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KIDNEY WEEK 2022 Nov. 3–6 | Orlando, FL

Chinook Therapeutics

Changing the Course of Kidney Care

ASN Kidney Week 2022
Investor Presentation

November 4, 2022

Note Regarding Forward-Looking Statements

Certain of the statements made in this presentation are forward looking, including those relating to Chinook's business, future operations, advancement of its product candidates and product pipeline, clinical development of its product candidates, including expectations regarding timing of initiation and results of clinical trials and sufficiency of its cash resources. In some cases, you can identify these statements by forward-looking words such as "may," "will," "continue," "anticipate," "intend," "could," "project," "expect" or the negative or plural of these words or similar expressions. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, our ability to develop and commercialize our product candidates, whether results of early clinical trials or preclinical studies will be indicative of the results of future trials, our ability to obtain and maintain regulatory approval of our product candidates, our ability to operate in a competitive industry and compete successfully against competitors that may be more advanced or have greater resources than we do, our ability to obtain and adequately protect intellectual property rights for our product candidates and the effects of COVID-19 on our clinical programs and business operations. Many of these risks are described in greater detail in our filings with the SEC. Any forward-looking statements in this presentation speak only as of the date hereof. Chinook assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this presentation.

Today's Presenters

Eric Dobmeier
President & CEO

Andrew King, DVM, PhD
Chief Scientific Officer

Charlotte Jones-Burton, MD, MS
SVP, Product Development & Strategy

Sreedhar A. Mandayam, MD, MPH, MBA, FASN
Professor of Nephrology at the University of Texas MD Anderson Cancer Center and Baylor College of Medicine

Laura Kooienga, MD
Practicing Nephrologist and Director of Research at Colorado Kidney Care

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Opening Remarks

Agenda

Introduction		Eric Dobmeier
TH-PO497	Atrasentan for the Treatment of IgA Nephropathy: Interim Results from the AFFINITY Study	Dr. Sreedhar A. Mandayam
FR-PO659	Updated Interim Results of a Phase 1/2 Study of BION-1301 in Patients with IgA Nephropathy	
BION-1301 PI Perspective		Dr. Laura Kooienga
FR-PO334	Preclinical Efficacy of CHK-336: A First in Class, Liver-Targeted, Small Molecule Inhibitor of Lactate Dehydrogenase for The Treatment of Primary Hyperoxalurias	Dr. Andrew King
TH-PO419	Single Nuclei RNA-seq Reveals Cell-type Specific Responses to Disease and Enalapril in the gddY Mouse Model of IgAN	
FR-OR60	A Multi-Omics Approach to IgA Nephropathy Characterization in the NURTuRE Cohort Enables Precision-Based Treatment Approaches	
Atrasentan Program Update		Dr. Charlotte Jones-Burton
BION-1301 Program Update		
Closing		Eric Dobmeier
Q&A		

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AFFINITY

Atrasentan for the Treatment of IgA Nephropathy: Interim Results from the AFFINITY Study

Anjay Rastogi[1], Michelle N. Rheault[2], Sung Gyun Kim[3], Nam D. Vo[4], Dwarakanathan Ranganathan[5], Lesley A. Inker[6], David K. Packham[7], Mark Vishnepolsky[8], Khushboo Sheth[9], Todd DeVries[9], Marianne Camargo[9], Andrew J. King[9], Charlotte Jones-Burton[9], Muh Geot Wong[10]

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Presented at ASN Kidney Week, November 3 2022, TH-PO497
(adapted from poster)
Data cut-off October 19, 2022

Atrasentan is an investigational agent and has not been approved for any uses in patients.

Speaker Disclosures

Grant Funding:	Akebia, CareDx, Horizon
Consultant:	Alexion, Chinook, Horizon, Sanofi, Travere
PI on IgAN trials:	Alexion, Chinook, Novartis, Omeros, Otsuka, Travere, Vera, Visterra
Speaker Bureau:	Alexion, Bayer, Otsuka, Natera
Ownership:	Prolato Clinical Research Center, Medingenii Capital, Prosalus Capital

Background

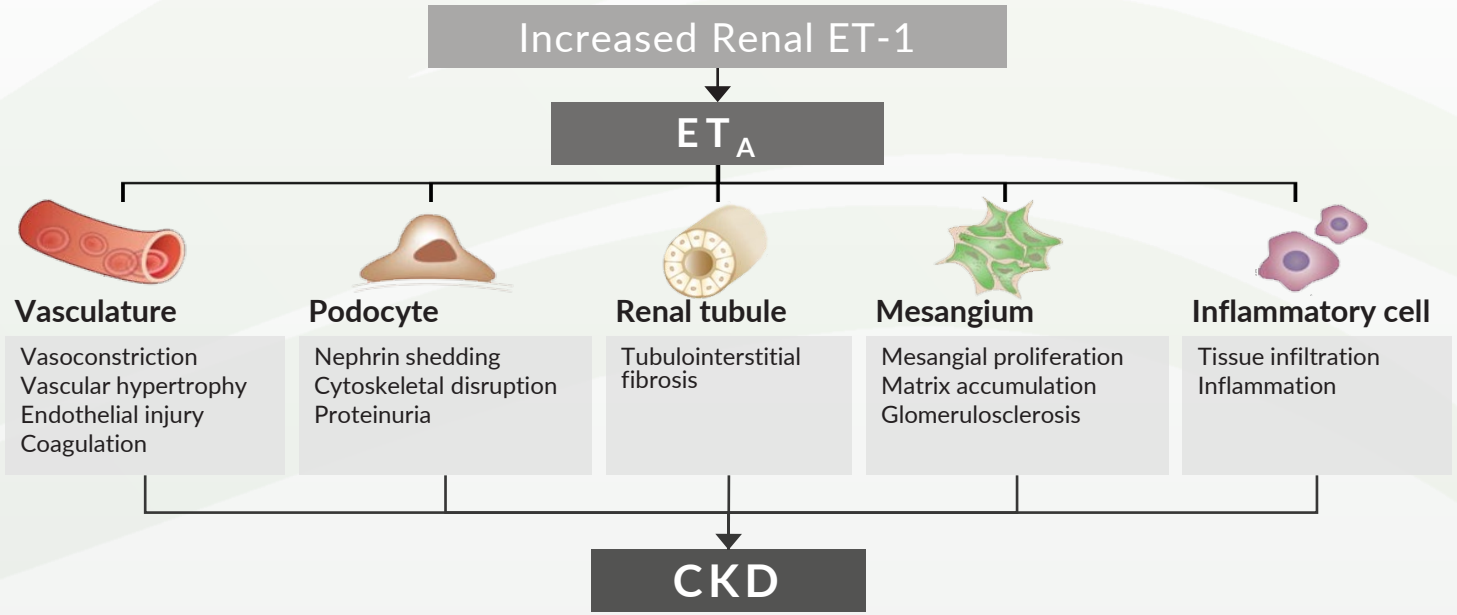
IgA Nephropathy (IgAN)

- IgAN is the leading cause of primary glomerulonephritis, with a global incidence of 2.5 per 100,000 individuals per year[1]
- Approximately 30-45% of IgAN patients progress to end-stage kidney disease (ESKD) over a period of 20-25 years[2-5]
- Proteinuria is strongly associated with kidney disease progression in IgAN[2,6-7] and treatments that reduce proteinuria result in improved clinical outcomes in IgAN[8-9]

Endothelin System Activation in IgAN

Endothelin (ET-1) is a key contributor to progression of IgA nephropathy

- Elevated kidney ET-1 expression strongly & prospectively predicts progression of IgAN 12 months following kidney biopsy[10]
- Endothelin A (ETA) receptor activation drives mesangial cell activation, kidney inflammation & fibrosis, and proteinuria, all hallmarks of IgAN[11-12]
- Kidney ET-1 & ETA receptor levels are elevated in proteinuric patients with IgAN[13-14]



1. Mcgrogan et al, 2011, NDT; 2. Reich et al, 2007, JASN; 3. Moriyama et al, 2014, PLOS ONE; 4. Rauen et al, 2020, Kidney Int; 5. Hastings et al, 2018, Kidney Int Rep; 6. Thompson et al, 2019, CJASN; 7. Barbour et al, 2019, JAMA Int Med; 8. Inker et al 2016 AJKD; 9. Inker et al, 2019, CJASN; 10. Tycova et al, 2018, Physiol Rev; 11. Kohan et al, 2014, Kidney Int; 12. Raina et al 2020 Kidney Dis; 13. Lehrke et al, 2001, JASN; 14. Zanatta et al, 2012, Renal Failure

AFFINITY Study Design

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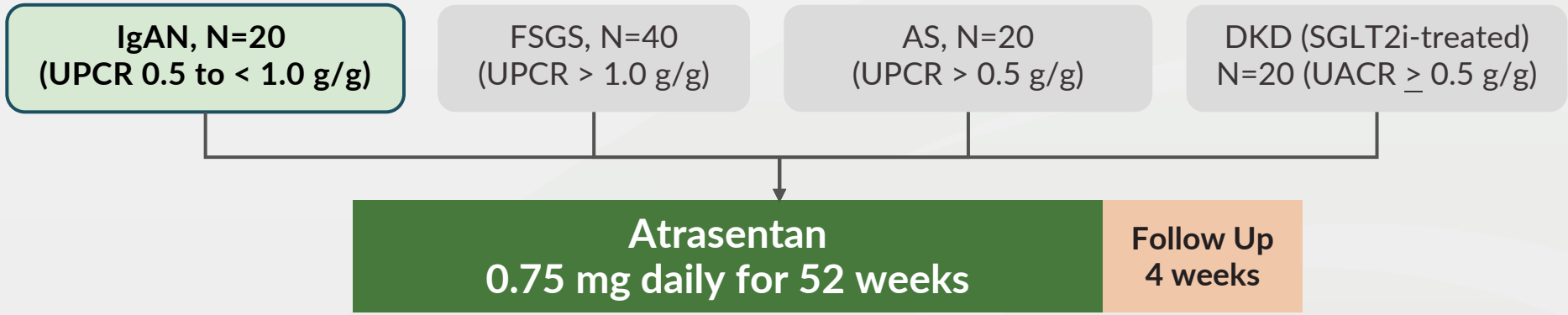
AFFINITY is a global, phase 2, open label basket study to assess the efficacy and safety of atrasentan in patients with proteinuric glomerular diseases (IgAN, focal segmental glomerulosclerosis [FSGS], Alport syndrome [AS], and DKD) at risk of progressive kidney function loss (NCT04573920)



Key Eligibility Criteria: IgAN Cohort

- Biopsy-proven IgAN
- Maximally-tolerated and optimized dose of a RAS inhibitor (RASi) for ≥ 12 weeks prior to screening
- UPCR of 0.5 to < 1.0 g/g (56.5 mg/mmol to <113 mg/mmol) based on first morning void urine collected at screening
- eGFR ≥ 30 mL/min/1.73 m^2

Key Study Endpoints

- Change from baseline at week 12 in UPCR, based on average of two 24-hour collections
- Analysis based on an MMRM model of change from baseline in UPCR
- Adverse Event (AE) type, incidence, severity, seriousness and relatedness

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Baseline and Safety

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AFFINITY IgAN Cohort

- The AFFINITY IgAN cohort enrolled 20 patients with biopsy-confirmed IgAN
- All patients received concurrent, max-tolerated and optimized RASi at least 12 weeks prior to study and throughout the study period
- 70% of patients had baseline total urine protein >1 g/day despite optimized RASi treatment, representing an IgAN population at high risk for progression
- Mean treatment duration was 45 weeks (range 13-53 weeks) as of data cut-off October 19, 2022

Demographics, N=20	
Age, years, *median (Q1,Q3)*	45 (35, 58)
Women, *n (%)*	10 (50)
Race, *n (%),* **Asian**	9 (45)
White	9 (45)
Other	2 (10)
Baseline Characteristics	***Median (Q1, Q3)***
Time from biopsy, years	3.9 (0.9, 11.8)
Blood pressure (mmHg) – Systolic	128 (116, 132)
– Diastolic	82 (77, 86)
BMI	26.2 (24.8, 29.2)
Brain Natriuretic Peptide (pg/mL)	12.5 (8.8, 42.0)
UPCR (g/g), First morning void at screening	0.6 (0.5, 0.7)
24-hour UPCR (g/g)	0.8 (0.7, 1.1)
24-hour urine protein excretion (g/day)	1.2 (0.9, 1.5)
Urine protein excretion (g/day) ≥ 1, n (%)	14 (70)
eGFR (mL/min/1.73 m^2) §	46 (37, 74)
Concurrent RASi, n (%)	20 (100)
ACEi	8 (40)
ARB	12 (60)

§ eGFR by CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration

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Safety and Tolerability

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- Atrasentan was generally well-tolerated with no treatment-related severe AEs to date
- One treatment-emergent AE (headache) led to study withdrawal

AE Category (N=20)		n (%)
Treatment emergent AEs (TEAEs), Severe AEs	Subjects with any TEAE	16 (80)
	Any TEAE occurring in N>1 subjects	
	COVID-19	7 (35)
	Dizziness	3 (15)
	Peripheral edema	2 (10)
	Headache	2 (10)
	Any Moderate TEAE	6 (30)
	Any Severe TEAE	0 (0)
	TEAE leading to discontinuation (headache)	1 (5)
	Serious AE (traffic accident unrelated to study drug)	1 (5)
Treatment-related AEs	Any treatment-related AE	5 (25)
	Moderate related AEs	3 (15)
	Headache	1
	Creatinine increase/Renal impairment	1
	Peripheral edema	1

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No Evidence of Significant Fluid Retention

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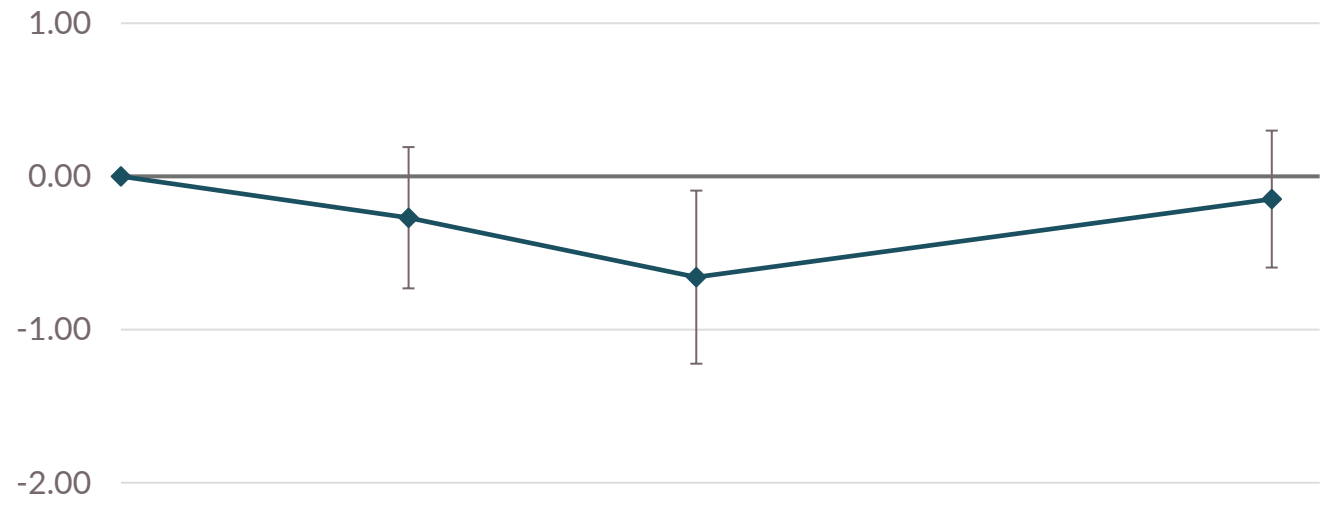
- No increase in mean body weight
- No significant elevation in BNP (median change of 2.9 pg/mL at week 12)
- No meaningful change in systolic or diastolic BP
- Minimal acute change in eGFR (0.15 mL/min/1.73 m2 averaged across Weeks 2 and 6)

Body Weight
Mean Change from Baseline ± SE (kg)



Wk	0	6	12	24
N	20	20	20	20

Data cut-off Oct. 19, 2022

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Proteinuria Reduction in Patients with IgAN

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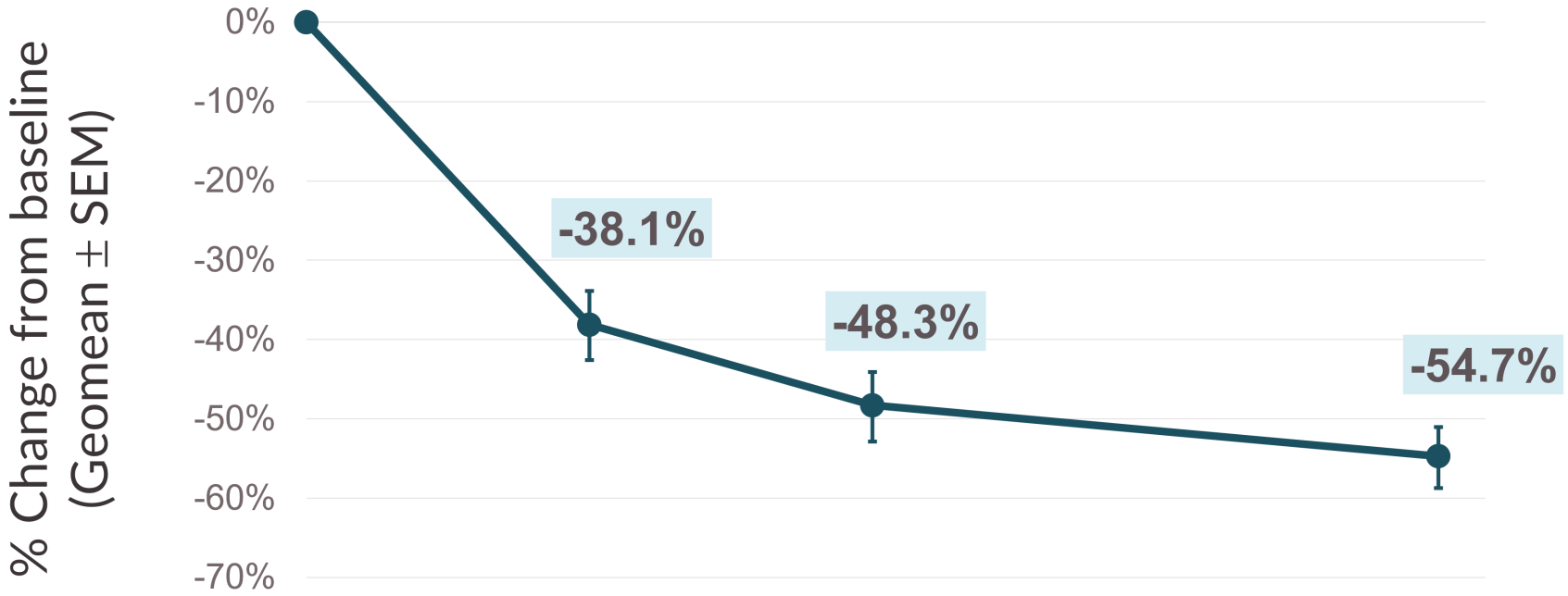
% Reduction in UPCR

Data cut-off Oct. 19, 2022



Wk	0	6	12	24
N	20	20	20	19

Median (range) baseline protein excretion: 1.2 (0.9, 1.5) g/day

Proteinuria Reduction in Patients with IgAN

Treatment with atrasentan results in a durable and clinically meaningful proteinuria reduction in patients with IgAN receiving optimized standard-of-care

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Proteinuria Reduction in Patients with IgAN

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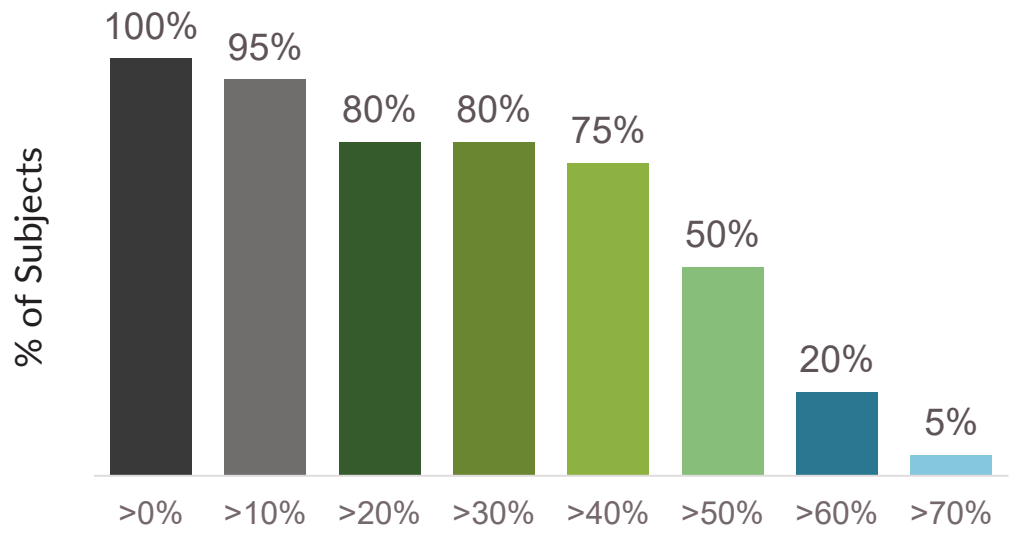
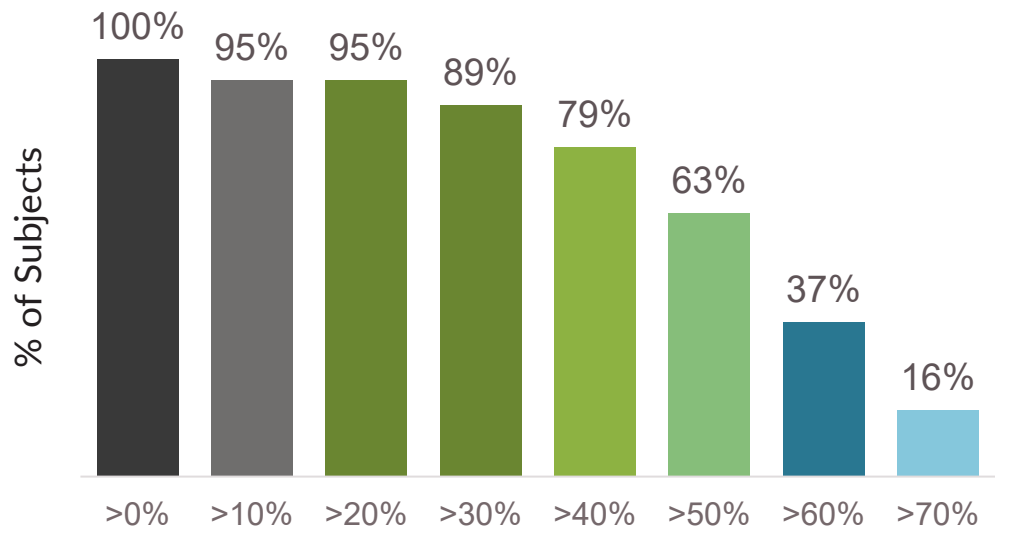
79% of patients achieved >40% reduction in proteinuria at Week 24

Week 12 (n=20)
UPCR Cumulative % Reduction



Week 24 (n=19)
UPCR Cumulative % Reduction



Data cut-off Oct. 19, 2022

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Summary/Conclusion

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In this Phase 2 study of 20 patients with biopsy-proven IgAN, 70% of patients had baseline total urine protein >1 g/day despite optimized SOC treatment, representing an IgAN population at high risk for kidney disease progression

Treatment with atrasentan resulted in clinically meaningful reductions in proteinuria at weeks 6, 12 and 24

There were no meaningful changes in blood pressure nor acute eGFR changes, suggesting proteinuria reductions were not primarily due to hemodynamic effects of atrasentan

Atrasentan was generally well-tolerated with no treatment-related SAEs

There was no increase in BNP or mean bodyweight, suggesting minimal fluid retention

This analysis demonstrates that treatment with atrasentan results in **clinically meaningful proteinuria reductions** in patients with IgAN who remain at risk for progression with residual proteinuria despite optimized standard-of-care treatment

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Updated Interim Results of a Phase 1/2 Study of BION-1301 in Patients with IgA Nephropathy

Jonathan Barratt[1], Laura Kooienga[2], Irfan Agha[3], Hanna Thomas[3], Biruh Workeneh[4], Rangaraj Narayanan[5], Bess Sorensen[5], Brian S. Schwartz[5], Andrew J. King[5], Charlotte Jones-Burton[5]

1. University of Leicester, Leicester, Leicestershire, United Kingdom; 2. Colorado Kidney Care, Denver, CO, United States; 3. Dallas Renal Group, Dallas, TX, United States; 4. The University of Texas MD Anderson Cancer Center, Houston, TX, United States; 5. Chinook Therapeutics Inc, Seattle, WA, United States

Presented at ASN Kidney Week, November 2022, FR-PO659
(adapted from poster)
Data cut-off October 13, 2022, unless otherwise noted

BION-1301 is an investigational agent and has not been approved for any uses in patients.

Background: IgAN and the APRIL Pathway

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IgA Nephropathy (IgAN)

- IgAN is the leading cause of primary glomerulonephritis, with approximately 2.5 per 100,000 individuals per year worldwide[1]
- Approximately 30-45% of IgAN patients progress to end-stage kidney disease (ESKD) over a period of 20-25 years[2-5]
- Proteinuria is strongly associated with kidney disease progression in IgAN[2,6-7] and treatments that reduce proteinuria result in improved clinical outcomes in IgAN[8-9]

The APRIL Pathway

A Proliferation Inducing Ligand (APRIL) is a TNF superfamily cytokine that drives IgA class switching and survival of IgA-secreting plasma cells[10]

Higher APRIL levels in patients with IgAN are correlated with higher pathogenic Gd-IgA1, proteinuria, and lower eGFR[11-12]

APRIL increases Gd-IgA1 secretion from lymphocytes of patients with IgAN[11]

1. Mcgrogan et al, 2011, NDT; 2. Reich et al, 2007, JASN; 3. Moriyama et al, 2014, PLOS ONE; 4. Rauen et al, 2020, Kidney Int; 5. Hastings et al, 2018, Kidney Int Rep; 6. Thompson et al, 2019, CJASN; 7. Barbour et al, 2019, JAMA Int Med; 8. Inker et al 2016 AJKD; 9. Inker et al, 2019, CJASN; 10. Suzuki et al, 2021, Sem Immunol; 11. Zhai et al, 2016, Medicine; 12. McCarthy et al, 2011, J Clin Invest

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BION-1301 in IgA Nephropathy

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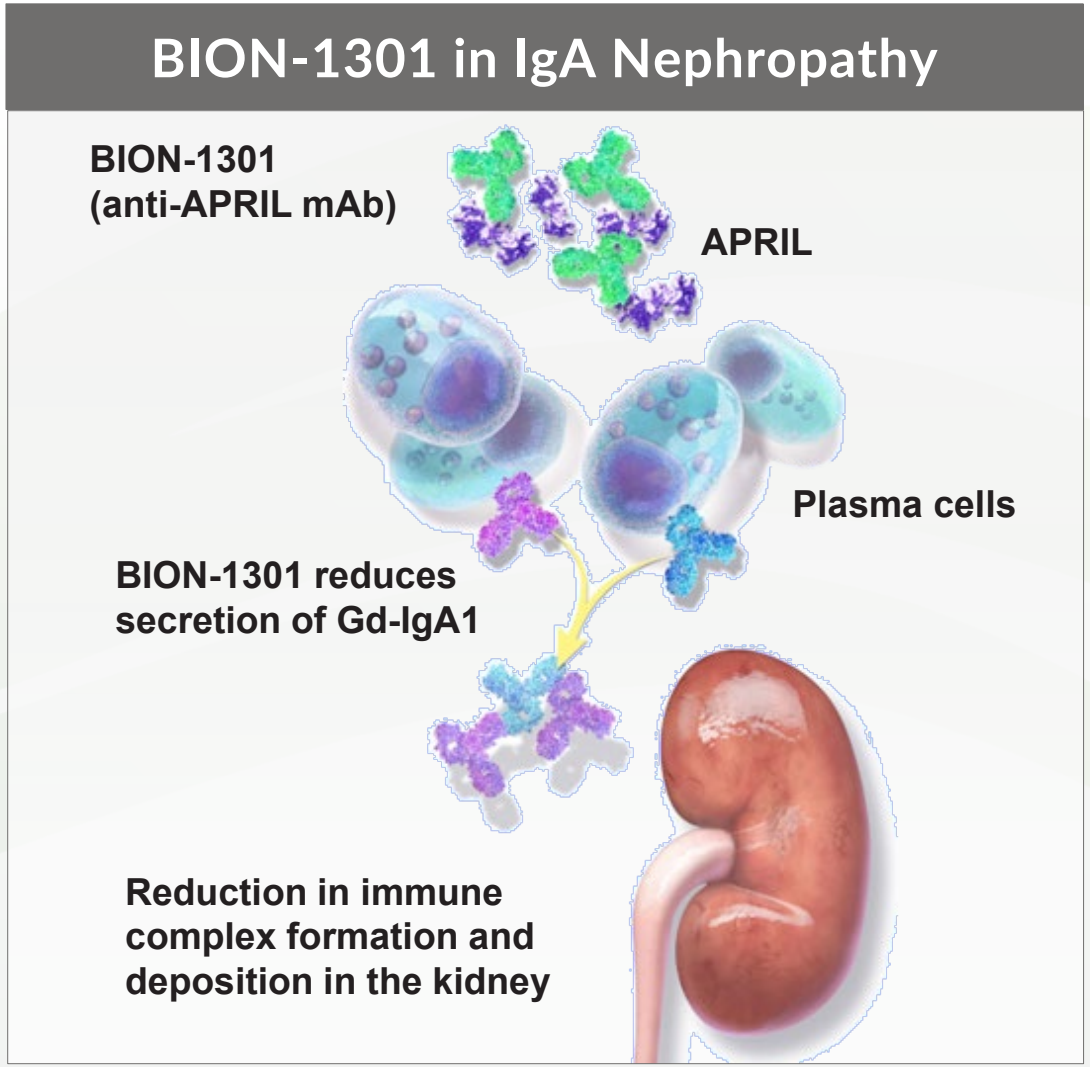
BION-1301* is a novel humanized monoclonal antibody that binds and blocks APRIL

- Potential disease-modifying approach by directly targeting the pathogenesis of IgAN
- BION-1301 was well-tolerated in patients with IgAN and resulted in depletion of Gd-IgA1 and sustained, clinically meaningful proteinuria reduction by 12 weeks of treatment[13]
- Phase 1 bioavailability study in healthy volunteers (HV) supports subcutaneous (SC) dosing[14]



* BION-1301 is an investigational drug that has not been approved by regulatory authorities. Efficacy and safety have not been established. There is no guarantee that it will become commercially available for the use(s) under investigation.

13. Barratt et al, 2022, ERA; 14. Lo et al, 2020 ERA-EDTA

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Study Design

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ADU-CL-19 (Part 3) is an ongoing phase 1/2 trial investigating BION-1301 in patients with IgAN (NCT03945318)

Cohort 1 (n=10)	450 mg Q2W IV → 600 mg Q2W SC, up to 104 weeks ‖†	**Ongoing**
Cohort 2 (n=30)	600 mg Q2W de novo SC, up to 104 weeks‖	**Enrolling**

†*Patients transitioned to SC at ≥24 weeks*

‖ *An optional 1-year treatment extension is available to both cohorts*

Objectives

- Safety, tolerability, PK, immunogenicity, biomarker effects, and preliminary effect on proteinuria in patients with IgAN
- Proof of mechanism
- Proof of concept
- Explore dose/schedule, IV and SC administration

Key Eligibility Criteria, Cohort 2

- Biopsy-proven IgAN diagnosis within past 10 years
- Total protein excretion ≥ 0.5 g/24h OR UPCR ≥ 0.5 g/g based on 24-hour urine collection at screening
- eGFR ≥ 30 mL/min per 1.73 m^2
- Stable/optimized dose of RASi for ≥ 3 months prior to screening (or intolerant to RASi)

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Demographics and Baseline Characteristics

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Demographics and Baseline Characteristics

Demographics	Cohort 1 (n=10**) 450 mg IV → 600mg SC	Cohort 2 (n=24) 600 mg de novo SC
Age, years, *mean (min, max)*	42 (27, 59)	40 (21, 74)
Sex, male, *n (%)*	9 (90)	15 (63)
Race, White, *n (%)*	10 (100)	11 (46)
Asian, *n (%)*	0	11 (46)
Black, *n (%)*	0	1 (4)
Missing, *n (%)*	0	1 (4)
Ethnicity, Hispanic, *n (%)*	2 (20)	2 (8)
Country, US, *n (%)*	10 (100)	16 (67)
Baseline characteristics	*Median (min, max)*	*Median (min, max)*
Time from biopsy, years	2.1 (0.3, 7.7)	3.3 (0.1, 7.6)
Blood pressure (mmHg), Systolic	127 (113, 133)	127 (110, 147)
Diastolic	83 (69, 88)	79 (57, 88)
eGFR (mL/min/1.73 m²)§	69 (30, 122)	75 (37, 131)
24-hour urine protein excretion (g/day)	1.2 (0.7, 6.5)	1.0 (0.6, 2.7)
24-hour UPCR (g/g)	0.5 (0.4, 4.6)	0.8 (0.2, 3.2)
Renin-angiotensin system inhibitor use (%)	100%	100%

§ eGFR by CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration
** Two patients withdrew from study for reasons unrelated to study drug

Cohort 1 enrollment and treatment duration:

- 10 patients enrolled; 8 patients continued to SC
- Mean treatment duration of 64 weeks (range 0.1 to 106 weeks)
  - Mean treatment duration of 450 mg IV prior to transition to SC was 37 weeks
  - Mean treatment duration after transition to 600 mg SC was 40 weeks

Cohort 2 enrollment and treatment duration:

- 24 patients enrolled (enrolling up to 30 patients)
- Mean treatment duration of 17 weeks (range 2 to 30 weeks)

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Safety and Tolerability

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In Cohort 1 and Cohort 2:

- BION-1301 is generally well tolerated in IgAN patients, with no reported deaths, SAEs, or AEs leading to discontinuation of study drug to date
- All infections in patients with IgAN have been Grade 1 or 2 in severity and only one infection, which was Grade 1 in severity, was assessed as treatment-related
- Injection site reactions have all been Grade 1 or Grade 2 in severity
- IgG level below the study defined threshold (< 3 g/L) occurred in one patient in Cohort 1, requiring protocol-mandated withholding of study drug. There have been no infections reported in this patient

AE Category (N=34)		n (%)
Treatment emergent AEs (TEAEs)	Patients with any TEAE	23 (67.6)
	Patients with Infection TEAE (Grades 1 or 2)	17(50.0)
	Infection TEAE occurring in N>1 patient	
	COVID-19	8 (23.5)
	Upper Respiratory Tract Infection	3 (8.8)
	Asymptomatic COVID-19	2 (5.9)
	Sinusitis	2 (5.9)
	Urinary Tract Infection	2 (5.9)
Treatment-related AEs	Patients with any treatment-related AE	8 (23.5)
	Related AEs occurring in N>1 patient	
	Fatigue	3 (8.8)
	Injection site erythema	3 (8.8)

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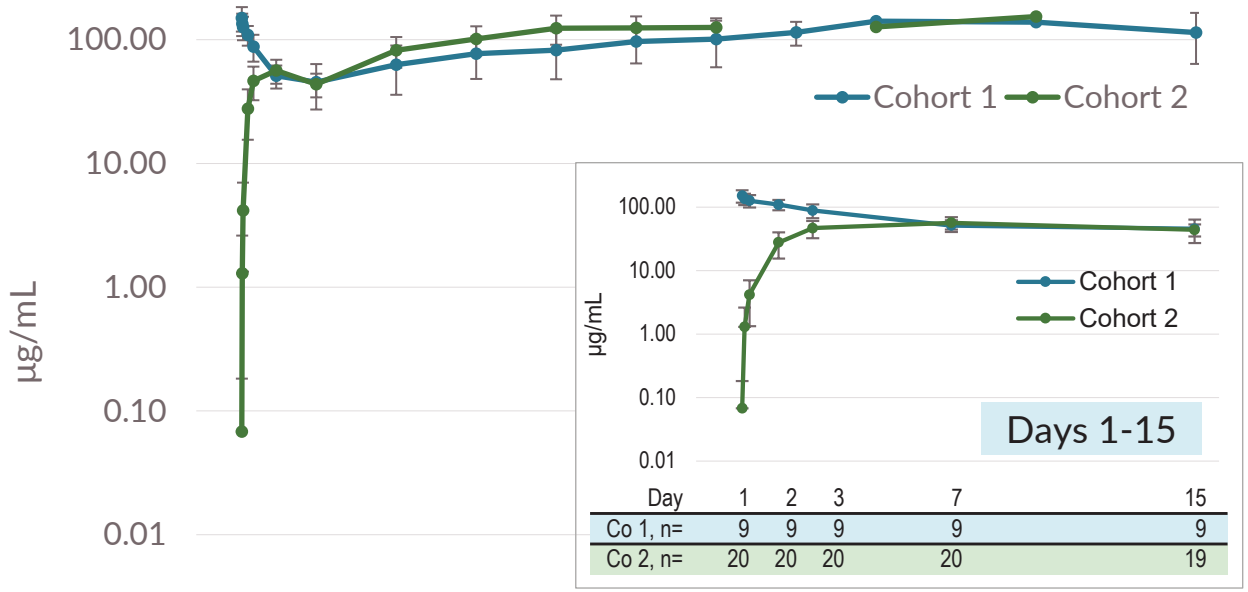
Pharmacokinetics

- Low inter-individual variability in BION-1301 serum concentrations following IV and SC administrations
- Trough concentrations of BION-1301 following 600 mg SC Q2W (Cohort 2) are consistent with trough concentrations observed following 450 mg IV Q2W (Cohort 1)
- No anti-drug antibodies observed in patients with IgAN to date

BION-1301 Serum Concentrations



Wk	1	4	10	12	16	20	24
Co 1, n=	9	9	8	8	2	2	4
Co 2, n=	20	17	8	9	9	4	0

Mean (± SD) BION-1301 serum concentrations following IV (Cohort 1) or SC (Cohort 2) administration Q2W‡. Data points after Day 7 are trough concentrations.

Data cut-off Sep 30, 2022

BION-1301 Results in Rapid and Durable Reduction in IgA and Gd-IgA1

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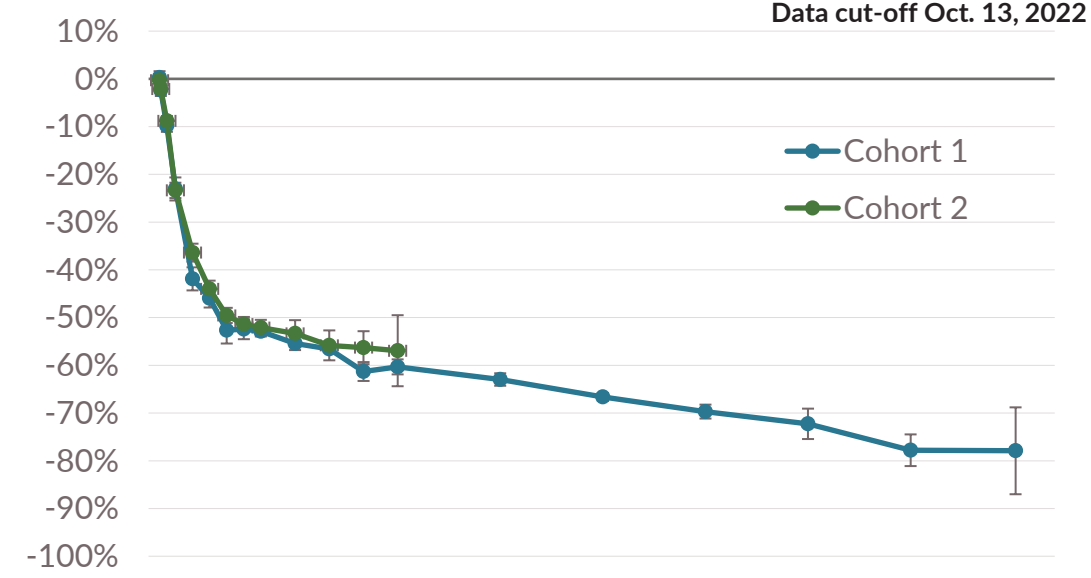
IgA % Change from Baseline (Mean ± SE)

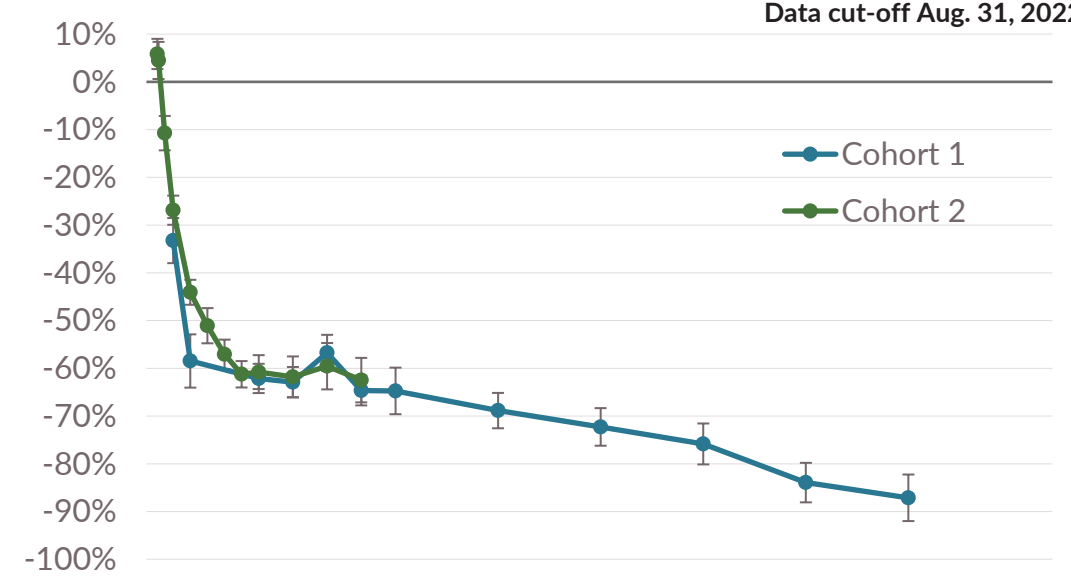
Data cut-off Oct. 13, 2022



Wk	4	8	12	16	20	24	28	40	52	64	76	88	100
Co 1, n=	8	8	8	8	2	5	6	8	7	7	4	3	2
Co 2, n=	23	18	15	10	10	9	3						

Gd-IgA1 % Change from Baseline (Mean ± SE)

Data cut-off Aug. 31, 2022



Wk	4	8	12	16	20	24	28	40	52	64	76	88	100
Co 1, n=	8	0	8	8	2	5	7	8	6	6	4	2	
Co 2, n=	20	13	9	10	8	2							

Mean Gd-IgA1 are not available at week 100

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Reductions in IgM, and to a Lesser Extent IgG, Were Also Observed

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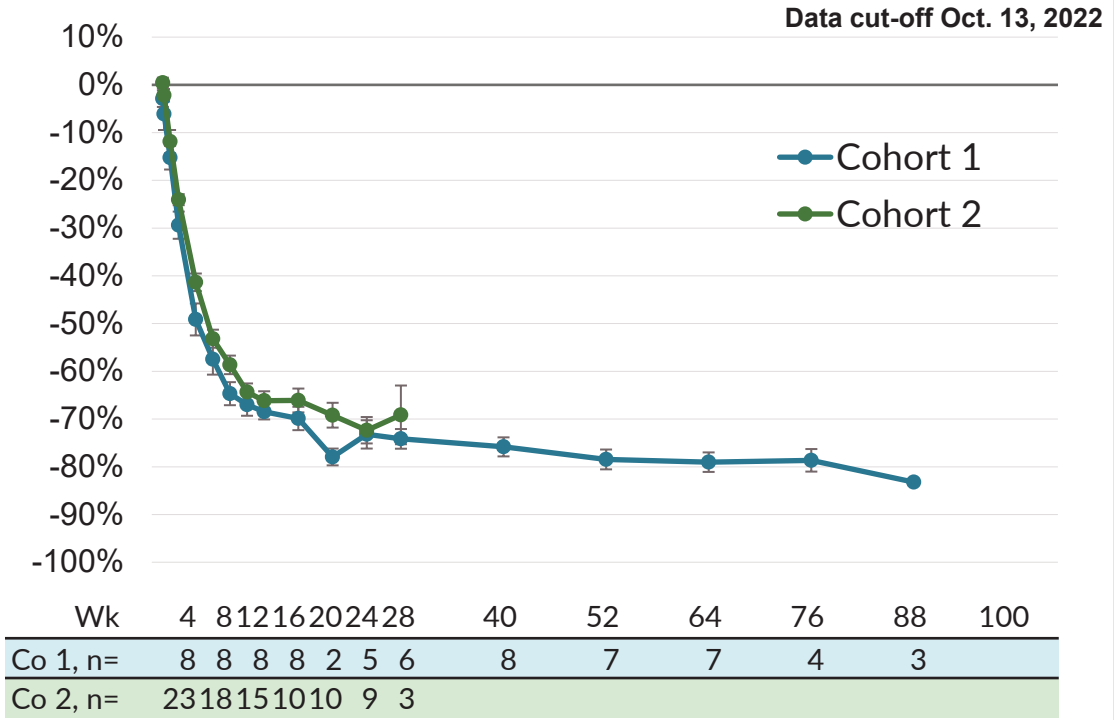
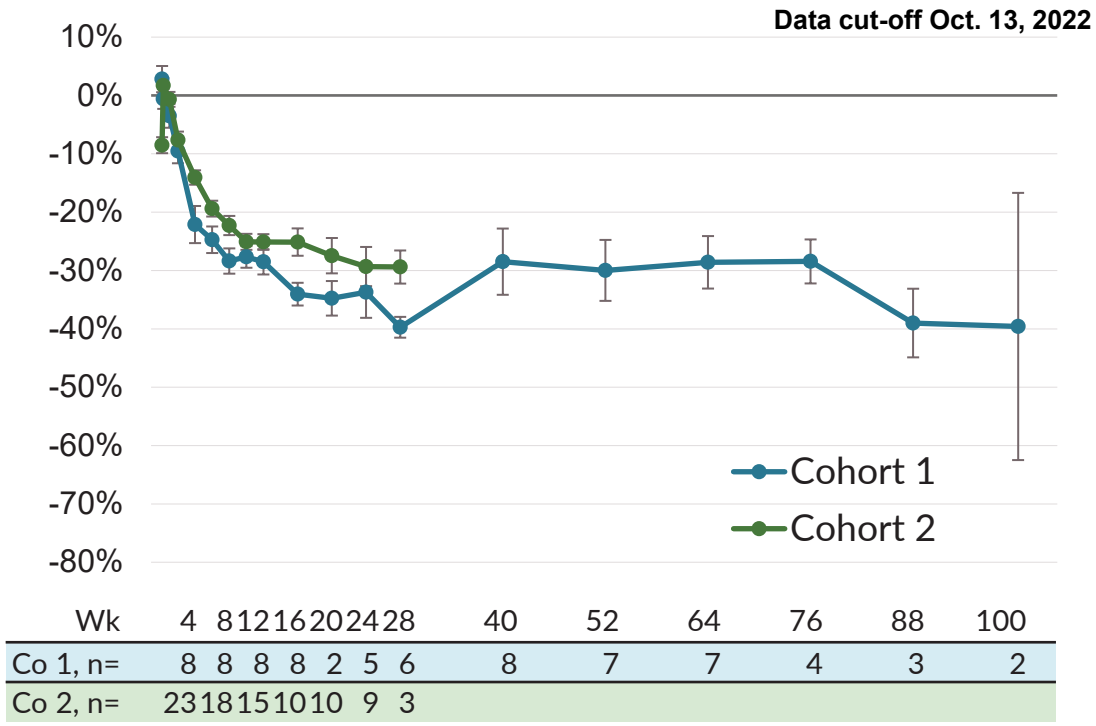
IgM % Change from Baseline (Mean ± SE)



IgG % Change from Baseline (Mean ± SE)



Mean IgM are not available at week 100

Data cut-off Oct. 13, 2022

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BION-1301 Treatment Results in Sustained, Clinically Meaningful Proteinuria Reductions

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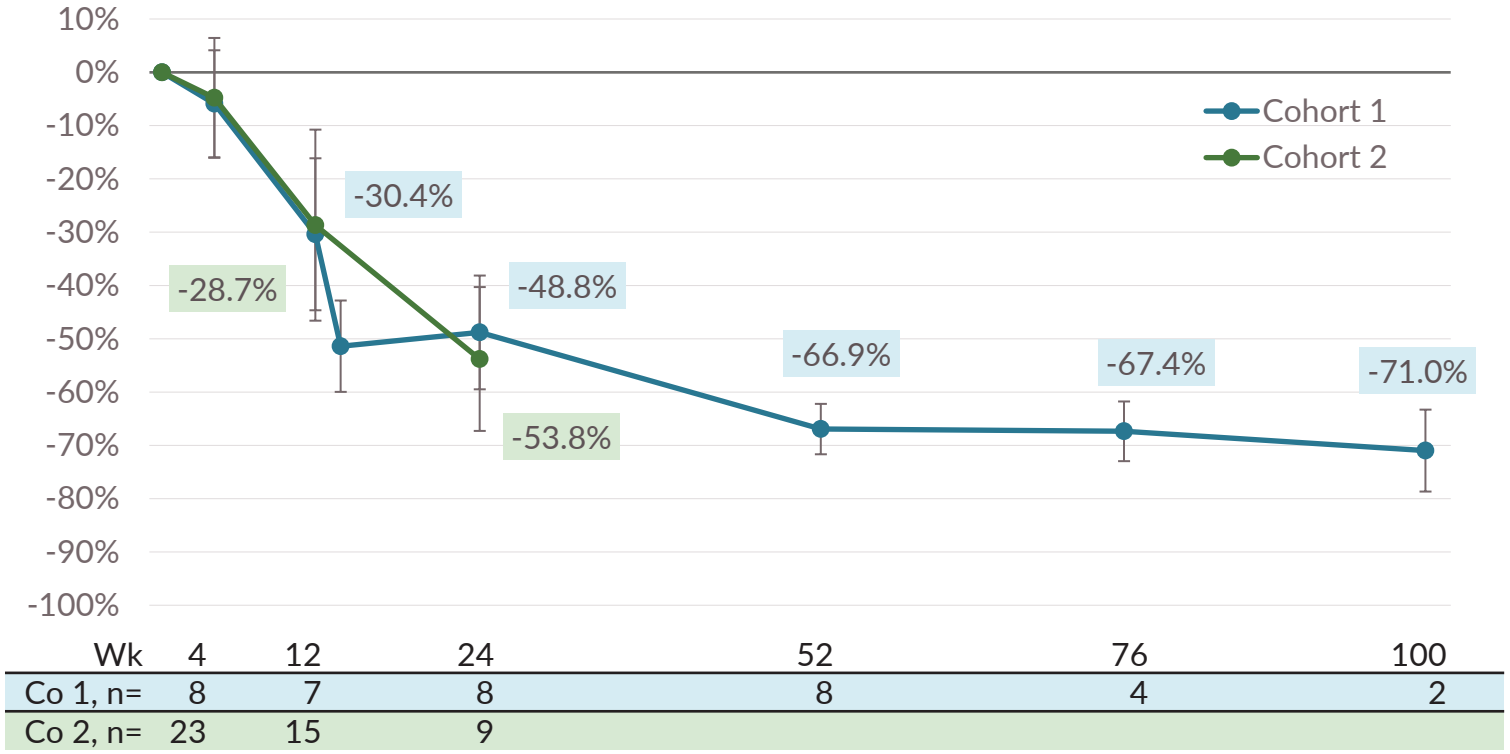
UPCR % Reduction (Geometric Mean ± SE)

Data cut-off Oct. 13, 2022



Wk	4	12	24	52	76	100
Co 1, n=	8	7	8	8	4	2
Co 2, n=	23	15	9			

Median (range) baseline protein excretion: Cohort 1, 1.2 (0.7, 6.5) g/day ; Cohort 2, 1.0 (0.6, 2.7) g/day

Cohort 1 (IV → SC):

- Clinically meaningful reductions in UPCR from baseline were seen in patients with IgAN across a wide range of baseline proteinuria levels by Week 12
- UPCR continued to decline through one year and then was maintained through two years, providing evidence of sustained efficacy
- Among patients with available data up to Week 52, 7/8 patients demonstrated a greater than 50% reduction in UPCR from baseline at Week 52

Cohort 2 (de novo SC):

- Mean reduction in UPCR of 53.8% at 24 weeks in Cohort 2 with de novo SC administration are consistent with those observed in Cohort 1

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Conclusions

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Nov. 3–6 | Orlando, FL

Interim Data Continues to Demonstrate Disease-Modifying Potential of BION-1301 in Patients with IgAN

- BION-1301 results in rapid and durable reductions in IgA and Gd-IgA1, the pathogenic IgA variant which drives IgAN pathogenesis
  - Reductions in IgM, and to a lesser extent IgG, were also observed
- BION-1301 is generally well-tolerated with no ADAs observed to-date in patients with IgAN
- BION-1301 results in clinically meaningful reductions in proteinuria in patients receiving optimized RASi
- Results are consistent across Cohort 1 (450 mg Q2W IV → 600 mg Q2W SC after 24 weeks) and Cohort 2 (600 mg Q2W SC)

These data provide proof-of-concept for the disease-modifying potential of BION-1301 to:

- ✓ deplete pathogenic Gd-IgA1 in patients with IgAN
- ✓ reduce proteinuria in patients with IgAN who remain at risk for progression with residual proteinuria despite optimized standard-of-care treatment

Clinical data to date supports BION-1301 (600mg SC Q2W) is well-tolerated and results in clinically meaningful proteinuria reductions to be further explored in phase 3

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BION-1301 PI Perspective

Laura Kooienga, MD

Practicing Nephrologist and Director of Research at Colorado Kidney Care

Dr. Kooienga's Patients in Cohort 1

DEMOGRAPHICS	COHORT 1 (n=4) 450 mg IV → 600mg SC
Age, years, *median (min, max)*	47.5 (30, 58)
Sex, male, *n (%)*	4 (100)
Race, White, *n (%)* **Asian,** *n (%)* **Black,** *n (%)*	4 (100) 0 0
Ethnicity, Hispanic, *n (%)*	0
Country, US, *n (%)*	4 (100)
BASELINE CHARACTERISTICS	*Median (min, max)*
Time from biopsy, years	2.4 (0.13, 7.6)
Blood pressure (mmHg), Systolic **Diastolic**	128 (118, 133) 84.5 (84, 87)
eGFR (mL/min/1.73 m^2)*	70 (47, 122)
24-hour urine protein excretion (g/day)	1 (0.7, 3.5)
24-hour UPCR (g/g)	0.5 (0.4, 0.9)
Renin-angiotensin system inhibitor use (%)	100%

* eGFR by CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration, n=4

To date, Dr. Kooienga's 4 patients in Cohort 1 have been on treatment for 56 – 76 weeks

Dr. Kooienga's Patients in Cohort 2

DEMOGRAPHICS	COHORT 2 (n=6) 600 mg de novo SC
Age, years, *median (min, max)*	37 (27, 56)
Sex, male, *n (%)*	5 (83.33)
Race, White, *n (%)* **Asian,** *n (%)* **Black,** *n (%)*	4 (66.67) 2 (33.33) 0
Ethnicity, Hispanic, *n (%)*	0
Country, US, *n (%)*	6 (100)
BASELINE CHARACTERISTICS	*Median (min, max)*
Time from biopsy, years	4.1 (0.67, 7.95)
Blood pressure (mmHg), Systolic **Diastolic**	128.5 (118, 137) 84.5 (72, 88)
eGFR (mL/min/1.73 m^2)*	58.5 (49, 75)
24-hour urine protein excretion (g/day)	1.5 (0.8, 5.1)
24-hour UPCR (g/g)	0.9 (0.4, 3.2)
Renin-angiotensin system inhibitor use (%)	100%

* eGFR by CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration, n=5

To date, Dr. Kooienga's 6 patients in Cohort 2 have been on treatment for 1 – 34 weeks

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Dr. Kooienga's Clinical Experience with BION-1301

- Very positive experience with BION-1301 phase 1/2 study to date
- All of Dr. Kooienga's patients enrolled in Cohorts 1 and 2 have:
  - ✓Tolerated BION-1301 well
  - ✓Had clinically meaningful reductions in proteinuria as of their most recent visit
  - ✓Tolerated subcutaneous injections well
  - ✓Had no concerns around dosing frequency or subcutaneous delivery
  - ✓Been highly motivated, engaged and committed to study

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Preclinical Efficacy of CHK-336: A First-in-Class, Liver-Targeted, Small Molecule Inhibitor of Lactate Dehydrogenase for the Treatment of Primary Hyperoxalurias

Jennifer Cox[1], Marc-Olivier Boily[1], Alex Caron[1], Oliver Chong[1], Jim Ding[1], Samuel Gaudreault[1], Robert Gomez[1],John Knight[2], Jay Kuo[1], Jeff Lester[1], Xingsheng Li[2], W Todd Lowther[3], Renata Oballa[1], David Powell[1], Hannah Sandford-Crane[1], Tao Sheng[1], Jayakumar Surendradoss[1], Vincent Tong[1], Joyce Wu[1], Andrew King[1]

1. Chinook Therapeutics, 2. University of Alabama at Birmingham, 3. Wake Forest University

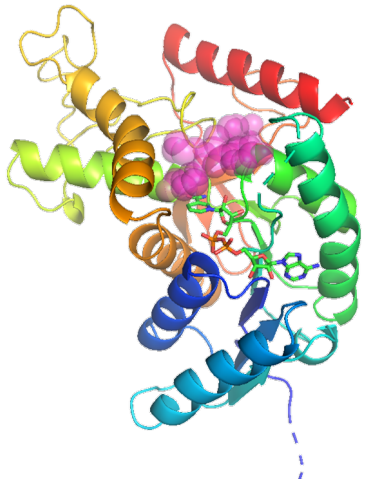
Presented at ASN Kidney Week, November 2022, FR-PO334
(adapted from presentation)

CHK-336 is an investigational agent and has not been approved for any uses in patients.

Results

KIDNEY WEEK 2022
Nov. 3–6 | Orlando, FL

A CHK-336 is a potent LDHA inhibitor in enzyme and hepatocyte assays across multiple species



Compound design and sub-nM potency guided by structural biology and X-ray crystallography of LDHA-inhibitor complexes

	Assay	CHK-336 IC_{50}
Enzyme	Human LDHA	0.2 nM
	Mouse LDHA	0.3 nM
Hepatocyte	Mouse Fresh Hepatocytes	52 nM
	Mouse Cryopreserved Hepatocytes	80 nM
	Rat Cryopreserved Hepatocytes	130 nM
	Monkey Cryopreserved Hepatocytes	130 nM
	Human Cryopreserved Hepatocytes	121 nM
PH1 Hepatocyte	Mouse *Agxt* Knockdown Hepatocytes (Oxalate Production)	165 nM

- CHK-336 demonstrates potent inhibition of LDHA in enzyme assays (IC_{50} = 0.2-0.3 nM) and primary hepatocyte assays across multiple species (IC_{50} = 52-165 nM)
- CHK-336 also demonstrates tight LDHA binding with a very slow off-rate (hours-days)

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Results

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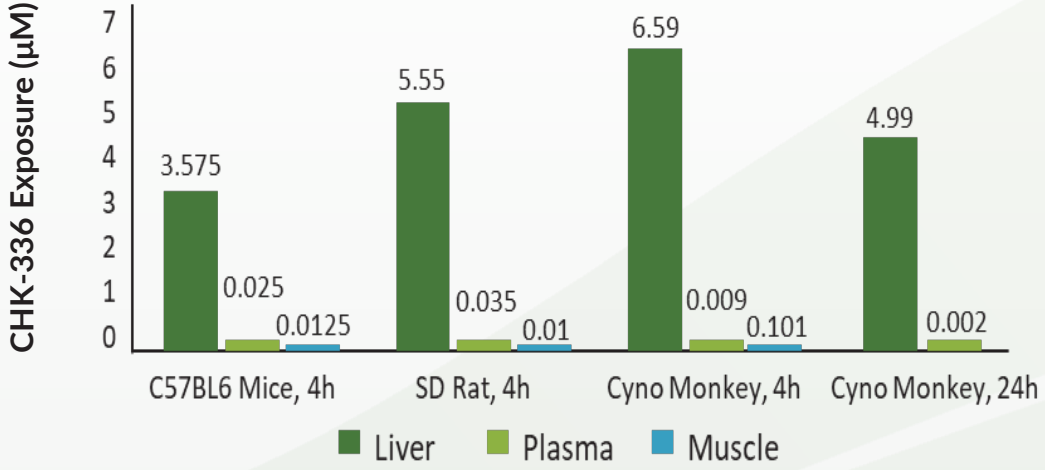
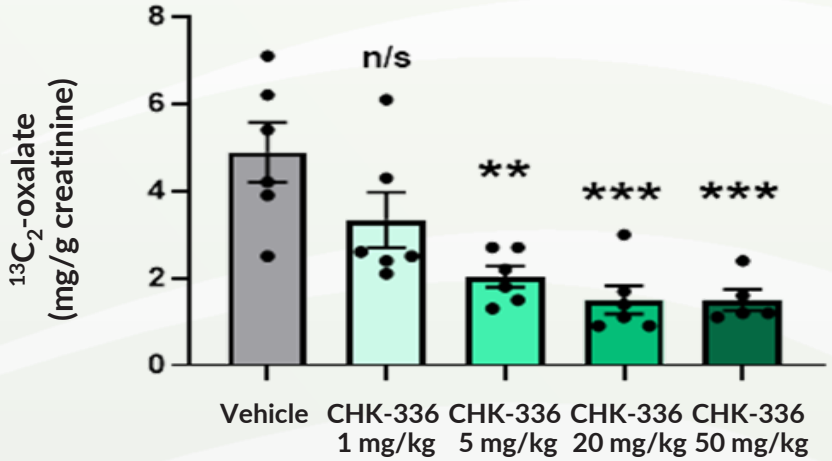
Nov. 3–6 | Orlando, FL

B Liver-targeted tissue distribution of CHK-336 and pharmacodynamic effect on the conversion of 13C2-glycolate into 13C2-oxalate

Tissue Distribution Profile of CHK-336 Across Species
(normalized to 5 mg/kg oral dose)



CHK-336 Dose Dependently Blocks $^{13}C_2$-Oxalate Production in Rats



- CHK-336 exhibits a liver-targeted tissue distribution profile in mice, rats and monkey with high liver concentrations and low extra-hepatic tissue exposures
- Liver-targeted profile driven by OATP-mediated uptake results in high liver/plasma unbound ratios of 180-fold (rat) to 450-fold (monkey)
- Since LDHA catalyzes the final step of oxalate production from glycolate, a 13C2-glycolate stable isotope tracer was used to assess CHK-336 target engagement by measuring urinary excretion of 13C2-oxalate in Sprague Dawley rats
- Human PK predictions suggest CHK-336 has the potential to be a low, once-daily oral dose therapeutic in humans

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Results

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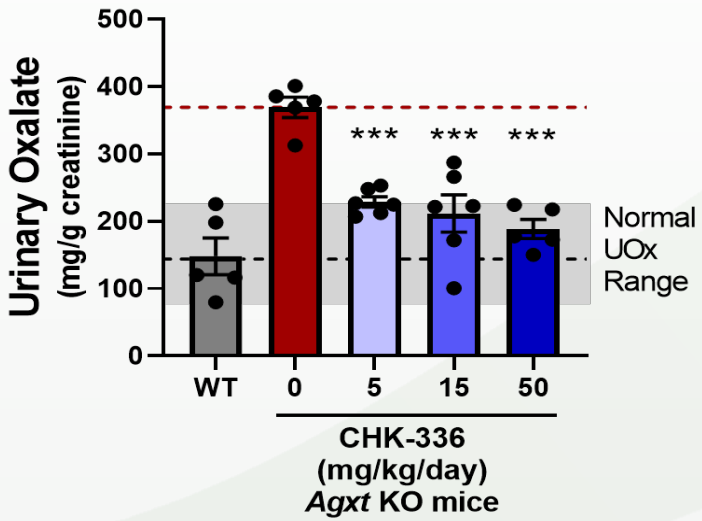
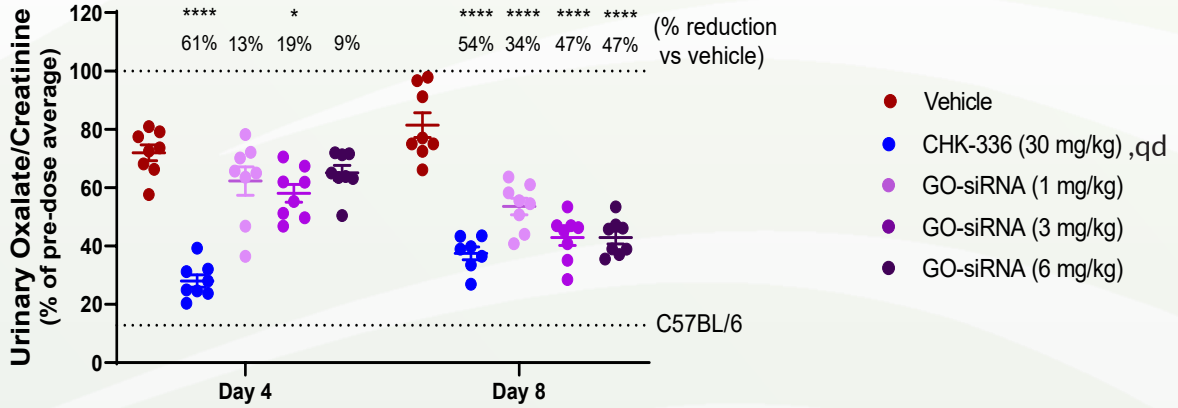
Nov. 3–6 | Orlando, FL

C CHK-336 produced significant and dose-dependent reductions in urinary oxalate in a PH1 mouse model

Urinary Oxalate Reduction by CHK-336 in a PH1 Mouse Model



Effect of CHK-336 Compared to GO siRNA on Urinary Oxalate in PH1 Mice



- CHK-336 was dosed orally, once-daily for 7 days in male Agxt KO mice and urinary oxalate concentrations were compared to a vehicle control group
- Low, oral, once-daily doses of CHK-336 significantly reduced urinary oxalate; majority of treated mice reached the normal range observed in wild-type mice
- CHK-336 had a more rapid onset of action and comparable magnitude of urinary oxalate reduction compared to a GO-targeting siRNA
- GO-siRNA was administered on day 0; Doses of 1, 3, and 6 mg/kg caused 56%, 75%, and 78% knockdown, respectively

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Results

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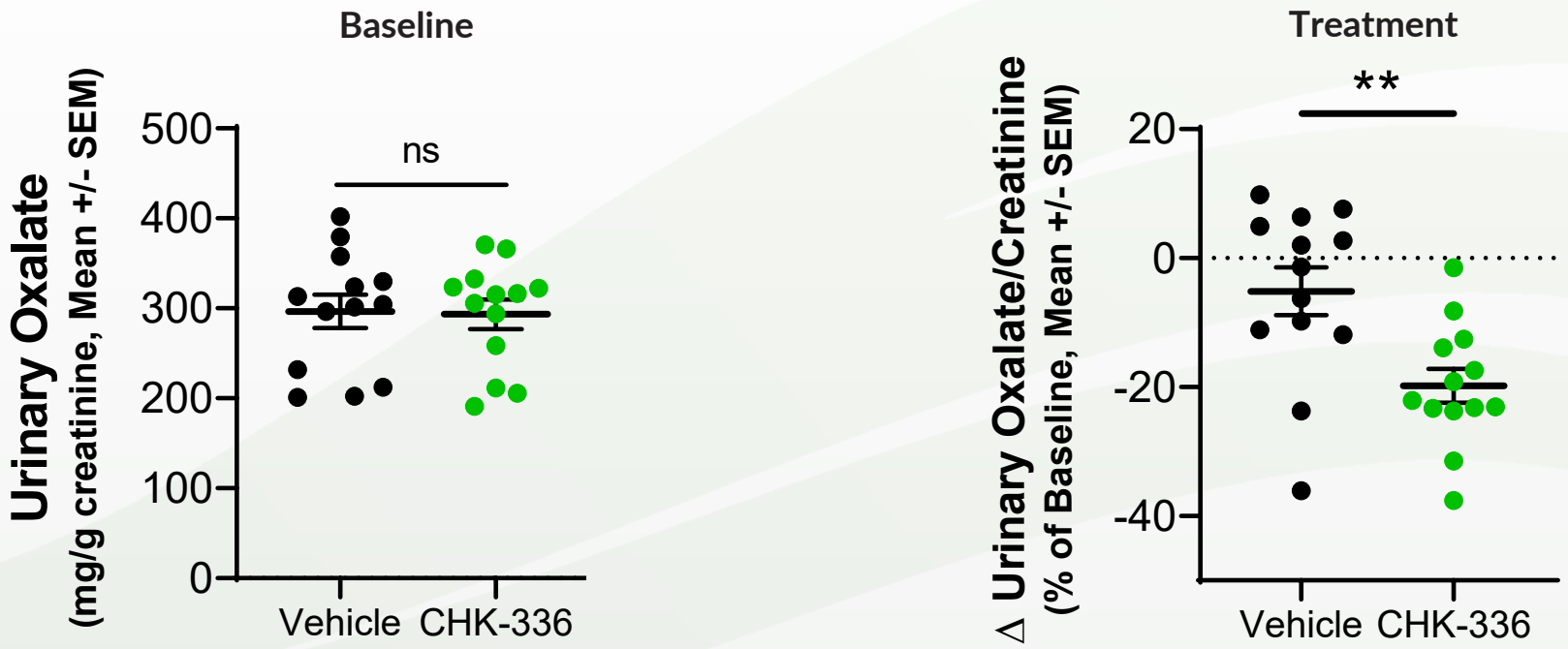
D CHK-336 significantly reduced urinary oxalate excretion in a genetic mouse model of PH2



CHK-336 was dosed orally, once-daily for 7 days at 25 mg/kg in male Grhpr KO mice and urinary oxalate concentrations were compared to a vehicle group

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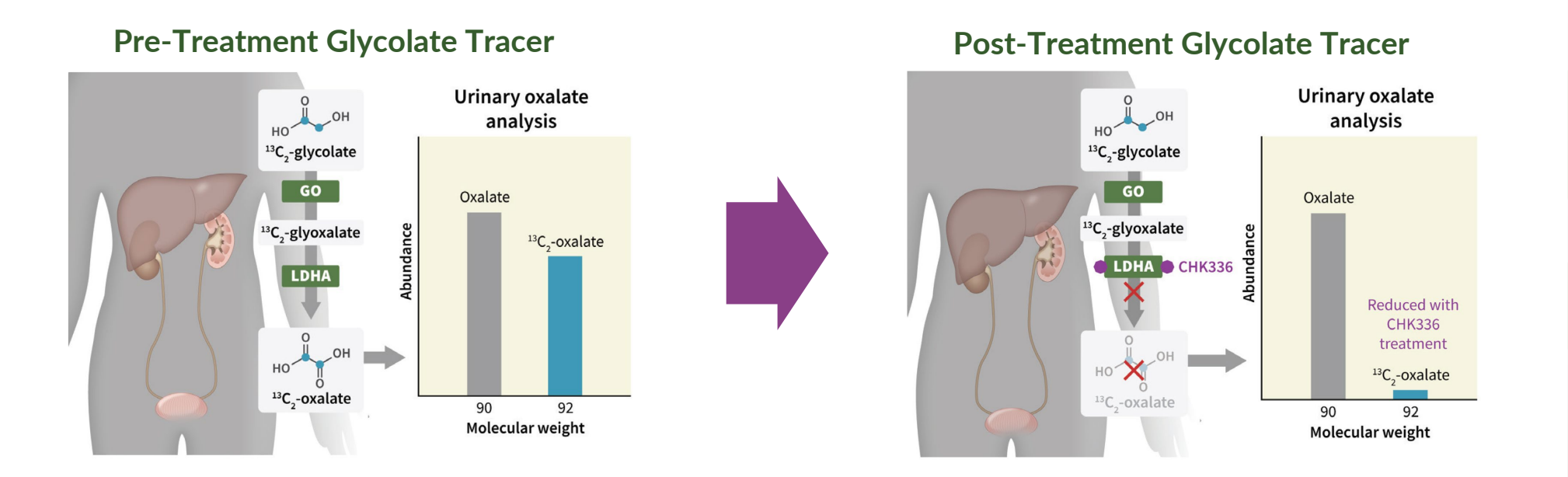
Conclusions

- CHK-336 is a potent LDHA inhibitor, with liver-targeted tissue distribution, that is efficacious in PH1 and PH2 mouse models of primary hyperoxaluria and has potential benefit in non-genetic hyperoxalurias caused by oxalate overproduction.
- The human safety and pharmacokinetic profiles of CHK-336 are currently under investigation in a healthy volunteer SAD/MAD study (NCT05367661).
- Target engagement will be assessed in humans using a novel stable isotope glycolate tracer approach (depicted below).



CHK-336 is a first-in-class oral LDHA inhibitor with the potential to treat all subtypes of primary hyperoxaluria as well as other disorders arising from oxalate overproduction

Single Nuclei RNAseq Reveals Cell-type Specific Responses to Disease and Enalapril in the gddY Mouse Model of IgAN

N. Eric Olson[1], Mark McConnell[1], Phillip J. McCown[2], Edgar A. Otto[2], Viji Nair[2], Marvin Gunawan[1], Sean Eddy[2], Jennifer H. Cox[1], Matthias Kretzler[1], Toshiki Kano[3], Yusuke Suzuki[3], Andrew J. King[1]

1. Chinook Therapeutics Inc, Seattle, WA, United States; 2. University of Michigan, Ann Arbor, MI, United States; 3. Juntendo University Faculty of Medicine, Tokyo, Japan

Disclosures: N. E. Olson, Mark McConnell, Marvin Gunawan, Jennifer H. Cox, Matthias Kretzler, Andrew J. King - Chinook Therapeutics, Employed, Equity

Presented at ASN Kidney Week, November 2022, FR-PO659
(adapted from presentation)

Atrasentan is an investigational agent and has not been approved for any uses in patients.

Cellular Composition

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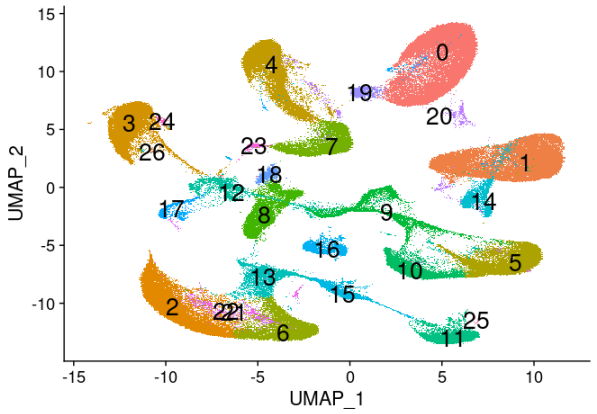
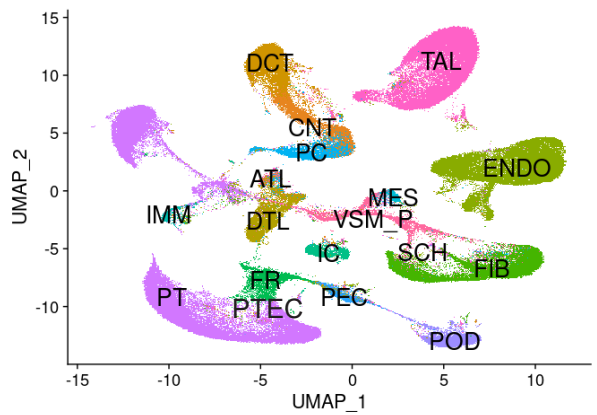
A Seurat Clusters



B Enhanced Azimuth L1 annotation



A Seurat clusters at resolution 0.3 generated 26 clusters'

B Cell types were annotated using azimuth level 1 annotation which was supplemented with mesangial cells from azimuth level 3 annotation. Additionally, failed repair proximal tubular epithelial cells (FR PTEC) were annotated using the approach described in Figure 2.

C Number of nuclei for each cell group by treatment. The majority of kidney cell types have well over 100 nuclei per treatment group, **providing good coverage of the tubulointerstitial and glomerular compartments**.

C

	Control	IgAN			
	Vehicle	Vehicle	Atrasentan	ACEi	Total
ATL	313	160	126	165	764
CNT	1,615	2,291	2,158	2,472	8,536
DCT	2,953	3,170	3,753	3,480	13,356
DTL	2,539	2,269	2,205	2,681	9,694
ENDO	5,267	7,874	8,408	9,744	31,293
FIB	3,291	5,780	4,950	6,915	20,936
FR PTEC	278	1,564	971	1,648	4,461
IC	771	886	899	983	3,539
IMM	42	650	380	490	1,562
MES	195	378	366	721	1,660
PC	2,432	1,698	1,418	1,929	7,477
PEC	509	765	737	1,005	3,016
POD	2,248	1,334	1,656	2,310	7,548
PT	8,308	10,768	15,287	15,356	49,719
SCH	74	189	132	322	717
TAL	10,120	7,785	7,830	9,550	35,285
VSM_P	667	1,435	1,278	2,649	6,029
Total	**41,622**	**48,996**	**52,554**	**62,420**	**205,592**

ATL – Ascending thin limb; CNT – connecting tubule; DCT - distal convoluted tubule; DTL – descending thin limb; ENDO – endothelial; FIB – fibroblast; FR PTEC– failed repair proximal tubular epithelial cells; IC – intercalated; IMM – immune; MES – mesangial; PC – principal; PEC – parietal epithelial; POD –podocyte; PT – proximal tubule; SCH – schwann; TAL – thick ascending limb; VSM_P – vascular smooth muscle / pericyte

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Results

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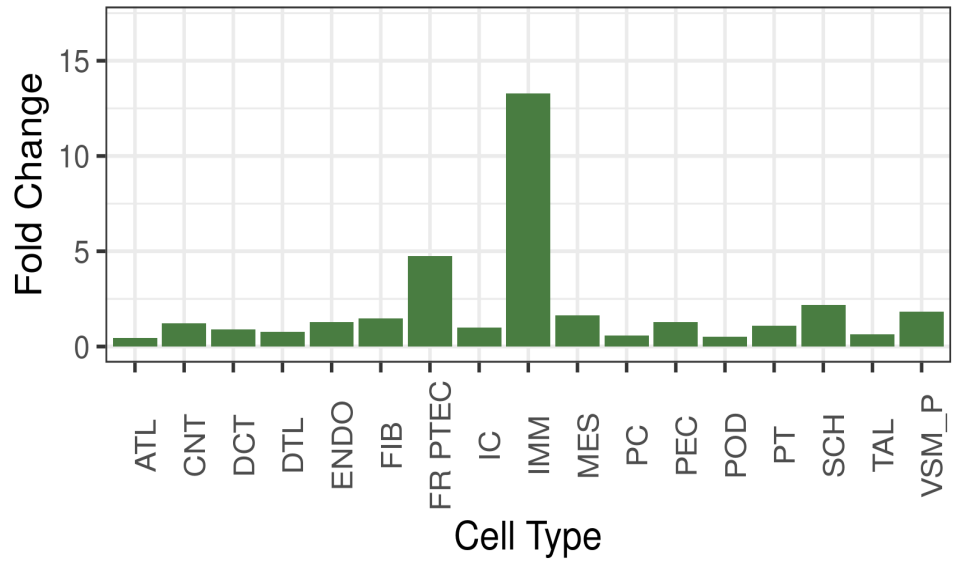
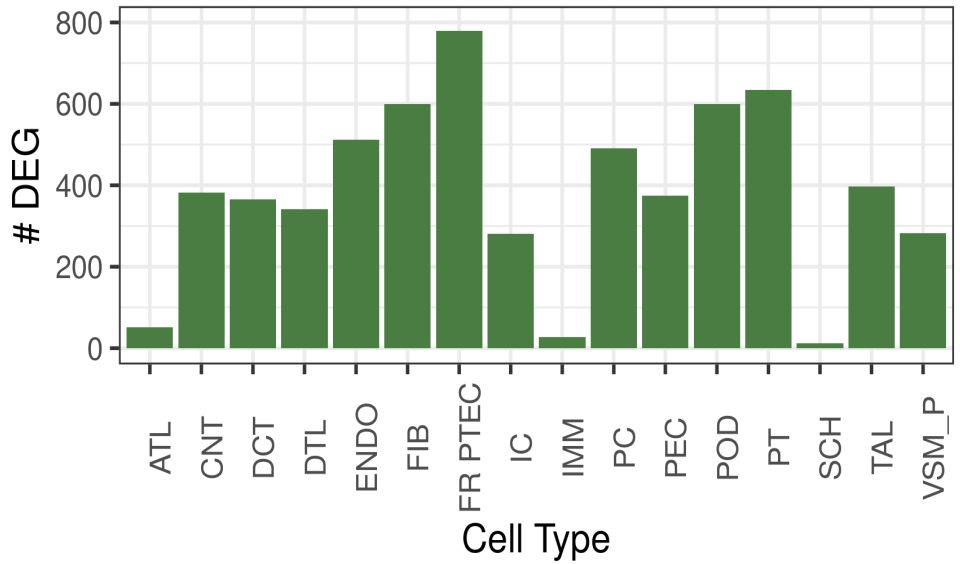
2 FR PTEC are the most expanded kidney cell type in gddY

A Cell proportion



B Differentially expressed genes



A FR PTEC are the most expanded kidney cell type in gddY compared to control, with ~4.7x the proportion of nuclei in gddY compared with control.

B FR PTEC have the largest number of differentially expressed genes (DEG), with 779 genes differentially expressed in gddY compared to control.

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Results

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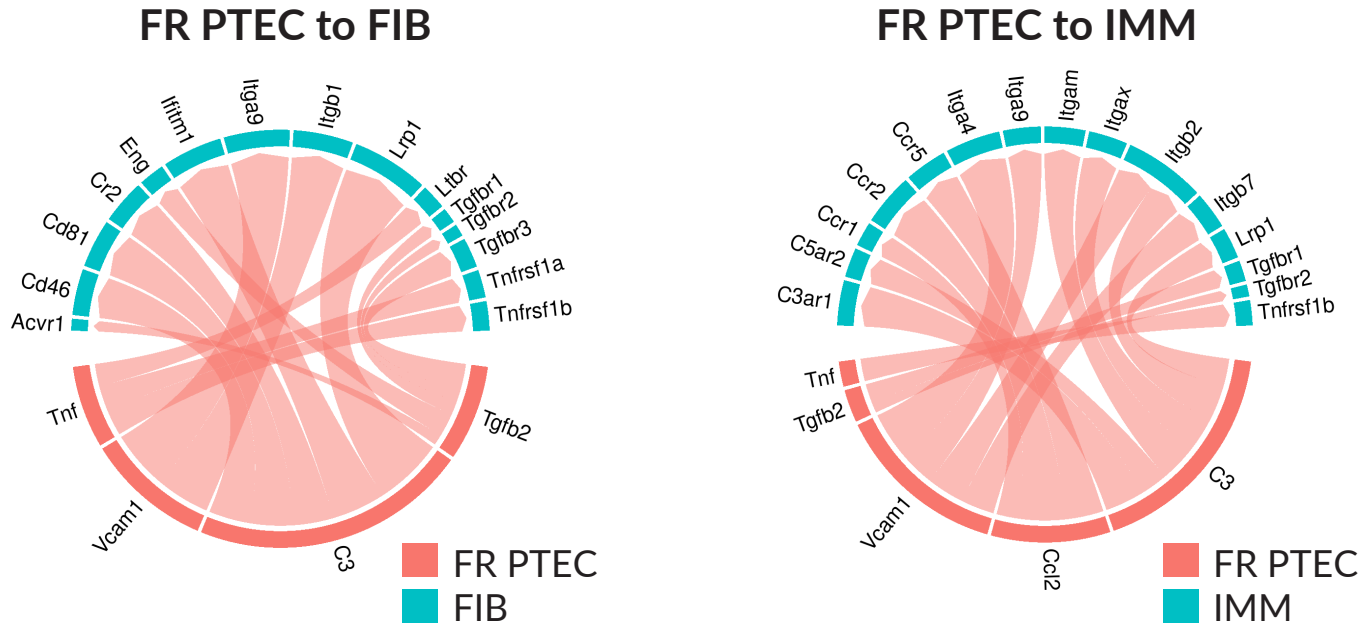
3 FR PTEC are a source of chemokines and cytokines for immune cells and fibroblasts



Putative relationships for key FR PTEC ligands and corresponding receptors on potential target cell types

- Pro-inflammatory and profibrotic effects on fibroblasts may be mediated through Tnf and Tgfb2 signaling from FR PTEC.
- FR PTEC may play a key role in recruitment of immune cells through their expression of Ccl2.

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Results

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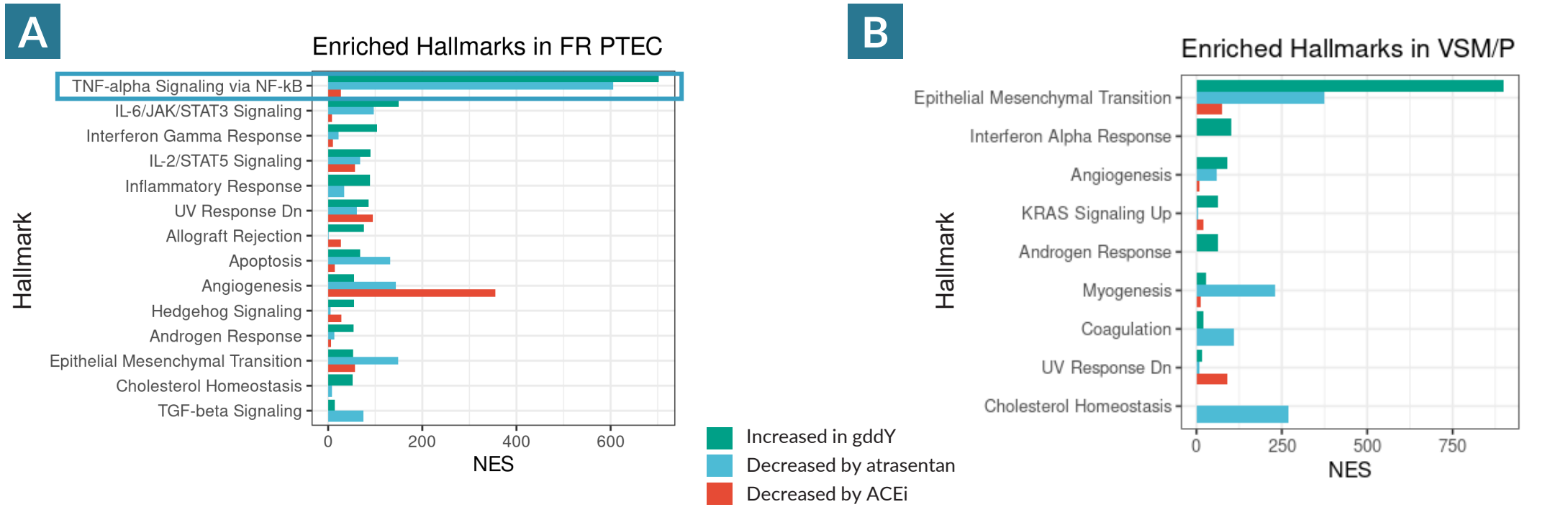
7 Comparison of pathway enrichments for atrasentan and ACEi treatment



A In FR PTEC, gddY-induced DEGs were highly enriched for TNF-α signaling. Atrasentan treatment of gddY mice led to downregulation of genes that are enriched in the TNF-α hallmark.

B In VSM/P cells, EMT was the primary hallmark increased in gddY. ACEi treatment had a modest effect on the increased expression of these genes.

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Conclusions

Failed repair proximal tubular epithelial cells (FR PTEC) are a prominent feature of the gddY mouse model of IgAN

- This study identified a cluster of cells that scored highly for a FR PTEC signature and a TNF signature and were the most highly expanded kidney cell type in gddY.
- We propose that these cells represent FR PTEC, and that the expansion of these cells is a major characteristic of the gddY model and may play a major role in tubulointerstitial. inflammation and fibrosis and progressive kidney function loss.
- We have also found that FR PTEC are a key characteristic of CKD progression in human disease[6].

Atrasentan and ACEi treatment resulted in different effects on gene expression

- Atrasentan induces the most gene expression changes in FR PTEC and these gene expression changes reverse pathogenic changes that are induced in the gddY disease model.
- ACEi treatment tends to induce new gene expression changes, most prominently in VSM/P.

Ongoing efforts to characterize gene expression associated with atrasentan response

- This atrasentan response signature is currently being evaluated in IgAN patient kidney biopsies and matched urine and serum samples are being screened for non-invasive surrogate biomarkers.

6. Bohnenpoll et al, Unsupervised Characterization of the NURTuRE Cohort Reveals Gene Expression and Tissue Remodeling Dynamics along a Synthetic CKD Progression Axis, ASN 2022 - SA-PO1011.

A Multi-Omics Approach to IgA Nephropathy Characterization in the NURTuRE Cohort Enables Precision-Based Treatment Approaches

N. Eric Olson, Jennifer Cox, I-Ju Lo, Seamus Ragan, Niklas Michel, Johannes Pospiech, Michaela Bayerlova, Simone Romoli, Taher Sathaliya, Tobias Bohnenpoll, Nikolas Stroth, Olivier Radresa, Andrew King, and Uwe Andag

FR-OR60, Glomerular Diseases: From Bench to Bedside [OR1300-1]

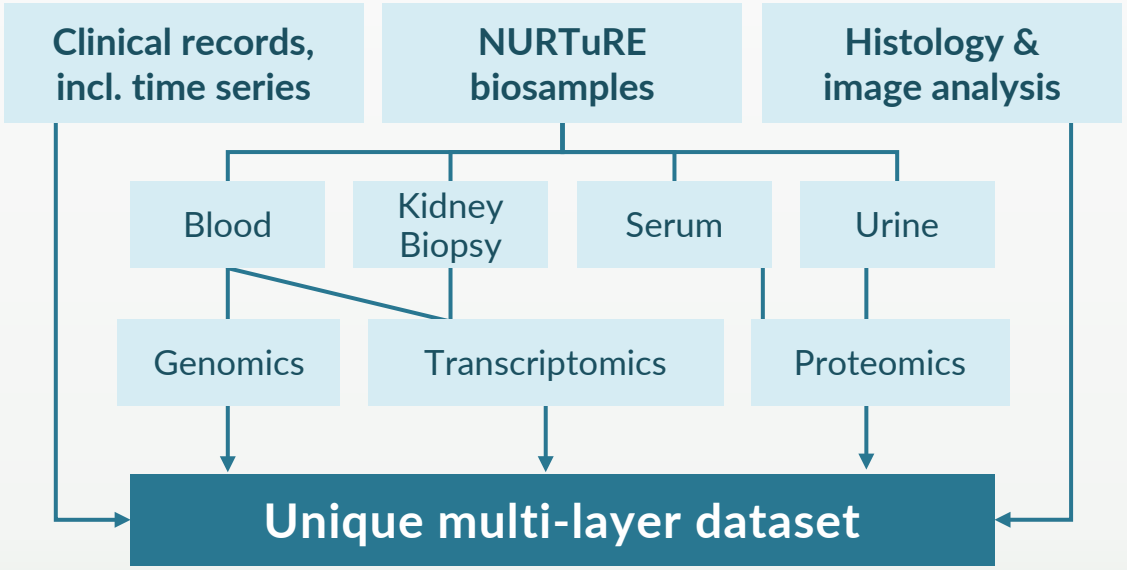
ASN Kidney Week, November 4, 2022

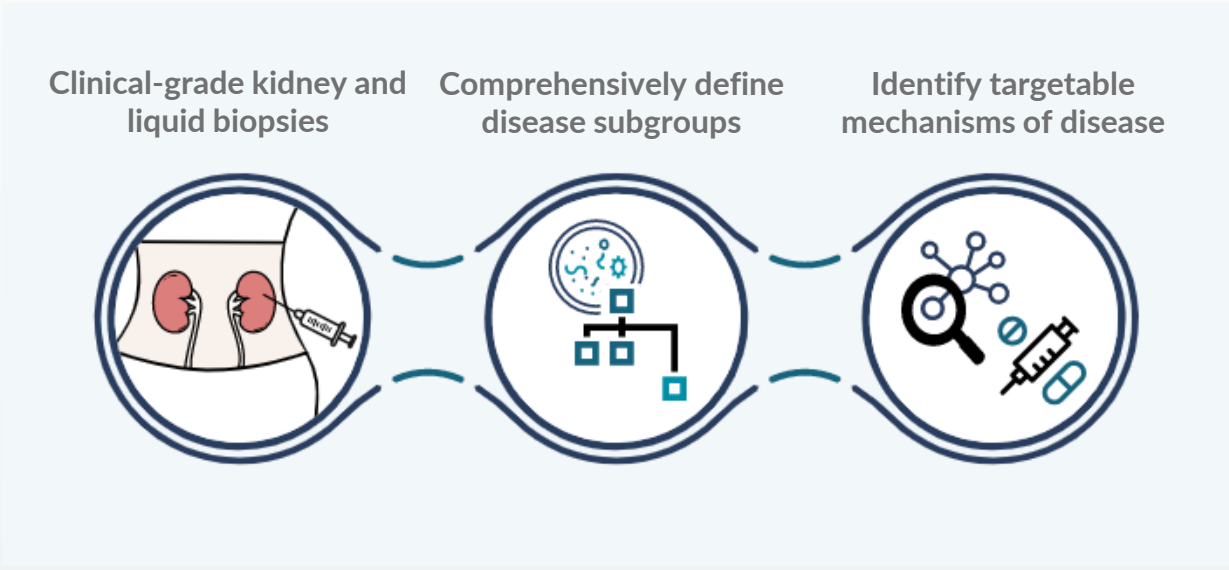
Integration of Real-World Clinical, Morphological and Molecular Data

KIDNEY WEEK 2022
Nov. 3–6 | Orlando, FL

Project Aims:

- The aim of this project is to use a multi-omics approach to the characterization of IgAN in the NURTuRE cohort, integrating clinical, histological, transcriptomic and serum proteomic data to gain deeper insights into patient stratification and disease biology.
- These learnings will be applied to clinical studies evaluating atrasentan, an endothelin receptor A antagonist, and BION-1301, an anti-APRIL antibody, for the treatment of IgAN.





https://www.nurturebiobank.org
Figure (lower left) adapted from Kidney Precision Medicine Project, accessed 4 May 2022, https://www.kpmp.org/about-kpmp

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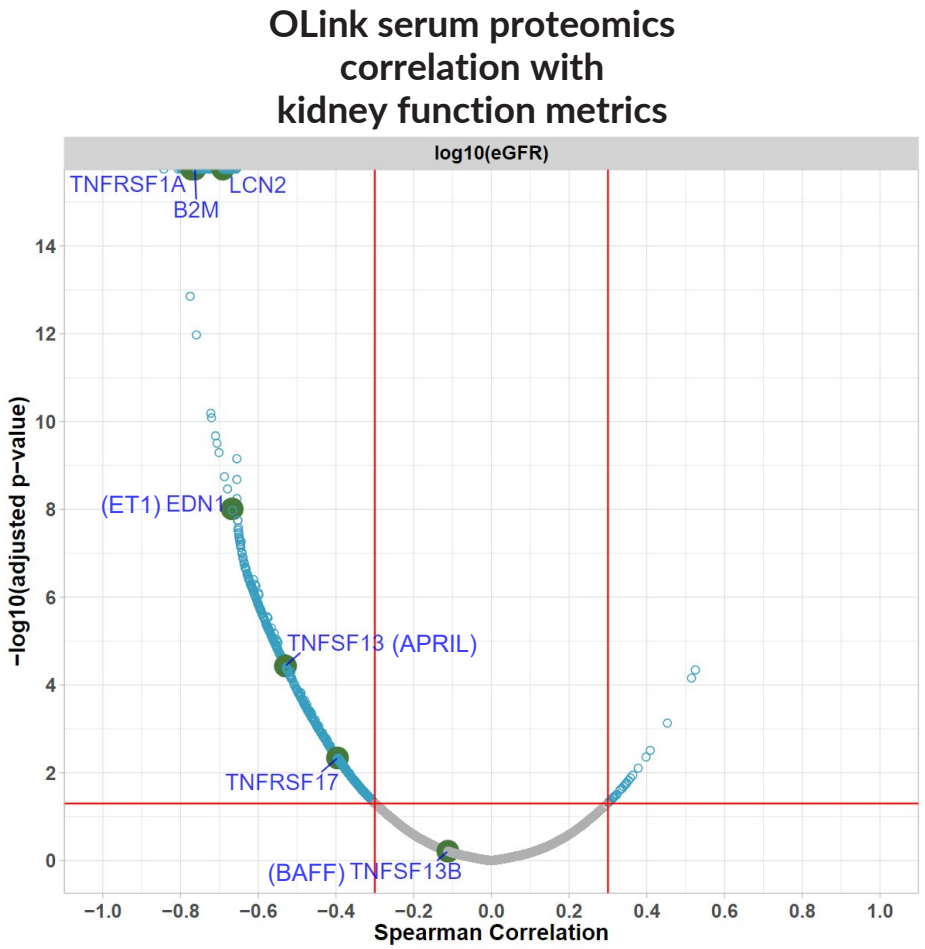
Serum Proteins Show Strong Relationship with Kidney Function



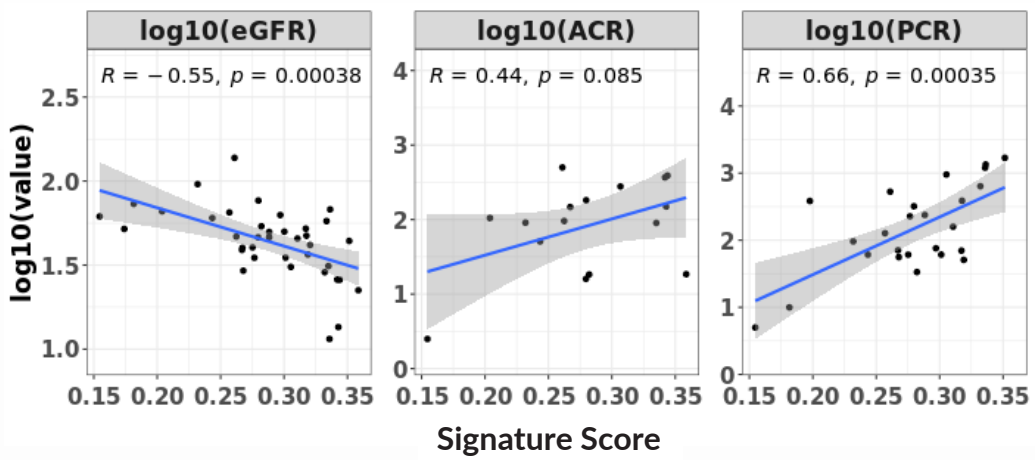
Highlight Select Targets with Significant Correlation
Significance Threshold: | Correlation | >=0.3; -log10(adjusted p-value) >=1.3

- In the NUTURE IgAN cohort, serum proteins had the strongest relationship with eGFR
  - Endothelin 1 (EDN1) is strongly and significantly correlated with eGFR
  - APRIL (TNFSF13) is strongly & significantly correlated with eGFR and is also correlated with UPCR
  - BAFF (TNFSF13B) is not significantly correlated with eGFR, UACR or UPCR

A Preclinical Model Derived Atrasentan Response Signature* is Correlated with Kidney Function

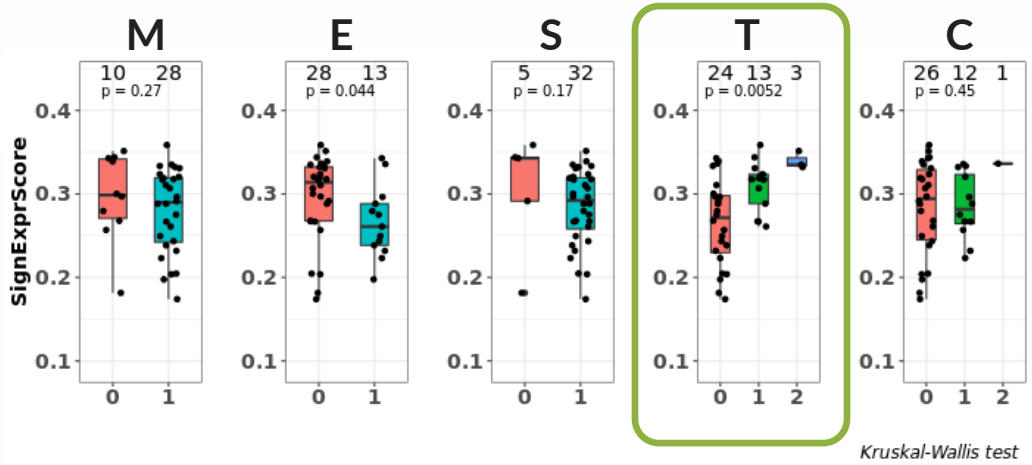
KIDNEY WEEK 2022 Nov. 3–6 | Orlando, FL

The atrasentan signature score from kidney biopsies is correlated with kidney function in the IgAN cohort



A 31-gene atrasentan response signature score was calculated using the gene expression data from kidney biopsies for the IgAN cohort. This score was correlated (spearman correlation test) with log10 eGFR, UACR and UPCR.

Increased atrasentan signature score is associated with tubular atrophy and interstitial fibrosis



A 31 gene atrasentan response signature derived from Failed Repair proximal tubule cells in the gddY IgAN model is significantly correlated with eGFR and UPCR in the IgAN cohort

The signature score is significantly higher in samples from subjects with an elevated T score

** See poster TH-PO419 for details*

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Future Plans

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Future steps	• Urine proteomics will be performed on matched urine samples from the NURTuRE IgAN cohort and used to identify urine biomarker for atrasentan signature score • Non-invasive surrogate biomarkers for the atrasentan response signature will be measured in atrasentan trials
Goals	• **To validate non-invasive surrogate biomarker strategy that can be used in clinical trials for atrasentan in IgAN and other indications** • **Assess the association of APRIL levels with baseline IgAN patient characteristics and kidney transcriptomics in support of patient stratification for BION-1301**

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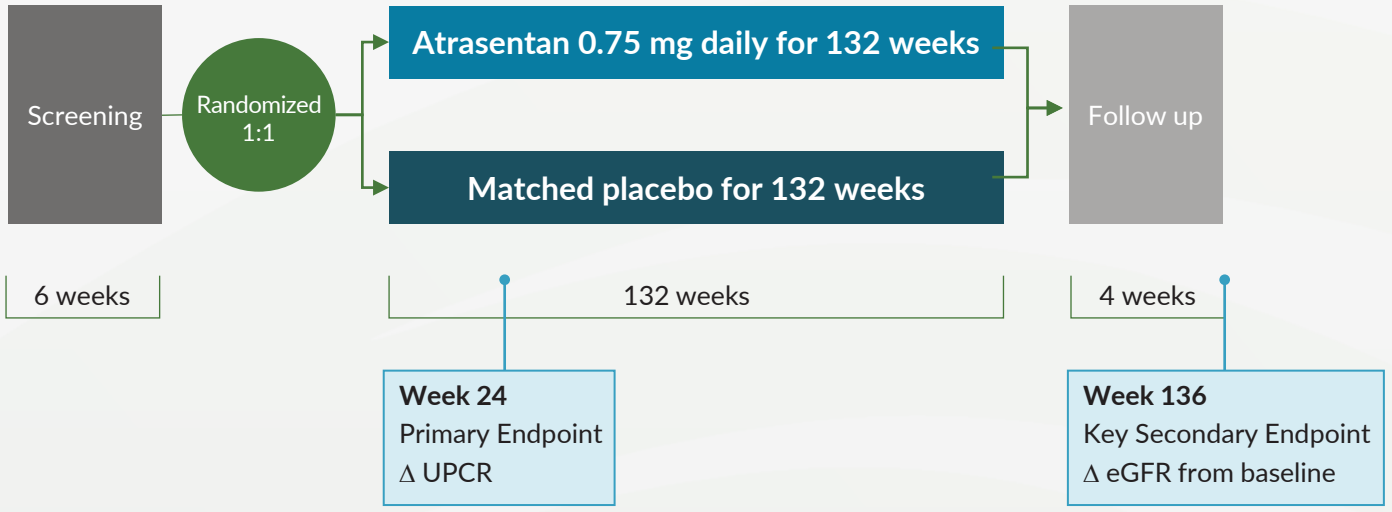
Atrasentan Program Update

Potent and Selective Endothelin A Receptor (ET_A) Antagonist

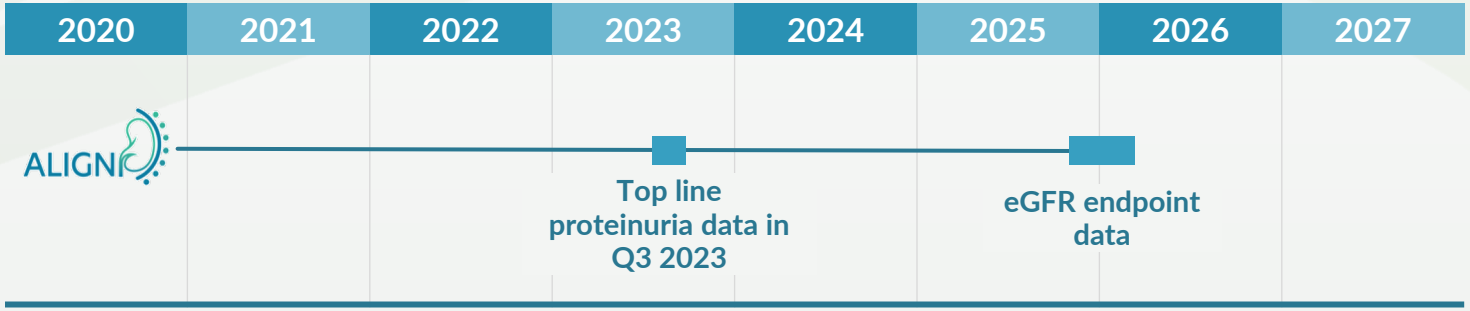
Phase 3 ALIGN Trial

Targeting patients with IgAN at high risk for disease progression

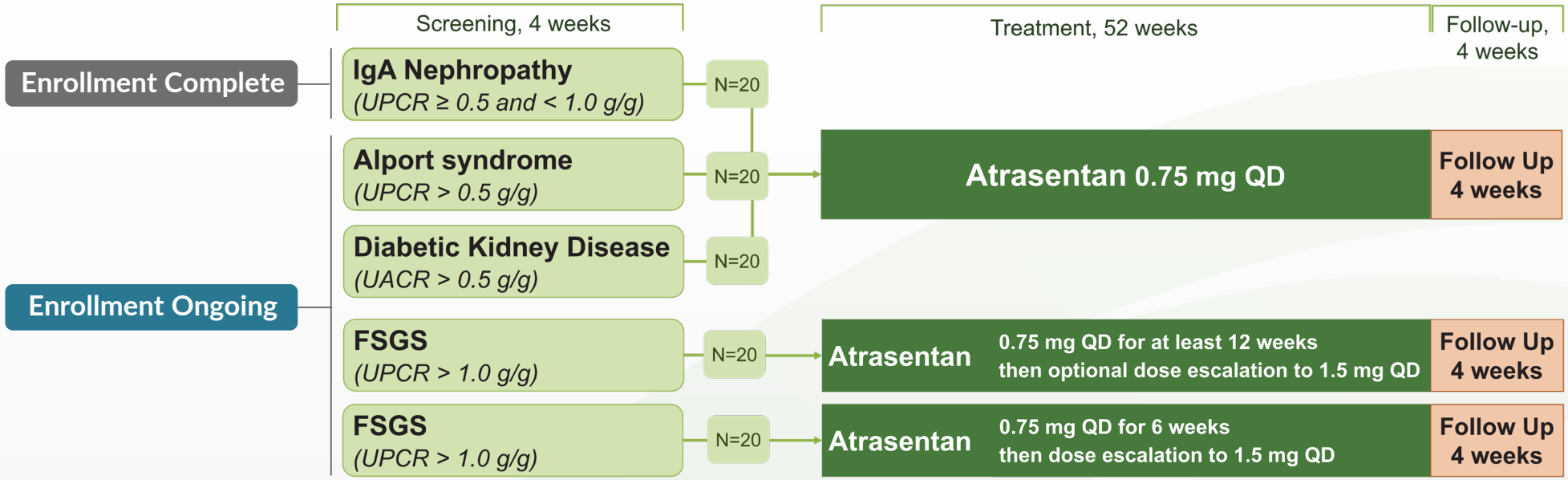
- Global double-blind placebo-controlled study (~170 sites)
- 320 patients, 1:1 randomization
- Biopsy-proven IgAN
- Patients on maximally-tolerated, optimized and stable dose of RASi, or RASi intolerant
- Proteinuria >1 g/day
- eGFR >30 ml/min/1.73m^2
- Primary endpoint 6-month proteinuria (accelerated approval)
- Secondary endpoint 2.5 year eGFR (full approval)



An additional stratum of up to 64 patients receiving a stable dose of SGLT2i for at least 12 weeks will be enrolled



Additional Atrasentan Clinical Trials Underway



AFFINITY

H1 2023 Phase 2 Study of Atrasentan + SGLT2i Combination in IgAN

- Data will support exploratory analysis from ALIGN atrasentan + SGLT2i combination strata
- Enroll IgAN patients at high risk for disease progression despite stable optimized RASi and stable SGLT2i
- Randomize patients 1:1 to placebo/atrasentan
- Primary endpoint: change in UPCR from baseline to week 12
- Goal is for data to support future use and is not required for approval

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BION-1301 Program Update

Anti-APRIL monoclonal antibody for patients with IgA nephropathy

BION-1301 Moving Forward

Plan to initiate pivotal trial in 2023, given strong clinical data and disease-modifying potential

Status

Cohort 1 in IgAN	450 mg IV → 600 mg SC q2w	Enrollment Completed
Cohort 2 in IgAN	600 mg SC q2w	Enrolling up to 30 patients

BION-1301

Continues to demonstrate disease-modifying potential, with rapid and durable reductions in IgA and Gd-IgA1 and clinically meaningful proteinuria reductions in patients with IgAN across Cohort 1 *(450 mg Q2W IV → 600 mg Q2W SC after 24 weeks)* **and Cohort 2** *(600 mg Q2W SC)*

Next Steps

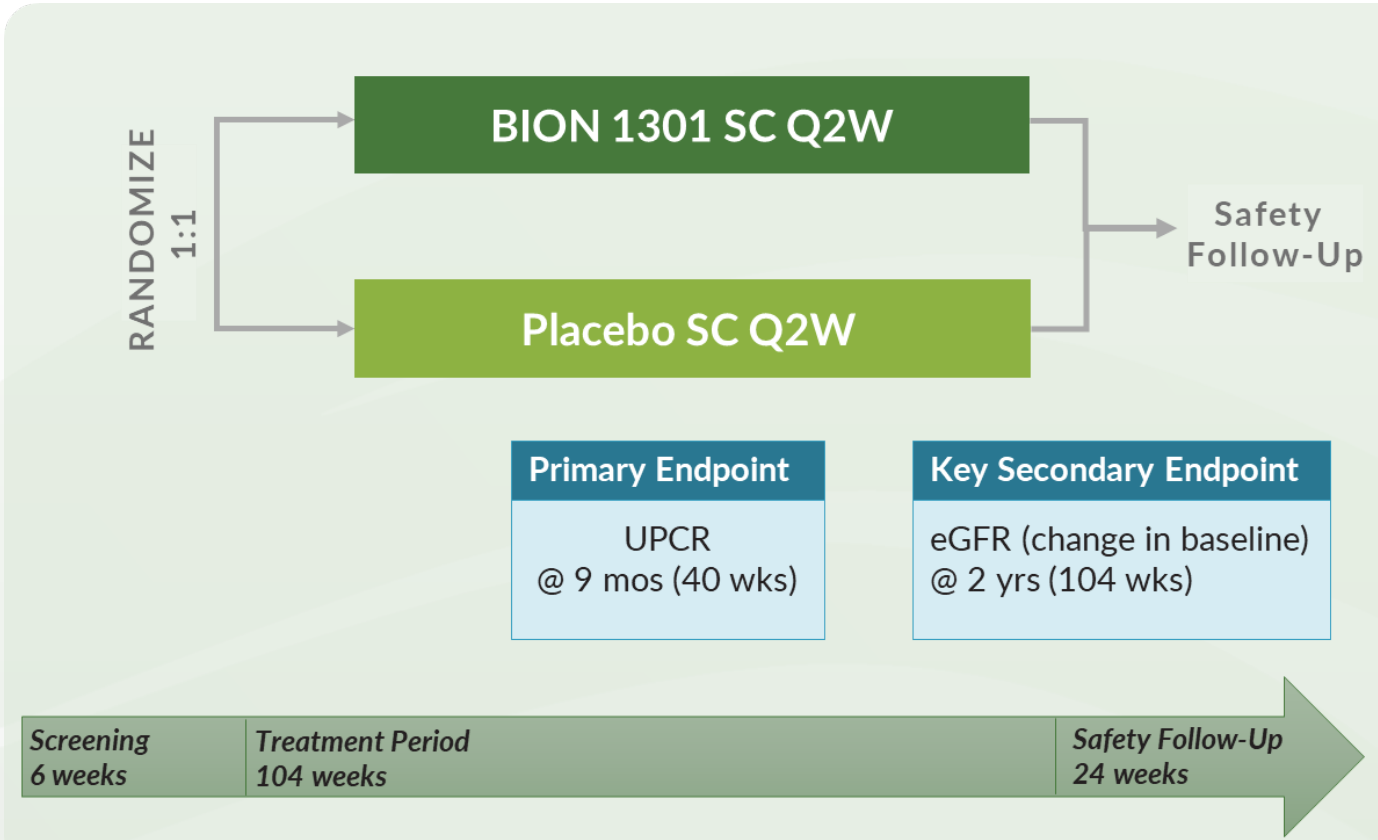
- Align with global health authorities *(ongoing)*
- Conduct site and country feasibility *(ongoing)*
- Initiate pivotal trial in 2023

Proposed BION-1301 Phase 3 Trial Design

Plan to initiate pivotal trial in 2023, given strong clinical data and disease-modifying potential

Proposed Phase 3 Targeting IgAN Patients at Risk for Disease Progression

- Global, double-blind, placebo-controlled
- 1:1 randomization
- Biopsy-proven IgAN
- Patients on maximally-tolerated, optimized and stable dose of RASi, or RASi intolerant
- Proteinuria >1 g/day
- eGFR >30 ml/min/1.73m2
- Primary endpoint 9-month proteinuria (accelerated approval)
- Secondary endpoint 2-year eGFR (full approval)



Trial design to be finalized following interactions with global health authorities

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Closing Remarks

Catalysts

Program	Indication	Catalyst	H1 2022	H2 2022	2023
Atrasentan	*IgA Nephropathy*	Present data from IgAN patient cohort of AFFINITY	✓	✓	
		Initiate phase 2 trial in combination with SGLT2i in IgAN			●
		Report topline proteinuria data from ALIGN in Q3 2023			●
	Glomerular Diseases	Present additional data from other AFFINITY cohorts			●
BION-1301	*IgA Nephropathy*	Present phase 1/2 data from Cohort 1 in IgAN	✓	✓	●
		Present phase 1/2 data from Cohort 2 in IgAN		✓	●
		Initiate phase 3 trial in IgAN			●
CHK-336	*Primary Hyperoxaluria*	Initiate phase 1 study in healthy volunteers	✓		
		Report phase 1 healthy volunteer data and advance towards initiation of phase 2 POC trials for patients with primary and idiopathic hyperoxalurias			●

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Q&A

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