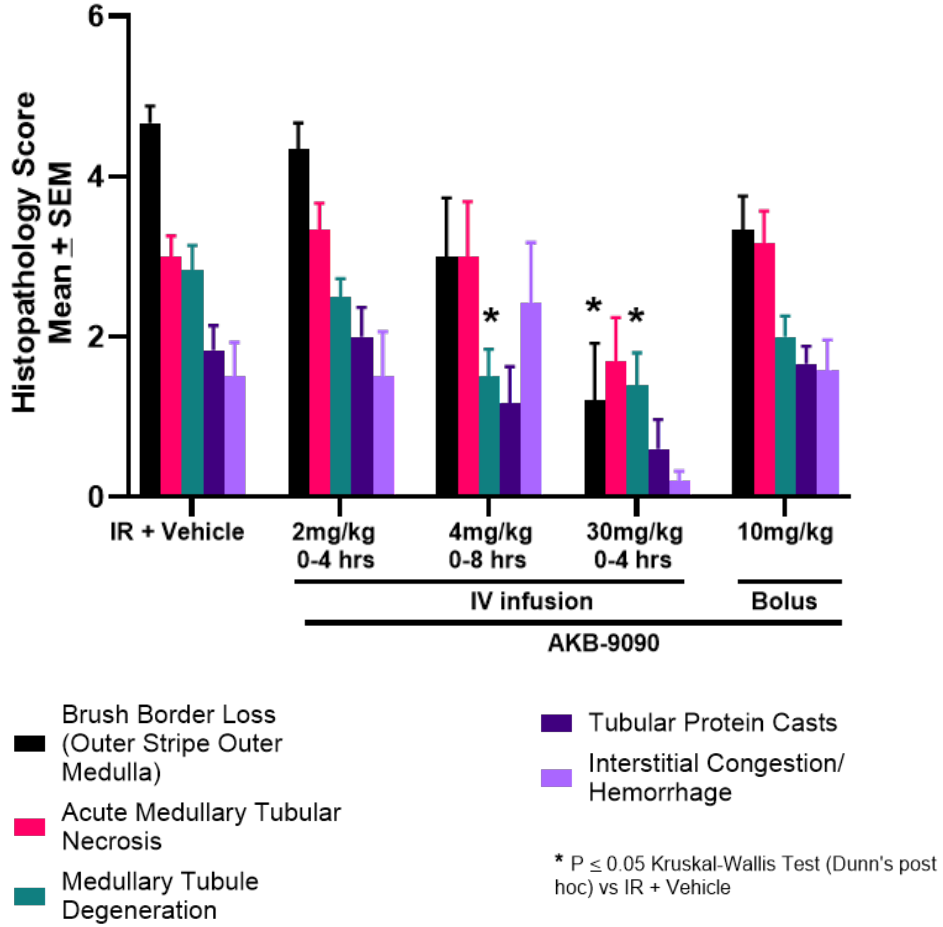
AKB-9090 reduced kidney injury in a kidney ischemia-reperfusion animal model

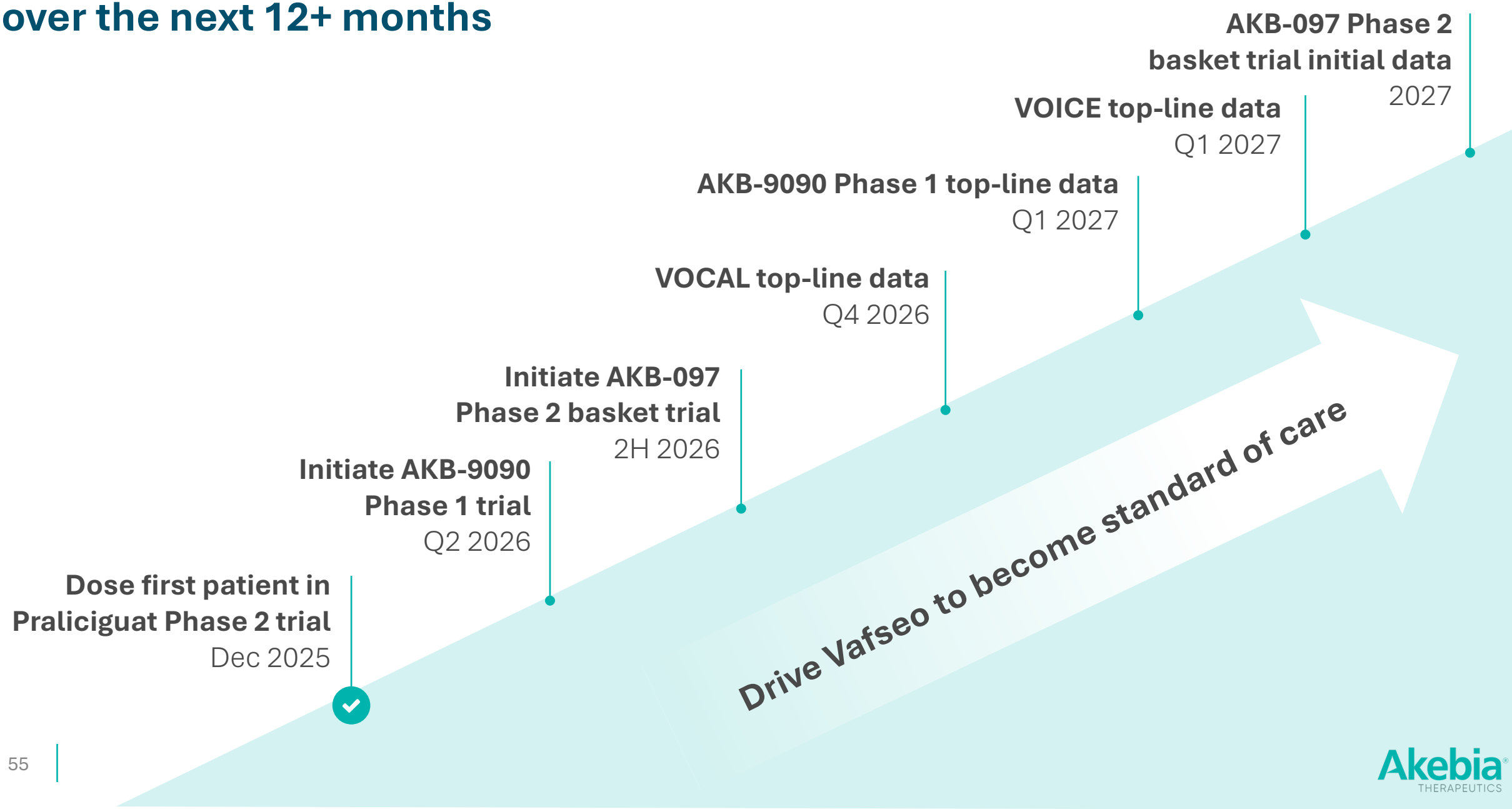




From Study Report IU-AKB-0017, 1520-2302890 and Addendum to 1520-2302890

Akebia® THERAPEUTICS

Multiple value enhancing milestones expected over the next 12+ months



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