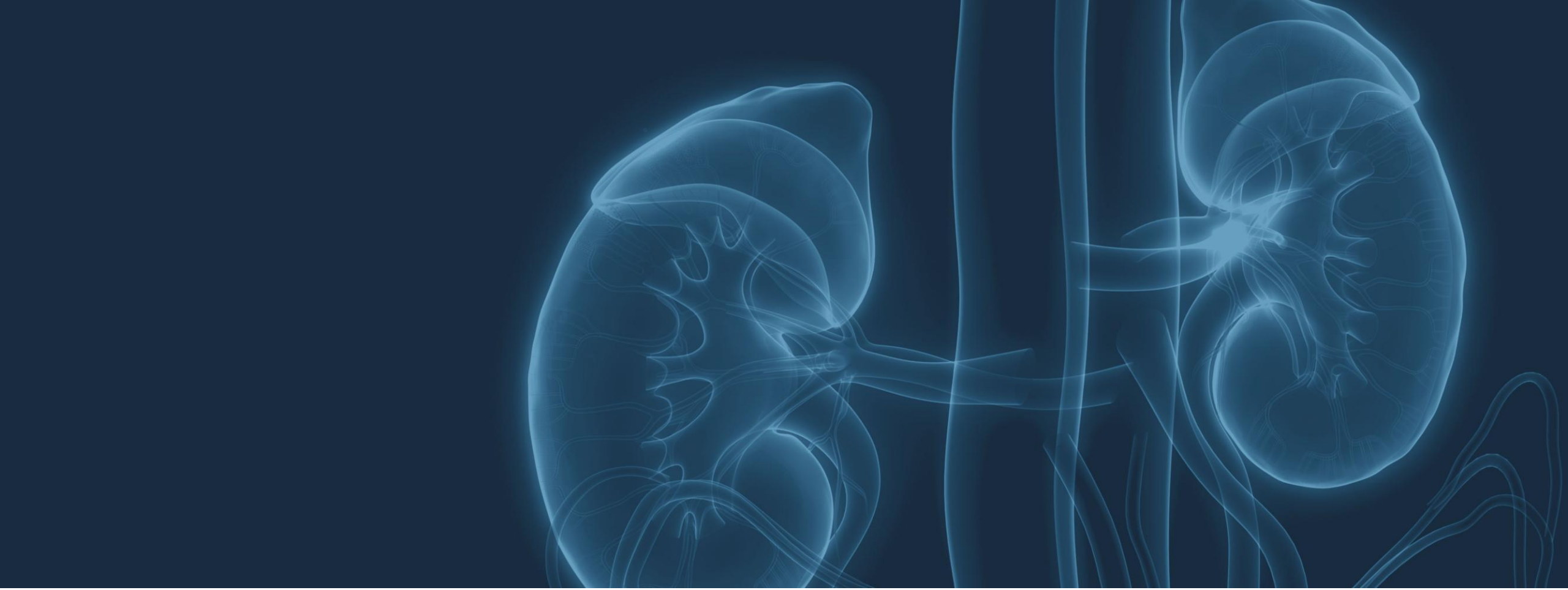


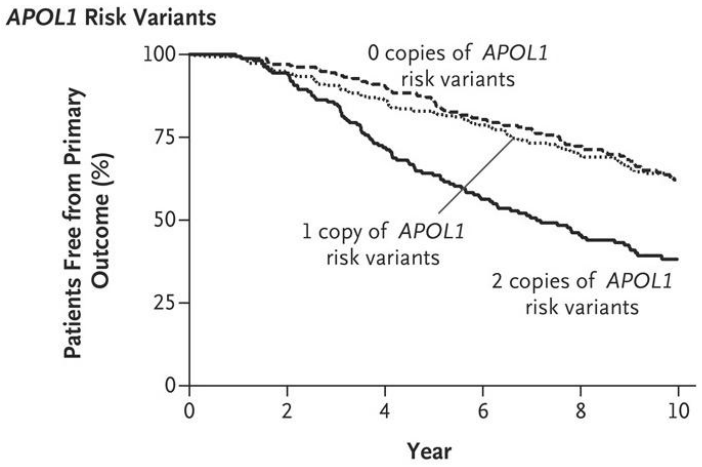
Evaluation of Safety, Tolerability and Efficacy of MZE829 in Adults with APOL1-Mediated Kidney Disease (HORIZON Study)

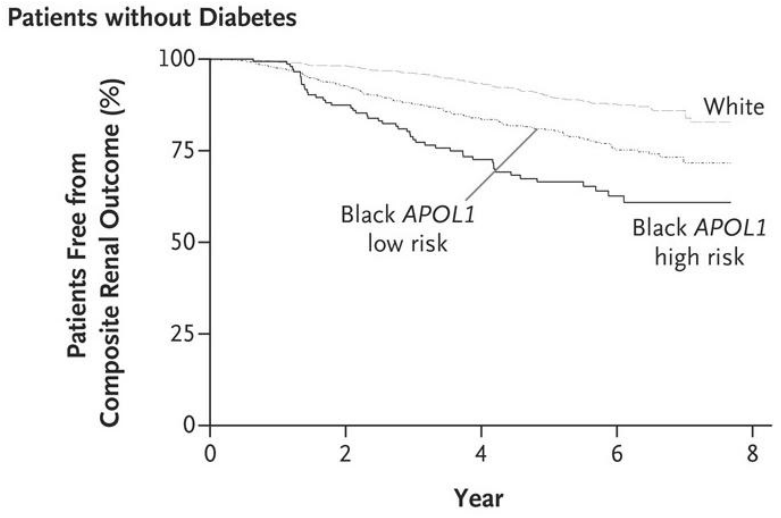
Presented by: Opeyemi A. Olabisi, MD, PhD

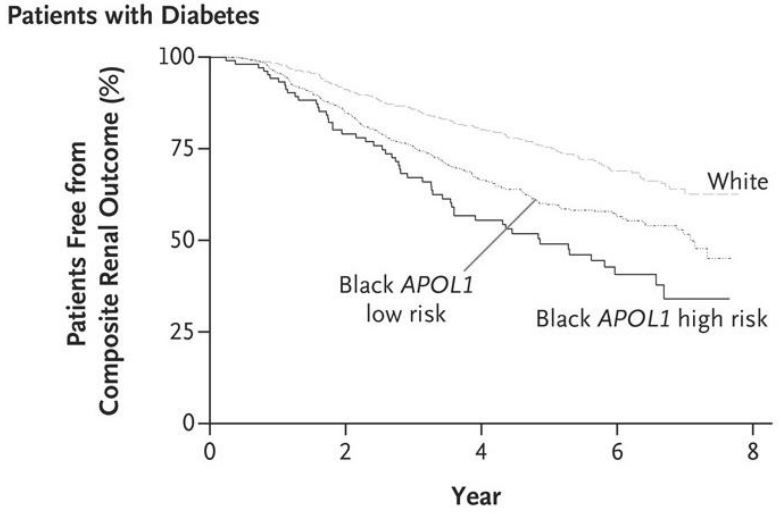
October 24, 2026

Background: APOL1-Mediated Kidney Disease (AMKD)

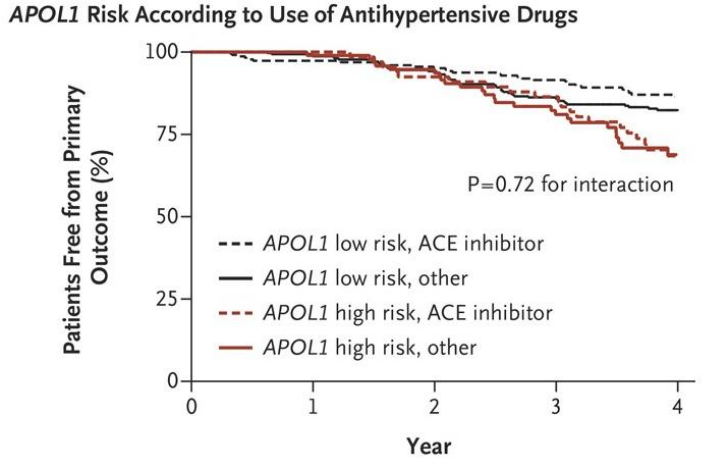
APOL1 high risk genotype increases incidence and progression rate of CKD





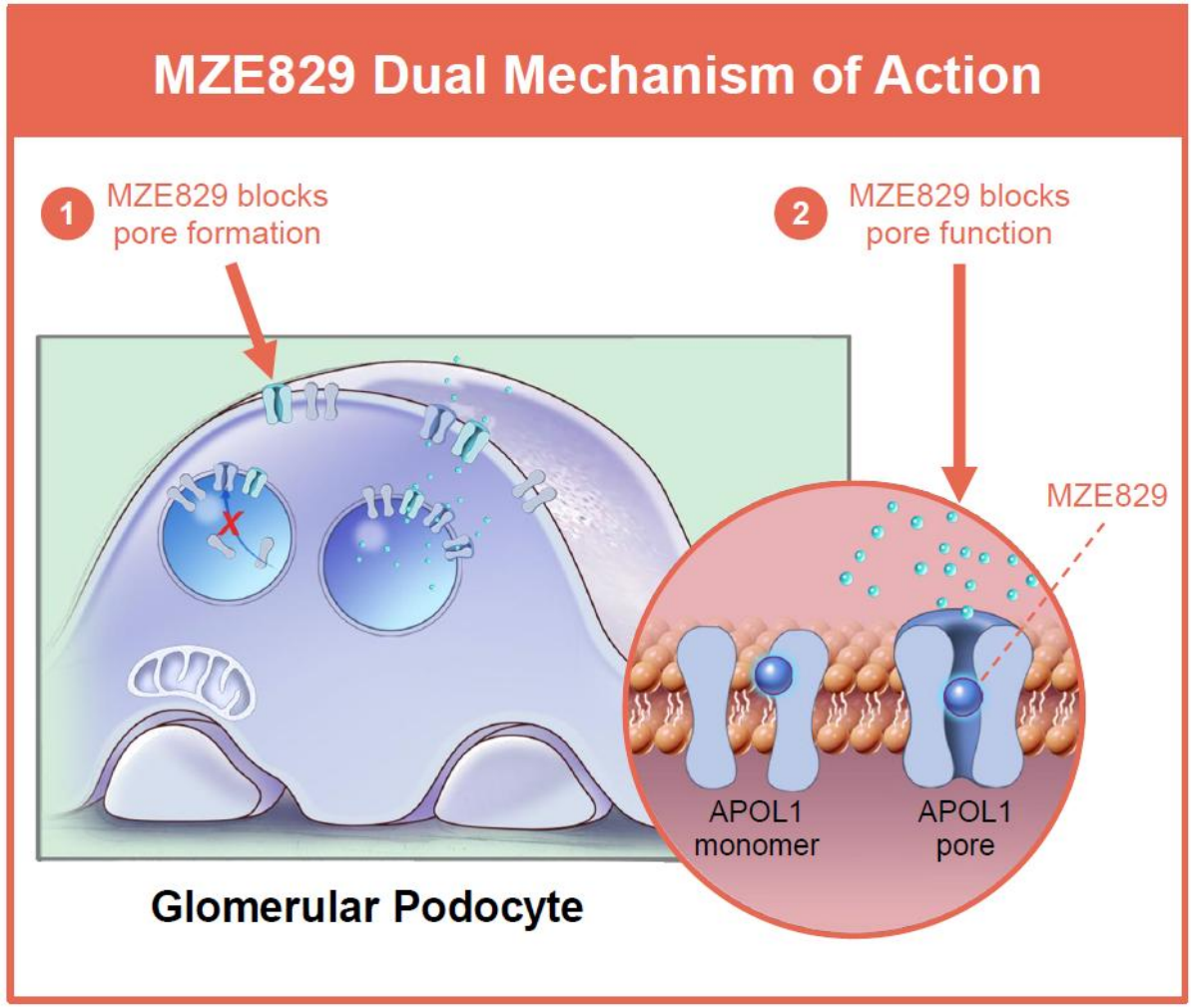


Current standard of care does not target genetic driver



Parsa A et al. NEJM 2013;369:2183-2196

Background: MZE829

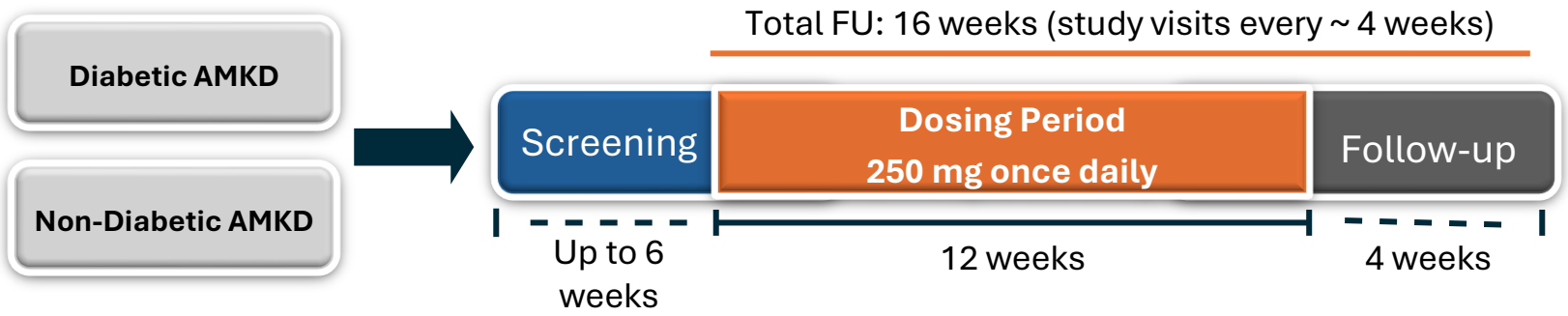


MZE829

- Selective, oral, once-daily small-molecule APOL1 inhibitor; blocks pore formation and function
- MOA supports broad AMKD phenotypes, including type 2 diabetes and FSGS

HORIZON Study Design

Open label basket study in adults with proteinuric diabetic and non-diabetic AMKD



Key Study Elements

➢ **Key Eligibility**

- Recent African ancestry with two copies of APOL1 risk variants
- Proteinuric CKD with diabetes, or attributed to HTN or FSGS without diabetes
- Baseline **uACR ≥300** mg/g and **eGFR ≥25** mL/min/1.73 m^2
- Stable background CKD regimen for ≥8 weeks prior to study (RAASi ± SGLT2i, MRA, GLP1, etc.)

➢ **Endpoints**

- Primary: safety, tolerability
- Secondary: uACR, PK
- Exploratory: uPCR

Demographics and Baseline Disease Characteristics

Characteristic	AMKD without diabetes (n=8)	AMKD with diabetes (n=7)	Total AMKD (n=15)[1]
Age — yr	46.4±13.4	52.3±10.3	49.1±12.0
Sex — no. (%)			
Female	4 (50.0)	3 (42.9)	7 (46.7)
Male	4 (50.0)	4 (57.1)	8 (53.3)
APOL1 genotype — no. (%)			
G1/G1	1 (12.5)	2 (28.6)	3 (20.0)
G1/G2	6 (75.0)	3 (42.9)	9 (60.0)
G2/G2	1 (12.5)	2 (28.6)	3 (20.0)
Body Mass Index[2]	32.9±6.0	34.1±8.0	33.4±6.7
uACR (mg/g)[3]	1371.0±946.1	819.7±555.2	1113.7±812.8
uPCR (mg/g)[3]	2046.2±1299.8	1356.5±962.7	1724.3±1169.9
eGFR (mL/min/1.73 m²)[4]	42.2±13.8	41.7±14.4	41.9±13.5
FSGS (biopsy diagnosed) (n)	5	0	5
RAASi + SGLT2i (%)	50	71	60

1. All 15 participants received ≥1 dose; 12 met the ≥80% compliance threshold and were included in the efficacy analysis
2. BMI expressed as kg/m^2; mean ± SD shown
3. uACR / uPCR at baseline was calculated as mean of 3 consecutive first morning voids during screening period; mean ± SD shown
4. eGFR based on CKD-EPI equation

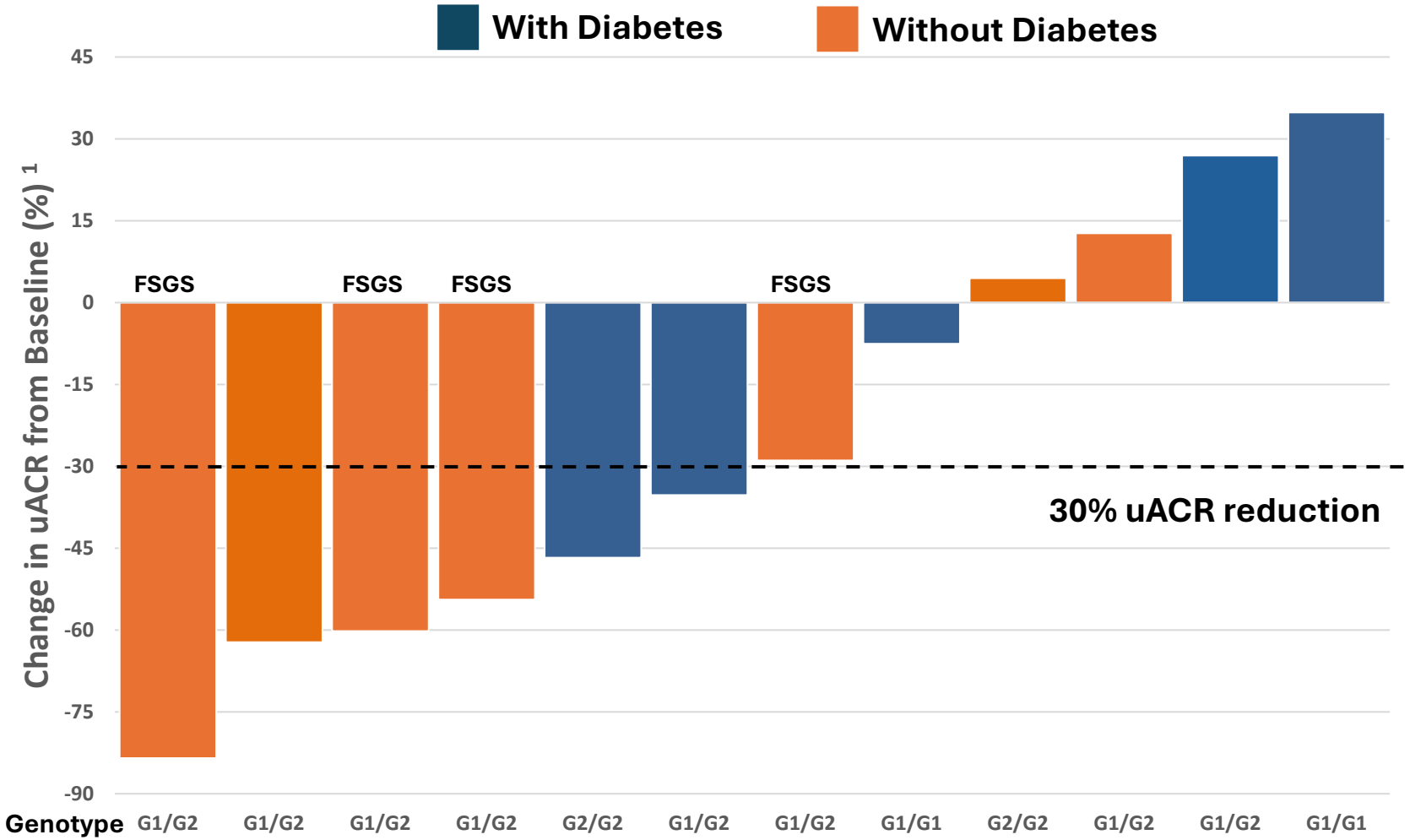
Summary of Safety

AE Category	Non-diabetic AMKD (n=8)	Diabetic AMKD (n=7)	Total AMKD (n=15)
Adverse event	6 (75.0)	4 (57.1)	10 (66.7)
TEAE based on severity	6 (75.0)	4 (57.1)	10 (66.7)
Mild	4 (50.0)	1 (14.3)	5 (33.3)
Moderate	2 (25.0)	2 (28.6)	4 (26.7)
Severe	0	1 (14.3)	1 (6.7)
Treatment-related TEAE	4 (50.0)	1 (14.3)	5 (33.3)
Mild	3 (37.5)	0	3 (20.0)
Moderate	1 (12.5)	1 (14.3)	2 (13.3)
Severe	0	0	0
Serious adverse event	0	0	0
TEAE leading to treatment discontinuation	1 (12.5)	0	1 (6.7)
Most common TRAEs			
Diarrhea	1 (12.5)	1 (14.3)	2 (13.3)
Headache	0	2 (28.6)	2 (13.3)

Safety data includes all patients that received at least one dose and either completed treatment or completed the Week 12 assessment.

- Safety profile generally consistent with that observed in healthy participants in the Phase 1 study
- No SAEs or treatment-related treatment-emergent severe AEs
- Most commonly reported AEs were GI complaints
- No clinically significant changes in labs, 12-lead ECG, vital signs, or physical exam findings

MZE829 demonstrates clinical proof-of-concept in AMKD



<u>Mean uACR Reduction</u>:

Overall: **36%**

FSGS: 62%

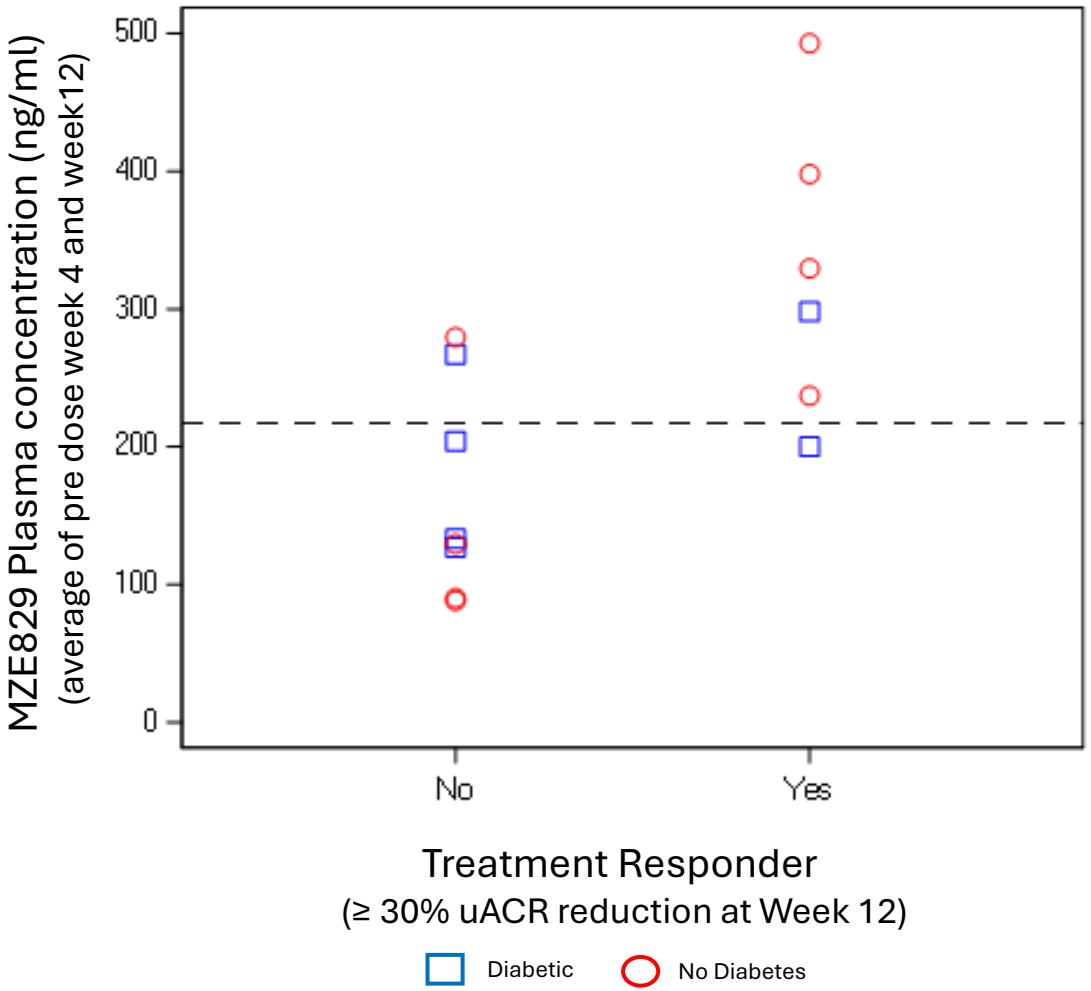
Non-diabetic AMKD: 49%

Diabetic AMKD: 12%

1. uACR at baseline was calculated as mean of 3 consecutive first morning voids during screening period
2. Mean uACR reduction is for the efficacy analysis population (12 of 15)

Plasma trough concentrations, not baseline characteristics, associate with response

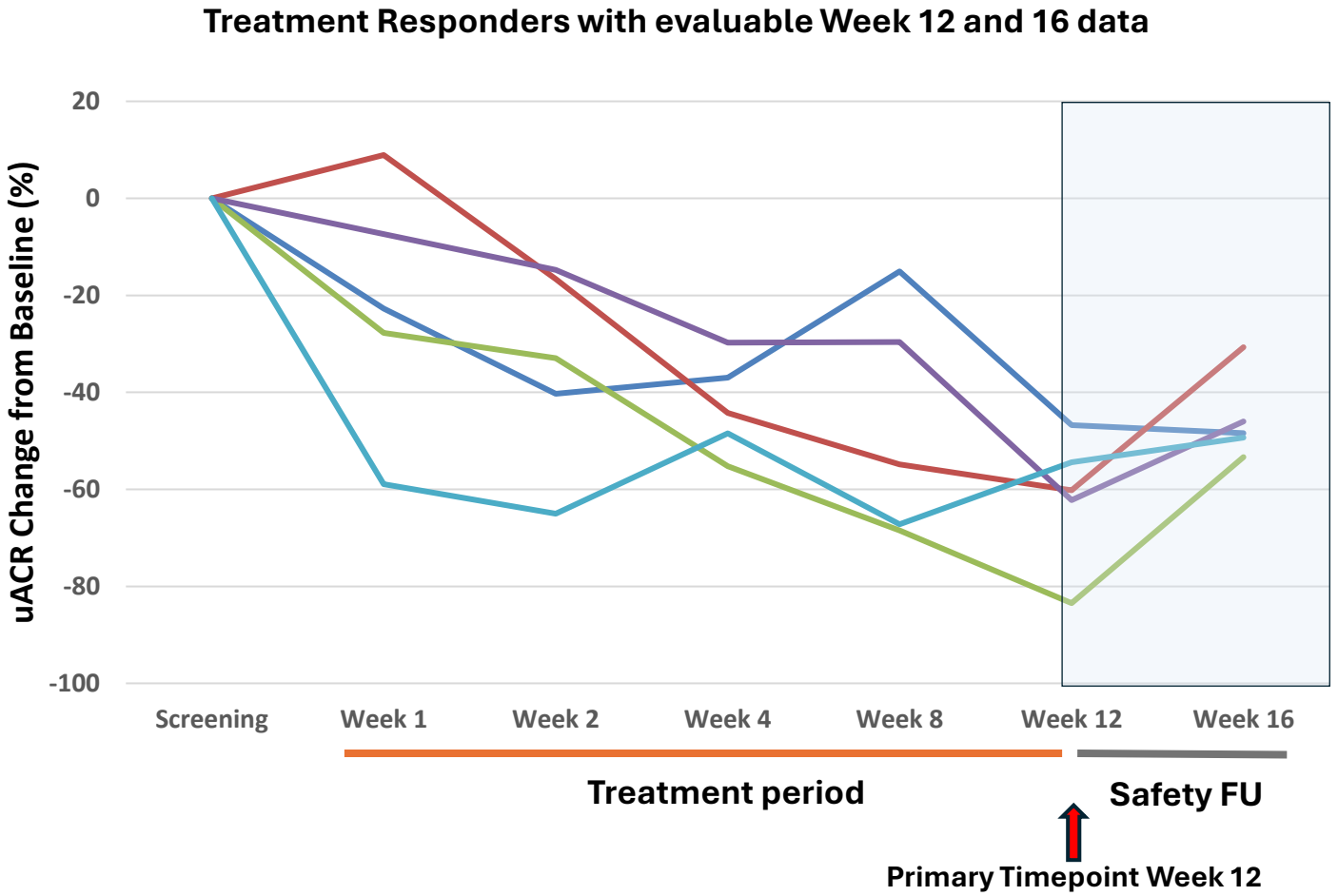
Higher plasma trough concentrations of MZE829 were associated with larger uACR reductions



Baseline disease characteristics did not predict treatment response

- Baseline disease severity as measured by uACR or eGFR does not appear associated with magnitude of uACR reduction
- Aside from PK and FSGS diagnosis, no other variables were found to be associated with treatment responses in this dataset, including
  - BMI
  - total albumin
  - comorbid conditions
  - concomitant medications
  - onset / duration of disease

uACR reduction in treatment responders reverses after end of treatment



- **Progressive uACR reduction through Week 12 (end of dosing)**
- **Trend returning towards baseline after end of treatment period indicates uACR reduction is a treatment effect**

Preliminary findings support further evaluation of MZE829 in AMKD

- **Preliminary analysis in 15 participants** with proteinuric AMKD with and without diabetes
  - Representative population:
    - moderate to severe CKD on at least 2 background CKD medications
    - Over 50% of participants were on combination RAASi and SGLT2i
    - Five biopsy-proven FSGS

- **Safety and tolerability**
  - Generally consistent with safety profile observed in previous Ph1 trial, with GI complaints as the most commonly reported AEs
  - No SAEs or severe TRAEs

- **Efficacy**
  - Data support efficacy of MZE829 in AMKD
  - Higher mean uACR reductions in non-diabetic patients with largest reductions observed in participants with FSGS
  - Individual responses in diabetic patients suggest potential efficacy

Acknowledgement

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