

# Phase 2 Study Design to Evaluate Safety and Efficacy of the Tyrosine Kinase Inhibitor ANG-3070 in Patients with Primary Proteinuric Kidney Disease

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# Disclosures

- Jai Radhakrishnan is a consultant for Angion Biomedica Corp.
- Shakil Aslam and John Neylan are employees of Angion Biomedica Corp. and may own stock/options in the company.
- Dana V. Rizk. serves as a consultant for Angion Biomedica Corp., Calliditas Therapeutics, George Clinical, Novartis, Otsuka Pharmaceuticals, received research funding from Achillion Pharmaceuticals, Calliditas Therapeutics, Otsuka Pharmaceuticals, Pfizer Pharmaceuticals, Reata Pharmaceuticals, Traverre Therapeutics, and has ownership in Reliant Glycosciences LLC.
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# Introduction - Primary Proteinuric Kidney Diseases (1/2)

- Focal segmental glomerulosclerosis (FSGS), and immunoglobulin (Ig)A nephropathy are among the most common primary proteinuric kidney diseases (PPKDs) in pediatric patients and adults
- PPKDs predominantly affect younger patients, significantly reducing quality of life, productivity, and longevity<sup>1,2</sup>
- Persistent proteinuria in patients with primary PPKD is associated with accelerated progression to end-stage kidney disease (ESKD) through induction of inflammation and fibrosis<sup>3-6</sup>
- Fibrosis is characterized by chronic inflammation, increased cellular proliferation, and extracellular matrix deposition in response to tissue injury<sup>3,7-9</sup>

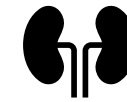
## Treatment and unmet need

- Standard of care (SOC) for symptom management of patients with PPKD includes renin-angiotensin-aldosterone system (RAAS) blockers, most commonly angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs)
- First-line therapy for patients at high risk for ESKD include immunosuppressive and/or cytotoxic agents primarily approved for other indications
  - Long-term treatment with these agents is complicated by their significant dose-limiting toxicity, need for close monitoring, high relapse rates, and drug resistance or dependence
- **There are currently no therapies approved specifically for PPKDs**

# Introduction (2/2)

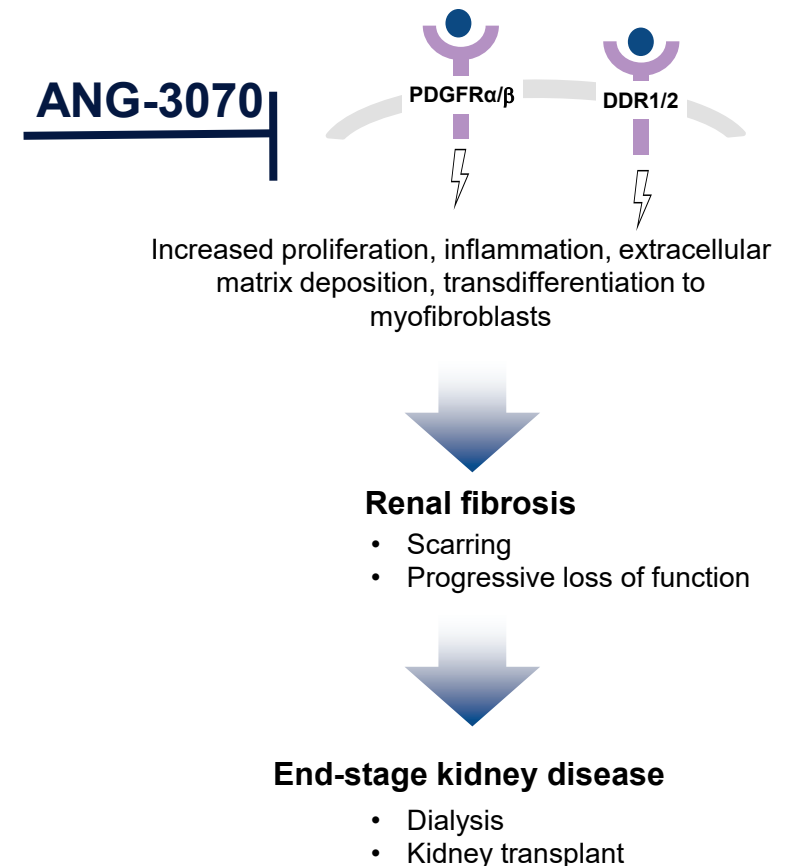
- Receptor tyrosine kinases (RTKs) such as platelet-derived growth factor receptor (PDGFR), and discoidin domain receptor (DDR) play important roles in the pathogenic process of renal fibrosis<sup>10-12</sup>
- ANG-3070 is a selective, oral tyrosine kinase inhibitor targeting PDGFR $\alpha/\beta$ , and DDR1/2
- ANG-3070 has demonstrated beneficial effects in animal models of kidney disease (see Posters PO1408, PO1201, and PO1400)<sup>13</sup>
  - In a Phase 1 study in healthy volunteers (NCT04196179), ANG-3070 had a favorable safety and tolerability profile, with no dose-limiting toxicities, although gastrointestinal side effects increased with dose level<sup>13</sup>
  - A Phase 2 study (NCT04939116) in patients with PPKD is underway

**Objective: To describe the design of the Phase 2, proof-of-concept study of ANG-3070 in the treatment of PPKD patients with persistent proteinuria while on SOC therapy**

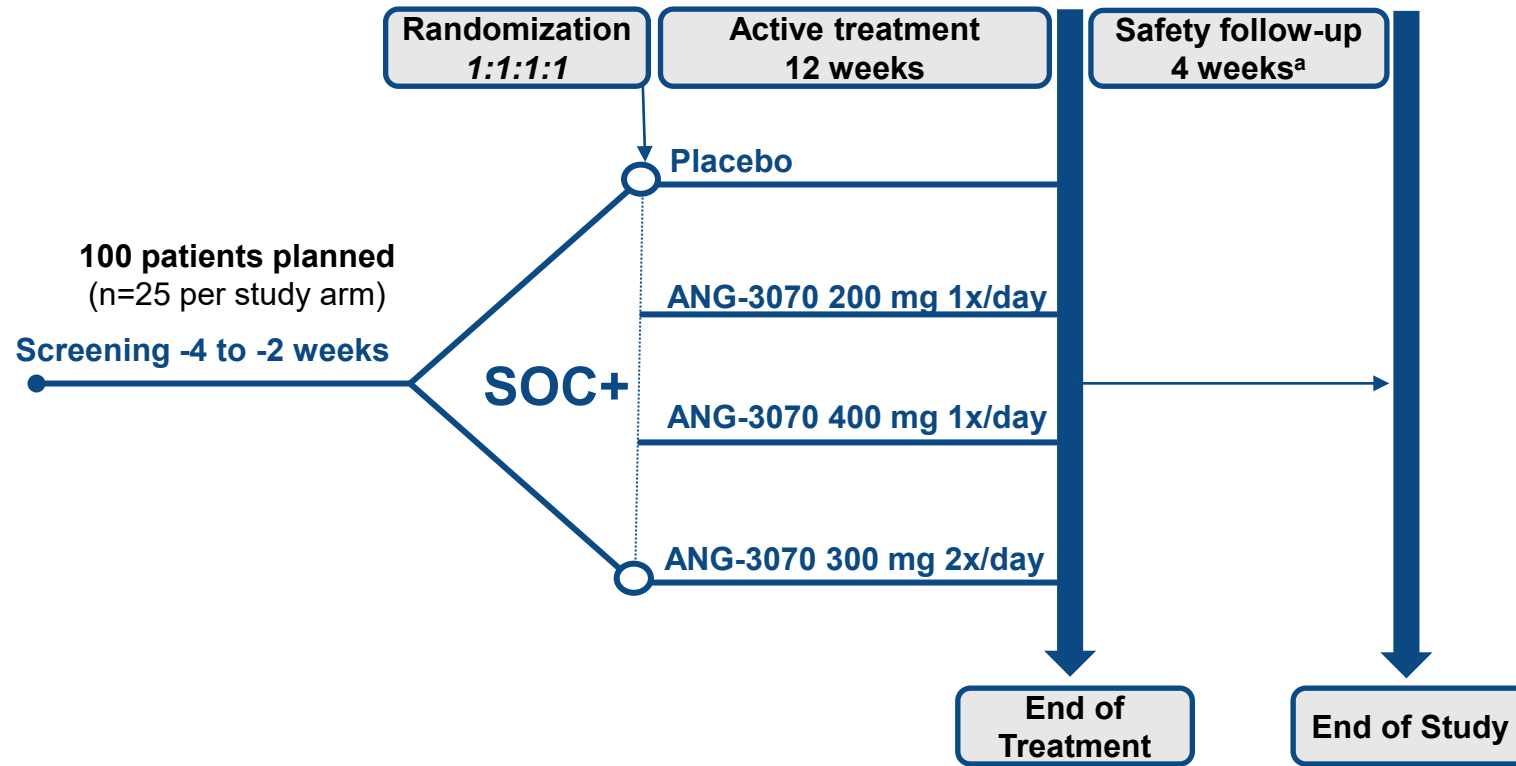


## Primary proteinuric kidney diseases (FSGS, IgA nephropathy, others)

- Proteinuria
- Disrupted glomerular filtration barrier and tissue integrity
- Aberrant tyrosine kinase signaling



# Phase 2, multicenter, double-blind, randomized, placebo-controlled study of safety and efficacy of ANG-3070



- SOC (must be stable for 12 weeks prior to randomization and throughout study period): Maximally tolerated or recommended dose of ACEi or ARB blockers (not both), RAAS blockers and SGLT-2 inhibitors
- All patients will take the study drug within 30 minutes of meals and at least 30 minutes apart from any other drugs
- ANG-3070 will be dosed once daily in the morning or twice daily in morning and evening

# Patient population



## Inclusion criteria

- Male or female participants aged 18 and older on SOC therapy
- Diagnosis of IgA nephropathy or primary FSGS confirmed from a past renal biopsy
- Genetic FSGS without a renal biopsy if the clinical picture is consistent with the genetic testing results
- eGFR by CKD-EPI  $\geq 40$  mL/min/1.73m<sup>2</sup>
- Urinary protein excretion  $\geq 1$  g/day on a 24-hour urine collection

## Exclusion criteria

- AST, ALT, or total bilirubin  $> 2$  x ULN
- HbA1c  $> 8.5\%$
- Hemoglobin  $< 8$  g/dL, or platelets  $< 50,000$ , or absolute neutrophil count  $< 1000$  cells/ $\mu$ L
- Known predisposition to bleeding and/or thrombosis
- Type I diabetes mellitus or histopathological evidence of diabetic kidney disease within 5 years
- Membranous nephropathy
- Renal disease secondary to systemic disease
- Positive HBV, HCV, or HIV viral screening

# Study Endpoints

## Primary

- Percentage change from baseline in 24-hour urinary protein excretion at Week 12

## Exploratory

- Plasma/urine biomarkers
- PK parameters
- ANG-3070 metabolites in plasma and/or urine

## Safety

- Number of AEs
  - SAEs
  - AEs emerging during treatment
  - SAEs and AEs leading to discontinuation of study treatment and within 4 weeks' post-treatment
- Laboratory parameters (hematology, chemistry, hepatic, coagulation, urinalysis), vital signs, electrocardiogram
- Proportion of patients showing an increase in MAP of  $\geq 10$  mm Hg from baseline on at least two visits or requiring the addition of new hypertensive medication or increases in the existing antihypertensive medications

# Statistical and safety analysis

- Sample size was selected to provide an assessment of safety and estimated beneficial effects to guide further clinical development of ANG-3070 in these patients
- For the primary efficacy endpoint, a Mixed Model Repeated Measures (MMRM) analysis will be performed, including treatment group, visit, treatment group by visit, and 24-hour urinary protein excretion value at baseline as covariates
- Safety analyses will include evaluation of the incidence of TEAEs, SAEs, and AEs leading to discontinuation of study treatment



# Conclusions

- There is a significant unmet medical need in patients with PPKDs and persistent proteinuria due to the lack of effective treatments
- Animal data suggest inhibition of the receptor tyrosine kinases PDGFR $\alpha/\beta$  and DDR1/2 have the potential to prevent renal function decline and the progression of CKD to ESKD<sup>1</sup>
- This Phase 2 proof-of-concept study will evaluate safety and efficacy of ANG-3070 in patients with persistent proteinuria on SOC; the first patient will be enrolled in late 2021

**Key Takeaway: This study will test the hypothesis the selective oral tyrosine kinase inhibitor ANG-3070 can reduce proteinuria, a surrogate marker of disease progression, hence informing the Phase 3 study design**