AFFINITY: A Phase 2 Basket Trial to Study the Safety and Efficacy of Atrasentan in Multiple Proteinuric Diseases

Marianne Camargo, MD, MSCR
Senior Medical Director
March 3, 2022

CHINOOK THERAPEUTICS

Chinook is a clinical-stage biopharmaceutical company discovering, developing and commercializing precision medicines for rare, severe chronic kidney diseases

Chinook's Commitment to Kidney Disease Drug Development

Advancing pipeline of precision medicines for kidney diseases

Program	Indication	Target Validation	Lead Optimization	IND-Enabling	Phase 1	Phase 2	Phase 3
Atrasentan	IgA Nephropathy	Phase 3 enrollment commenced in early 2021					
	Basket of glomerular diseases	Phase 2 enrollment commenced in early 2021					
BION-1301	IgA Nephropathy	Phase 1/2 ongoing					
CHK-336	Primary Hyperoxaluria	Ph1 initiation planned in for H1 2022					
Research Programs	Other rare, severe chronic kidney diseases						
Discovery Programs	Other rare, severe kidney diseases						

We continue to evaluate opportunities to add additional kidney disease programs to pipeline

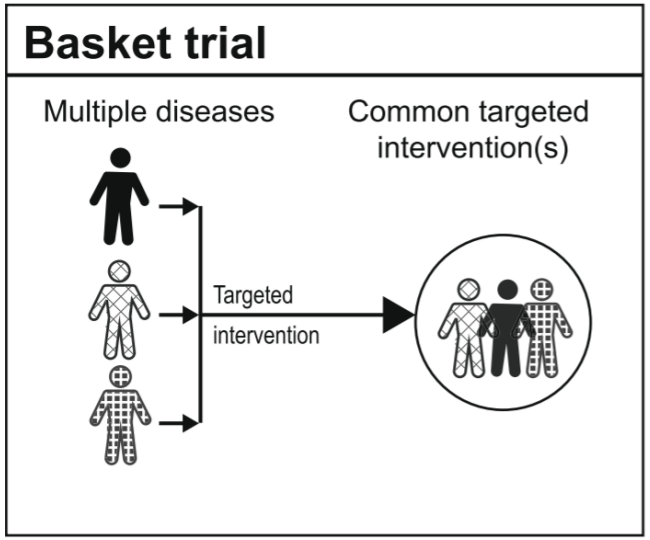
CHINOOK THERAPEUTICS

Modernization of Drug Development in Nephrology

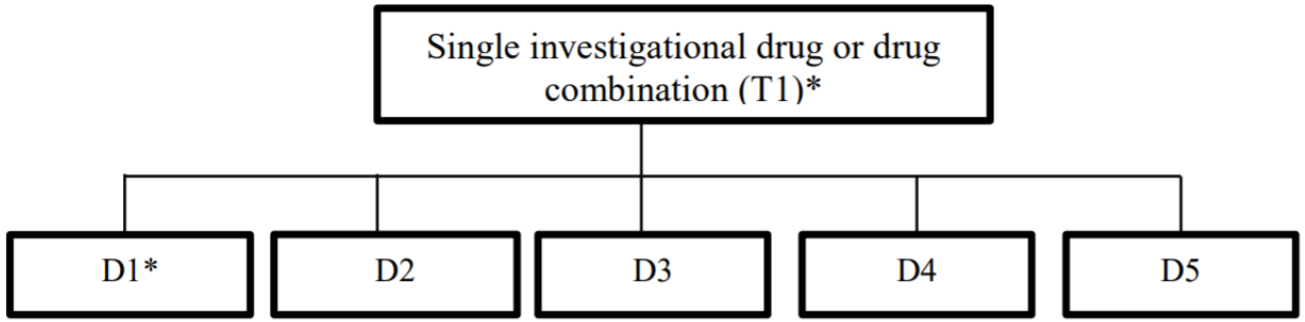
- Use of clinical trials with **master protocols**, a modern approach to expedite drug development
- Master protocols (basket trials, umbrella trials and platform trials) are novel designs that have the potential to explore multiple hypotheses through concurrent sub-studies
- The oncology field has pioneered these novel study designs
- A Basket Trial involves a single investigational drug (or drug combination) that is studied across multiple disease populations (can be defined by stage, histology, number of prior therapies, genetic or other biomarkers, demographic characteristics, etc.)

Advantages of Basket Trials

- Ideal for studying multiple diseases that have a common target
- Leverages the efficiency of one master protocol and one study system infrastructure
- The sub-studies within basket trials are usually designed as single-arm activity-estimating, in nephrology likely looking at proteinuria reduction or eGFR
- Each sub-study may have different objectives and endpoints



Park, J.J.H., Siden, E., Zoratti, M.J. *et al Trials* **20,** 572 (2019)



* T = investigational drug; D = protocol defined subpopulation in multiple disease subtypes.

Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics Guidance for Industry, FDA Draft Guidance 2018

Park, J.J.H., Siden, E., Zoratti, M.J. *et al.* Systematic review of basket trials, umbrella trials, and platform trials: a landscape analysis of master protocols. *Trials* **20,** 572 (2019). https://www.fda.gov/media/120721/download

CHINOOK THERAPEUTICS

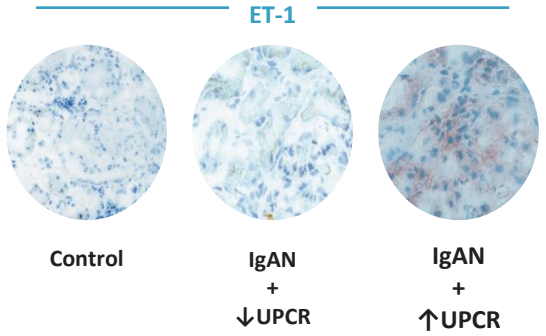
Atrasentan in a Basket Trial for Treatment of Glomerular Diseases

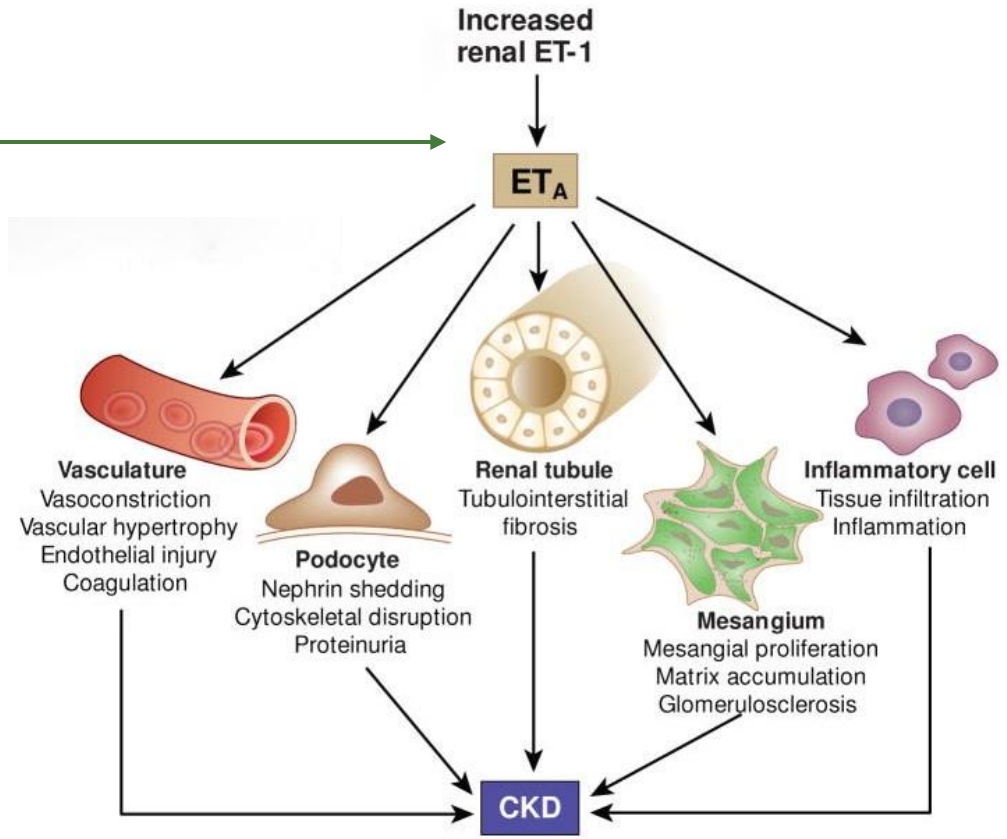
Atrasentan: An Investigational Potent and Selective ET_A Antagonist

ET_A Activation Drives Proteinuria Progression through Multiple Potential Mechanisms

ET_A receptor activation drives proteinuria, mesangial cell activation & kidney inflammation & fibrosis, all hallmarks of glomerular diseases

Intense kidney ET-1 & ET_A receptor immunostaining in IgAN patients with significant proteinuria





Proteinuria Inflammation & Fibrosis

ET system activation appears to be a key molecular determinant of the clinical course in glomerular diseases

Elevated kidney ET-1 expression strongly & prospectively predicted progression of IgAN, 12 months following kidney biopsy

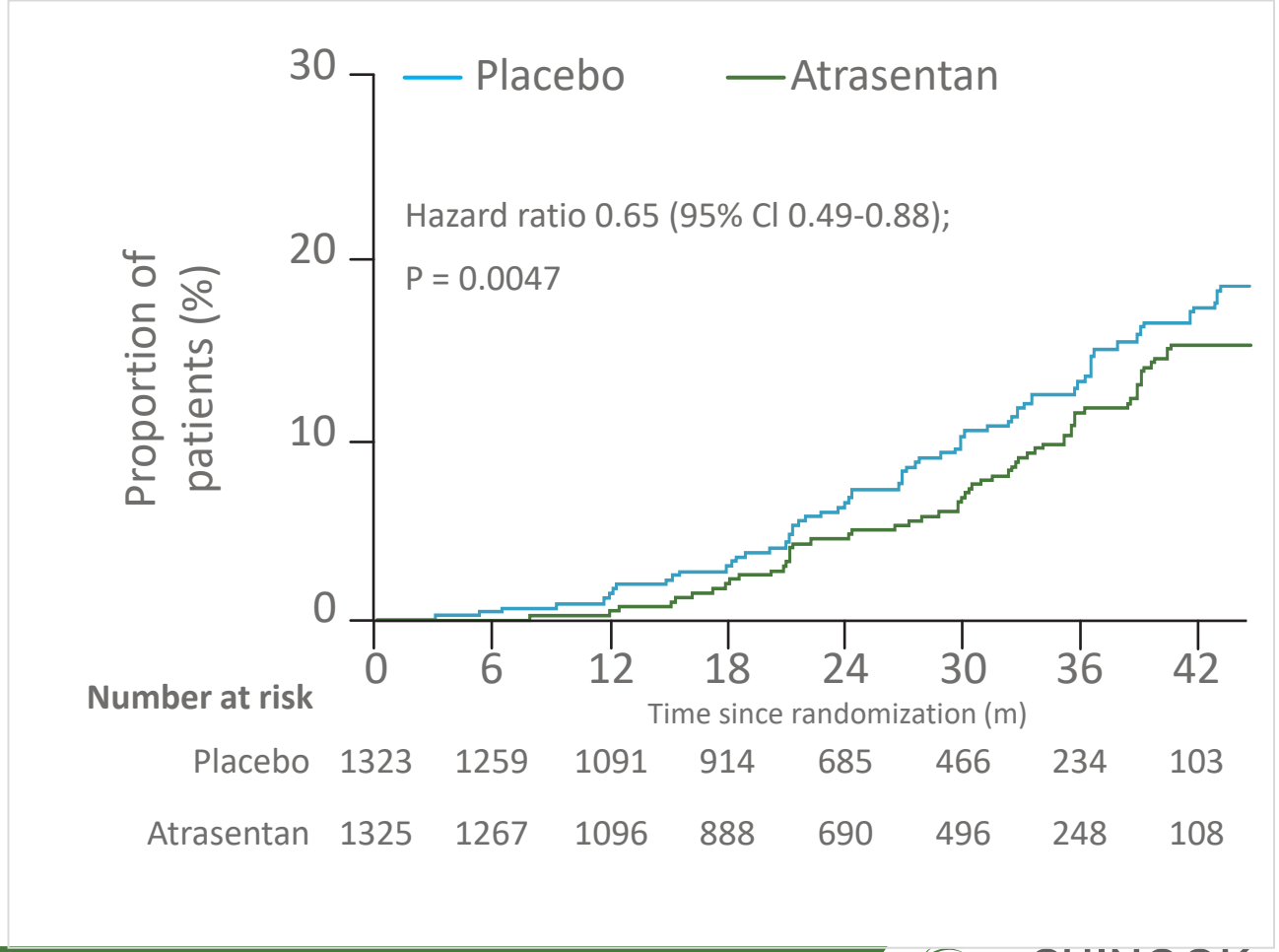
Blockade of the ET_A receptor through atrasentan represents a promising approach to treat glomerular disease

Tycova et al. Physiol. Res. 67: 93-105, 2018; Lehrke et al. J Am Soc Nephrol 2001 12: 2321–2329; Zanatta et al, Renal Failure, 2012, 34: 308–315; Kohan DE et al., Kidney Int. 2014

Topline Results from SONAR

Atrasentan and renal events in patients with type 2 diabetes and chronic kidney disease: a double-blind, randomized, placebo-controlled trial

- **3600** high-risk patients with DKD randomized
- **2** Years median treatment duration
- **35%** decreased risk of ESKD or doubling of serum creatinine in responders* (28% in all randomized)
- **27%** risk reduction of End Stage Kidney Disease
- **39%** risk reduction of doubling of serum creatinine

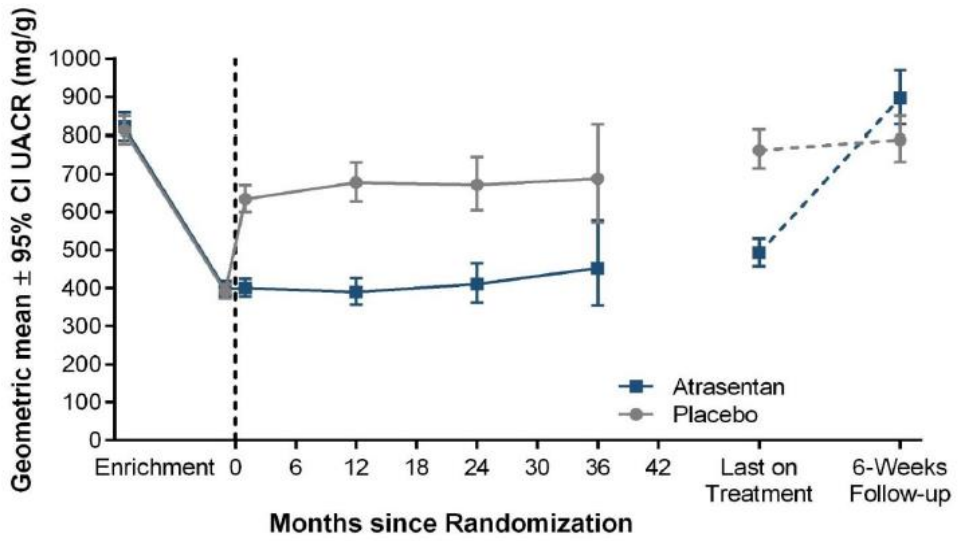


Heerspink et al, Diabetes Obes Metab. 2018;20:1369–1376, Heerspink et al, SONAR Trial, Lancet 2019

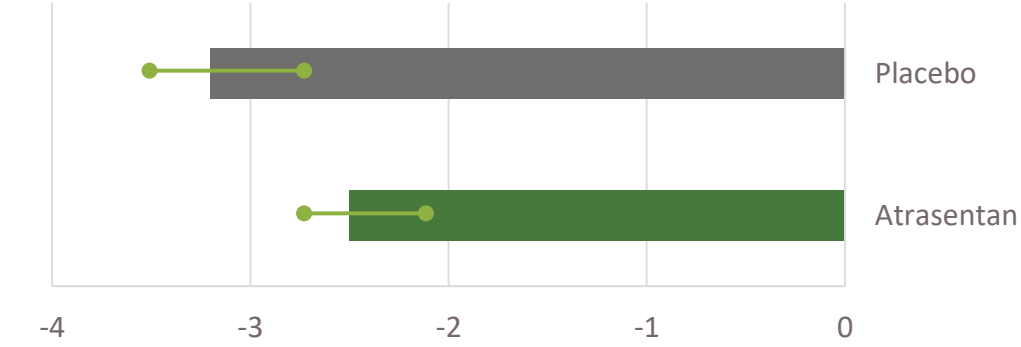
SONAR Outcomes Supportive of Success in Other Proteinuric Glomerular Diseases

Proteinuria reduction is recognized as an important surrogate endpoint in glomerular diseases

Proteinuria (UACR)*



Kidney Function (eGFR Slope)*



-2.4 ml/min/1.73m²/yr (95%CI -2.7 to -2.1)
-3.1 ml/min/1.73m²/yr (95%CI -3.4 to -2.8) **p=0.0005**

*In Responders (patients who achieved >30% reduction in proteinuria)

Heerspink et al, Diabetes Obes Metab. 2018;20:1369–1376, Heerspink et al, SONAR Trial, Lancet 2019

CHINOOK THERAPEUTICS

AFFINITY: A Basket Trial of Glomerular Diseases

AFFINITY Study Overview

Study Objective

- The Phase 2 AFFINITY study assesses the efficacy and safety of atrasentan in patients with proteinuric glomerular diseases at risk of progressive kidney function loss

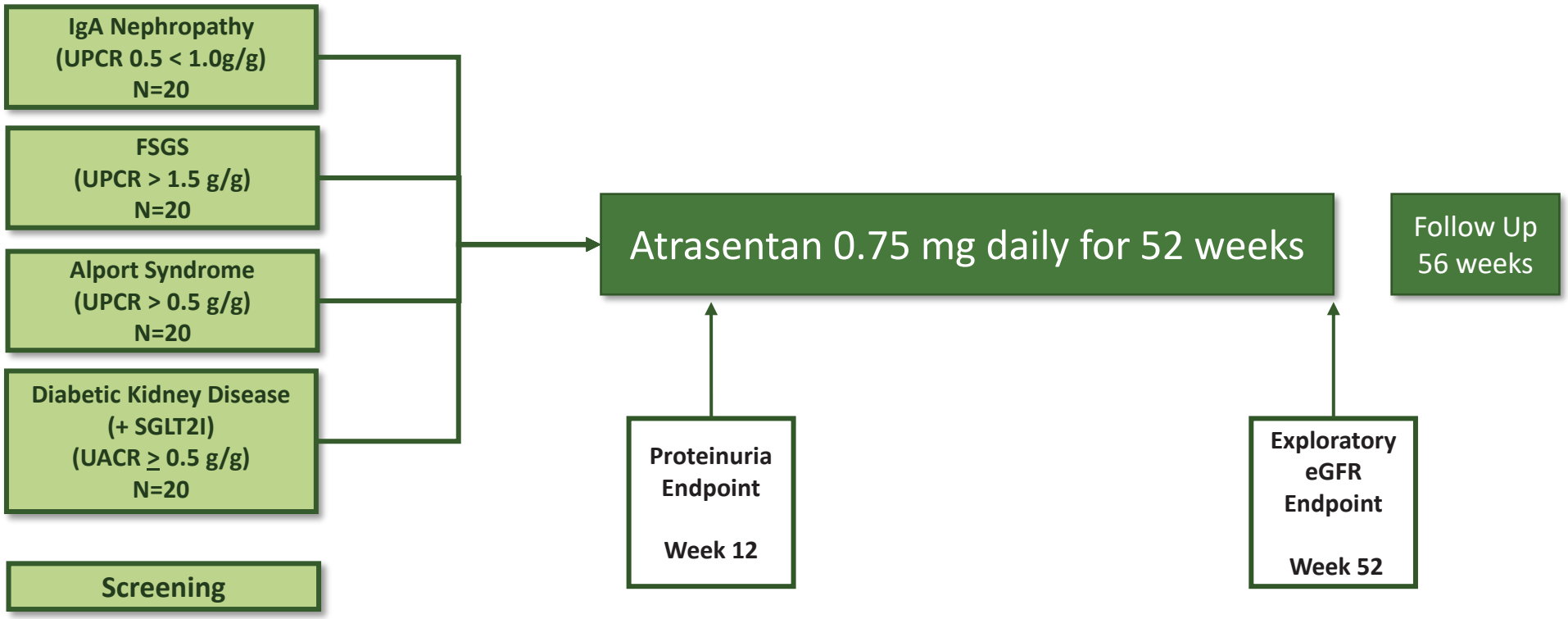
Study Design

- Approximately 80 patients (~20 per cohort) in the United States, Australia, South Korea, Italy, Spain and the United Kingdom with the following proteinuric glomerular diseases will receive 0.75 mg atrasentan for 52 weeks:
    - Cohort 1: IgAN
    - Cohort 2: FSGS
    - Cohort 3: Alport Syndrome
    - Cohort 4: DKD (on stable dose of SGLT2i)
- Patients must be on a maximally tolerated and stable dose of a RASi
- Where allowed by local regulations, options for remote study visits using telemedicine and home health may be offered
- Provides a flexible solution for patients and clinicians in the era of COVID-19 and reduces the burden to patients for trial participation

Methods

Study Objective

- AFFINITY is a global, phase 2, open label basket study to assess the efficacy and safety of atrasentan in patients with proteinuric glomerular diseases at risk of progressive kidney function loss



*All cohorts eGFR ≥30 ml/min/1.73m^2, except for DKD ≥ 45 ml/min/1.73m^2

AFFINITY Study Overview

Study Endpoints

- The primary endpoint is change in proteinuria from baseline at Week 12:
  - Cohort 1-3: UPCR from a 24-hr urine collection
  - Cohort 4: UACR from a First Morning Void
- Additional outcome measures include:
  - Evaluate atrasentan plasma concentration over time
  - Cohort 1: Percent of subjects achieving proteinuria reduction to less than 0.3 g/day
  - Cohort 2: Percent of subjects achieving UPCR < 1.5 g/g and > 40% reduction from baseline
  - Cohort 1-4: Change from baseline to Week 52
  - Cohort 1-4: Change from baseline in estimated glomerular filtration rate (eGFR) at Week 56

Inclusion Criteria, IgA Nephropathy

Subjects must meet ALL inclusion criteria to be enrolled

Types of Subjects and Disease Characteristics

Cohort 1- IgAN

Biopsy-proven IgAN that, in the opinion of the Investigator, is not due to secondary causes

- Biopsy could have occurred at any point in time prior to study
- A diagnostic report must be available for review by the Sponsor or designee

Receiving a maximally tolerated and optimized dose of a RAS inhibitor that has been stable for at least 12 weeks prior to screening

UPCR ≥ 0.5 and < 1.0 g/g (≥ 500 mg/g and < 1000 mg/g) based on a central laboratory assessment of first morning void urine collected at screening

eGFR ≥ 30 mL/min/1.73 m^2

Inclusion Criteria, FSGS

Subjects must meet ALL inclusion criteria to be enrolled

Types of Subjects and Disease Characteristics

Cohort 2- FSGS

Biopsy-confirmed FSGS or documentation of a genetic mutation in a podocyte protein associated with FSGS

UPCR > 1.5 g/g (>1500 mg/g) based on a central laboratory assessment of first morning void urine collected at screening

eGFR ≥ 30 mL/min/1.73 m^2

Receiving a maximally tolerated and optimized dose of a RAS inhibitor that has been stable for at least 12 weeks prior to screening

If receiving systemic corticosteroids or calcineurin inhibitors, dose (level) must be stable for 12 weeks prior to start of study drug and anticipated to remain on a stable dose at least through week 12

Body Mass Index (BMI) ≤ 40 kg/m^2

Inclusion Criteria, Alport Syndrome

Subjects must meet ALL inclusion criteria to be enrolled

Types of Subjects and Disease Characteristics

Cohort 3- Alport syndrome

Diagnosis of Alport syndrome by genetic testing (documented mutation in a gene associated with Alport syndrome, including COL4A3, COL4A4, or X-linked COL4A5 in the subject or a family member) OR patients with a new mutation that, in the opinion of the Investigator, has significant supporting evidence of Alport syndrome (biopsy, familial genetics, family history & familial biopsy, microscopic hematuria, hearing loss pattern, fleck retinopathy)

UPCR > 0.5 g/g (>500 mg/g) based on a central laboratory assessment of first morning void urine collected at screening

Receiving a maximally tolerated and optimized dose of a RAS inhibitor that has been stable for at least 12 weeks prior to screening

eGFR ≥ 30 mL/min/1.73 m^2

Inclusion Criteria, DKD

Subjects must meet ALL inclusion criteria to be enrolled

Types of Subjects and Disease Characteristics

Cohort 4- DKD

Clinical diagnosis of type 2 diabetes mellitus (T2DM) as per guidelines

Diagnosis of DKD based on the opinion of the investigator, including the presence of the following criteria:

a. **UACR ≥ 0.5 g/g (500 mg/g) based on a central laboratory assessment of first morning void urine collected at screening**
b. **eGFR ≥ 45 mL/min/1.73 m^2**

Receiving a maximally tolerated and optimized dose of a RAS inhibitor that has been stable for at least 12 weeks prior to the screening visit and stable dose of SGLT2 inhibitor for at least 12 weeks prior to screening

Main Exclusion Criteria

Subjects must meet NONE of the following exclusion criteria to be enrolled
Concurrent diagnosis of another cause of chronic kidney disease including diabetic kidney disease or another primary glomerulopathy
Clinical suspicion of rapidly progressive glomerulonephritis (RPGN) based on KDIGO guidelines or clinical suspicion of IgA vasculitis (Henoch-Schonlein Purpura)
Known history of congestive heart failure, diastolic dysfunction, or prior hospital admissions for conditions relating to fluid overload such as pulmonary edema, uncontrolled peripheral edema, pleural effusion, or ascites
Confirmed blood pressure >150 mmHg systolic or >95 mmHg diastolic based on a mean of 3 measurements obtained at screening
With the exception of DKD (Cohort 4), use of an SGLT2 inhibitor within the past 30 days
HbA1c > 9.5% in Cohort 4 (DKD), HbA1c > 7.0% in Cohorts 1-3
Except for Cohort 2 (FSGS), use of systemic immunosuppressant medications including systemic steroids (prednisone or equivalent >10 mg/day for more than 2 weeks within 3 months prior to screening), mycophenolate, azathioprine, cyclosporine, tacrolimus, etc. for more than 2 weeks within the past 3 months prior to screening

CHINOOK THERAPEUTICS

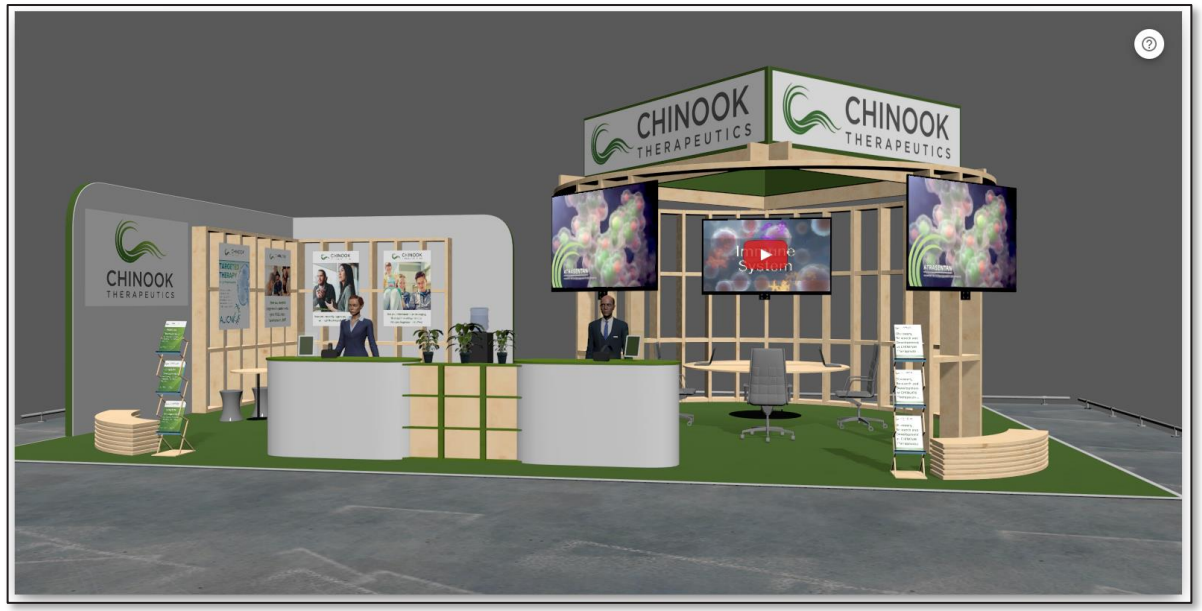
Chinook plans to present data from the IgAN patient cohort of the AFFINITY study in the first half of 2022!

Stay tuned!

Chinook Booth at the 59th ERA Congress

The 59th ERA Congress will take place on **May 19-22, 2022**, both virtual and live in Paris

Visit Chinook at our exhibit booth!



Join Us in our Mission to Discover and Develop Precision Therapies for Patients with Kidney Diseases

Contact us if you would like to learn more about any of our trials, would like to refer a patient or are interested in becoming one of our investigators!

mcamargo@chinooktx.com

CHINOOK
THERAPEUTICS