CHINOOK THERAPEUTICS

Chinook Therapeutics

Developing Precision Medicines for Kidney Diseases

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Investor Webcast & Conference Call

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Today's Presenters

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President & CEO

Andrew King, DVM, PhD
Chief Scientific Officer

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

Jonathan Barratt, PhD, FRCP
Mayer Professor of Renal Medicine at
University of Leicester &
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Opening Remarks

Agenda

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FC052	Atrasentan for the Treatment of IgA Nephropathy: Interim Results from the AFFINITY Study	Muh Geot Wong, PhD
MO212	Updated Interim Results of a Phase 1/2 Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Clinical Activity of BION-1301 in Patients with IgA Nephropathy	Jonathan Barratt, PhD, FRCP
MO264	Selective Endothelin A Receptor Antagonist Atrasentan Attenuates Mesangial Cell Injury, Proteinuria and Intra-Renal Proliferative, Inflammatory and Fibrotic Transcrptional Networks in a Rat Model of Mesangioproliferative Glomerulonephritis	Andrew King, DVM, PhD
FC080	A Systems Nephrology Framework for the Molecular Classification of Chronic Kidney Disease	
Atrasentan Program Update		Charlotte Jones-Burton, MD, MS
BION-1301 Program Update		
Closing		Eric Dobmeier
Q&A		

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

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1 Hallym University Sacred Heart Hospital; 2 MTN Kidney and Hypertension; 3 Kyung Hee University Medical Center; 4 Royal Brisbane & Women's Hospital;
5 Tufts Medical Center Keck-USC; 6 Keck- USC School of Medicine; 7 Chinook Therapeutics, Seattle, WA , USA; 8 Concord Repatriation General Hospital

Disclosures for Presenting Author:

Current Employer:	Concord Repatriation General Hospital, Sydney, Australia
Honoraria:	Baxter, Amgen, AstraZeneca, CSL Behring, Dimerix, Otsuka, Chinook and Travere
Scientific Advisor or Membership:	Member of the Steering Committee for PROTECT, DUPLEX and VISIONARY trials

Previous Employer, the George Institute for Global Health, holds research contracts for trials in cardiovascular and/or kidney disease in Asia Pacific region

IgA Nephropathy (IgAN): A Potentially Progressive, Chronic Glomerular Disease with Limited Treatment Options

#1

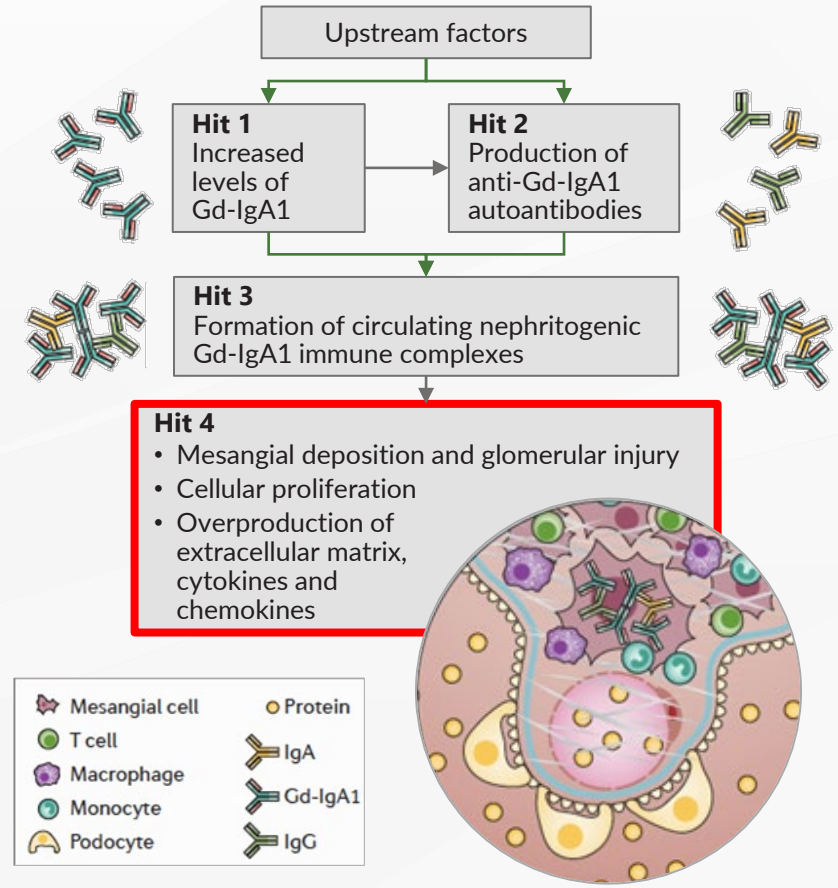
IgAN is the most common primary glomerulonephritis globally, though it is considered a rare disease

ESKD
30-45%

End-stage kidney disease (ESKD) is developed by about **30-45%** of IgAN patients over a period of 20-25 years

Limited treatment options for high-risk patients:

- RAS inhibition (ACEi/ARB) is frontline (KDIGO 1B)
- Steroids & immunosuppressive agents:
  inconsistent therapeutic benefit and accompanied by significant side effects (KDIGO 2B); Tarpeyo (budesonide) recently approved
- DAPA-CKD:
  suggests benefit of SGLT2i in non-diabetic CKD, including IgAN



Pathogenic model of IgA nephropathy

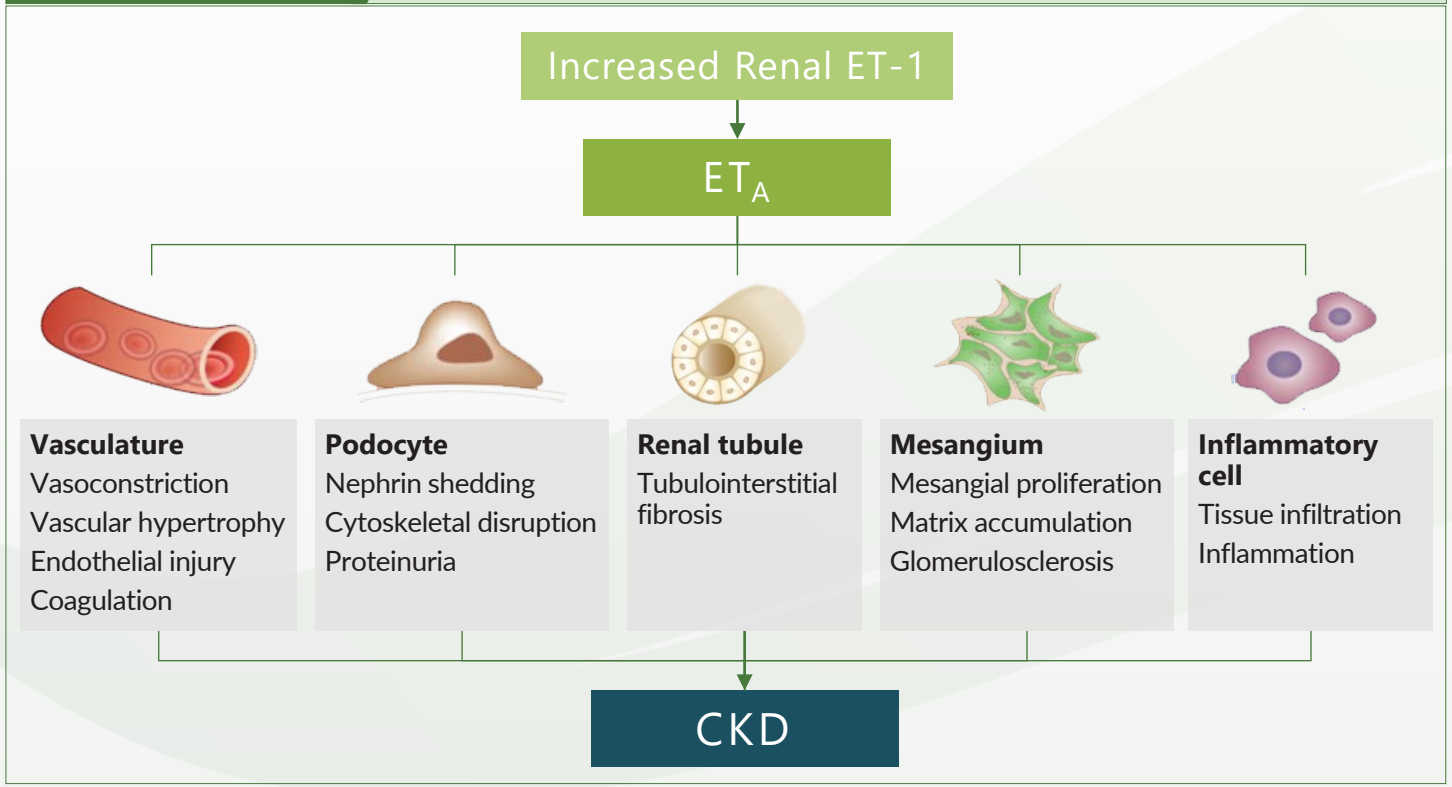
Wyatt, R. J., & Julian, B. A. (2013). IgA nephropathy. New England Journal of Medicine, 368(25), 2402-2414.
Lai, K., Tang, S., Schena, F. et al. IgA nephropathy. Nat Rev Dis Primers 2, 16001 (2016).

Endothelin System Activation in IgAN Disease Progression

ET_A activation reported to result in:

- Mesangial cell activation
- Proteinuria
- Kidney inflammation & fibrosis

… all hallmark characteristics of IgAN



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

Intense glomerular and TI ET-1 expression in IgAN patients with significant proteinuria

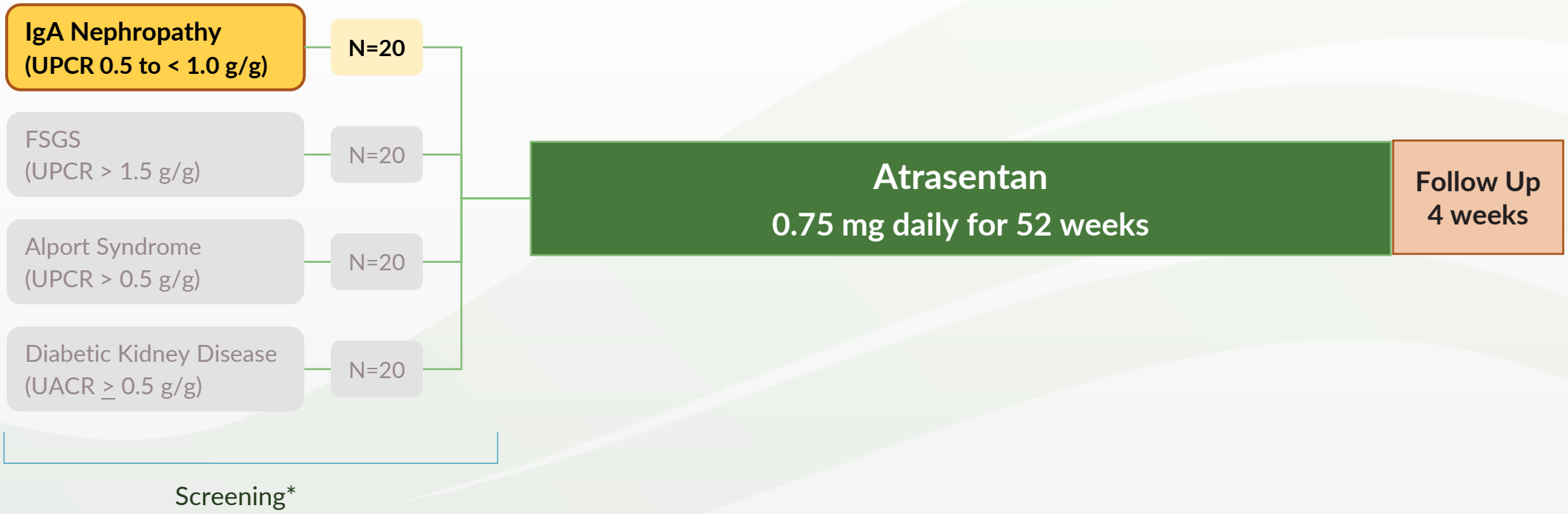
Blockade of the ET_A receptor with potent and selective **ET_A antagonist** atrasentan, represents a potential approach to treat IgAN patients at high risk of progression (**Hit 4**)

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.

AFFINITY Study Design:
Atrasentan in Patients With Proteinuric Glomerular Diseases

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



* Stable RASi for all cohorts (in addition to stable SGLT2i for diabetic kidney disease)
All cohorts eGFR ≥ 30 ml/min/1.73m2, except for DKD ≥ 45 ml/min/1.73m2

AFFINITY Study Protocol; ClinicalTrials.gov Identifier: NCT04573920

Study Methods

Key Eligibility Criteria

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

Receiving a maximally tolerated and optimized dose of a **RAS inhibitor** that has been stable for at least 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 m²

Key Study Endpoints

Primary Endpoint

- **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

AE type, incidence, severity, seriousness and relatedness

* Biopsy could have occurred at any point in time prior to study.
AE, adverse event; MMRM, mixed-effects model repeated measures (fixed effects of visit and baseline in UPCR)

Demographics & Baseline Characteristics

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)
BMI (kg/m2)	*Median (Q1, Q3)*	26.2 (24.8, 29.2)

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)
Brain Natriuretic Peptide (pg/mL)	12.5 (8.8, 42.0)

Baseline Characteristics (cont)	Median (Q1, Q3)
UPCR, First morning void at screening (g/g)	0.63 (0.54, 0.70)
24-hour UPCR (g/g)	0.80 (0.73, 1.10)
24-hour urine protein excretion (g/day)	1.17 (0.85, 1.46)
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

Safety and Tolerability

To date*, atrasentan has been well-tolerated in patients with IgAN (n=20)

AE Category	n (%)
Subjects with any TEAE	16 (80)
Any TEAE occurring in N>1 subjects	
COVID-19	5 (25)
Peripheral edema	2 (10)
Any Moderate TEAE	6 (30)
Any Severe TEAE	0 (0)
TEAE leading to discontinuation (headache)	1 (5)
SAE (traffic accident unrelated to study drug)	1 (5)

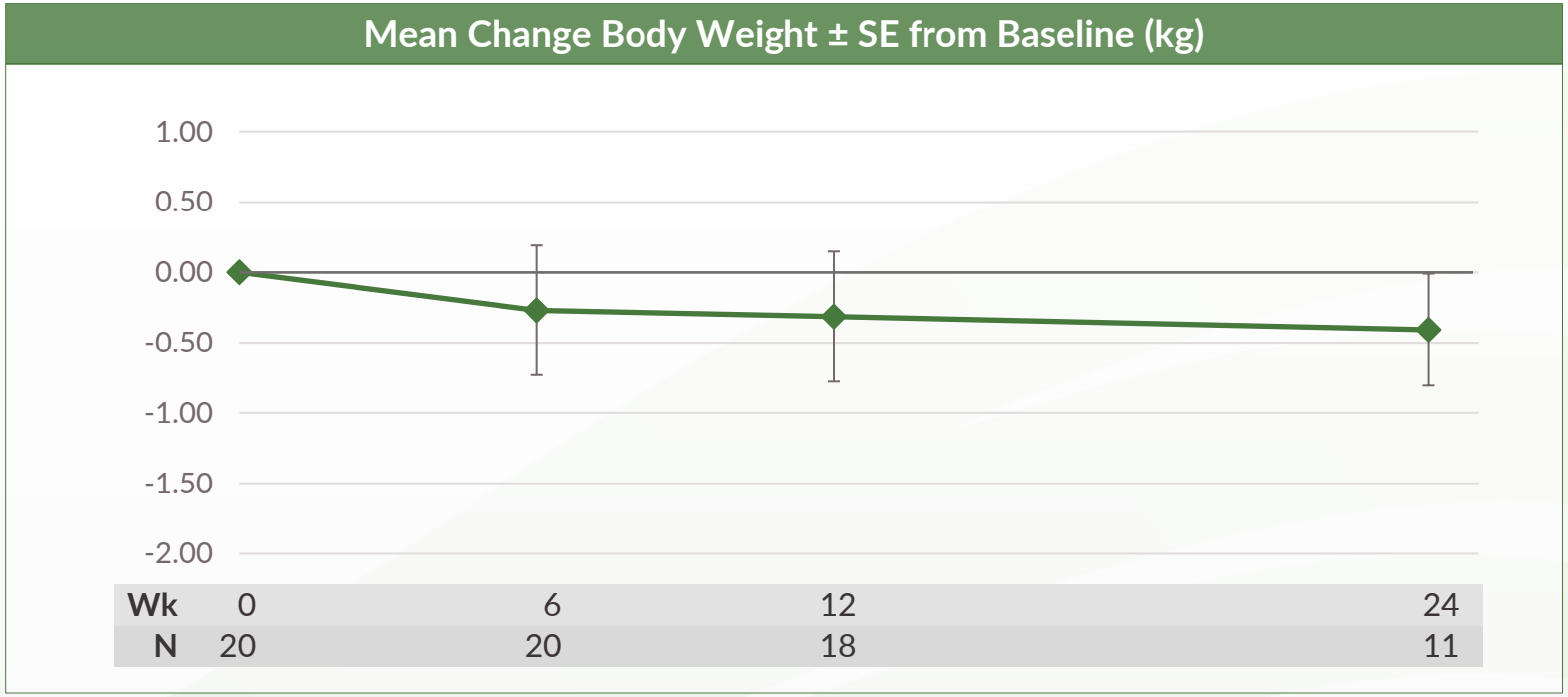
AE Category	n (%)
Treatment-related AE	5 (25)
Moderate related AE	3 (15)
Headache	1
Creatinine increase	1
Peripheral edema	1

- **No SAEs related to study drug to date**

18/20 patients remain on treatment, with time on treatment ranging from 6-52 weeks.
One patient discontinued treatment and one patient has completed 52 weeks.

*Data cut-off: April 22, 2022. AE, adverse event; TEAE, treatment-emergent adverse event; SAE, serious adverse event.

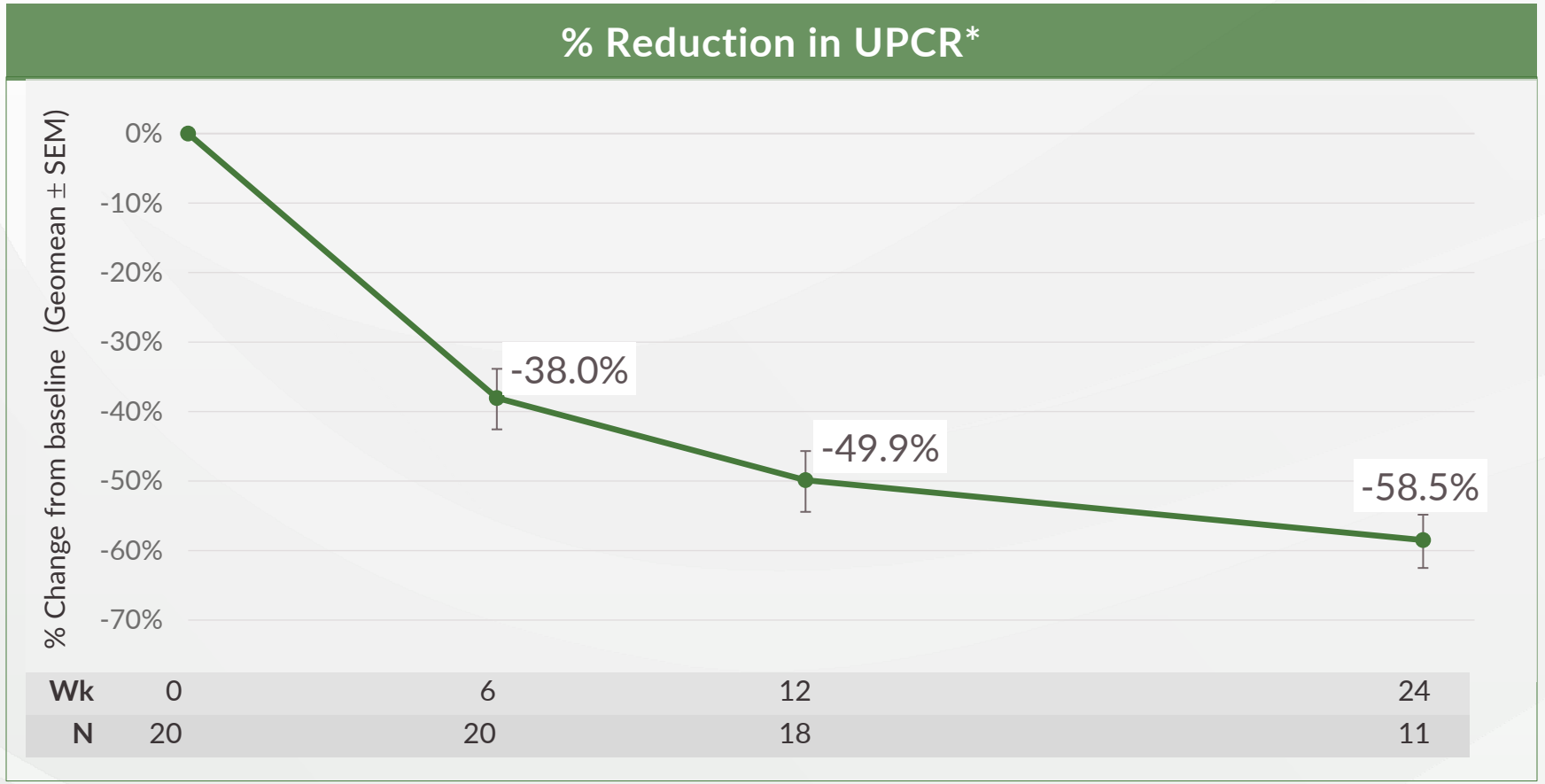
No Evidence of Significant Fluid Retention



- 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 m^2 averaged across Weeks 2 and 6)

Atrasentan Provides Clinically Meaningful Proteinuria Reduction in Patients with IgAN Receiving Optimized SOC

AFFINITY



Median baseline 24-h urine protein excretion: 1.17 g/day (Q1,Q3: 0.85, 1.46 g/day)

*Results plotted are based on the least squares mean +/- SE of change from baseline on natural log scale from the MMRM back-transformed to a percent reduction from baseline scale

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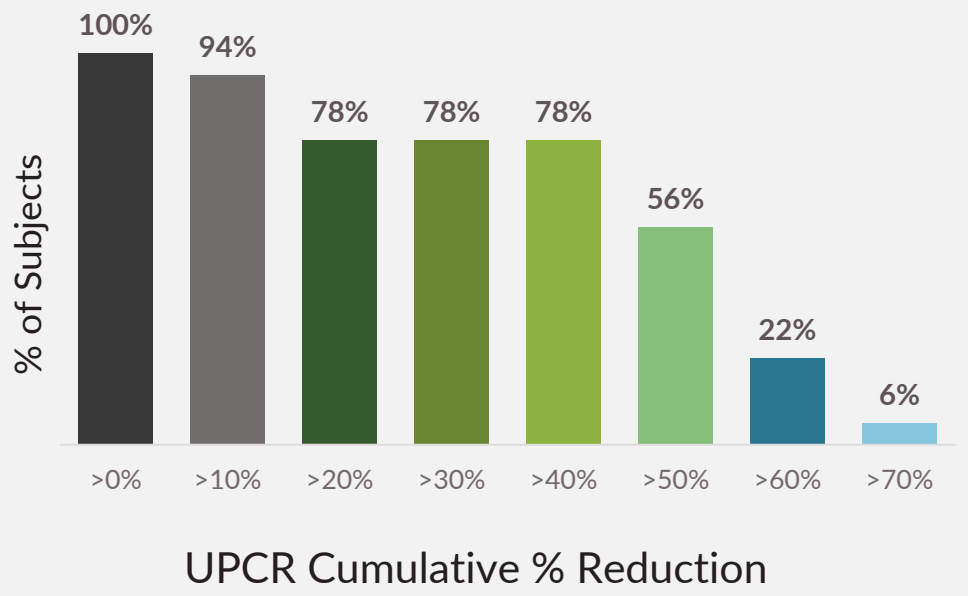
Atrasentan Provides Clinically Meaningful Proteinuria Reduction in Patients with IgAN Receiving Optimized SOC

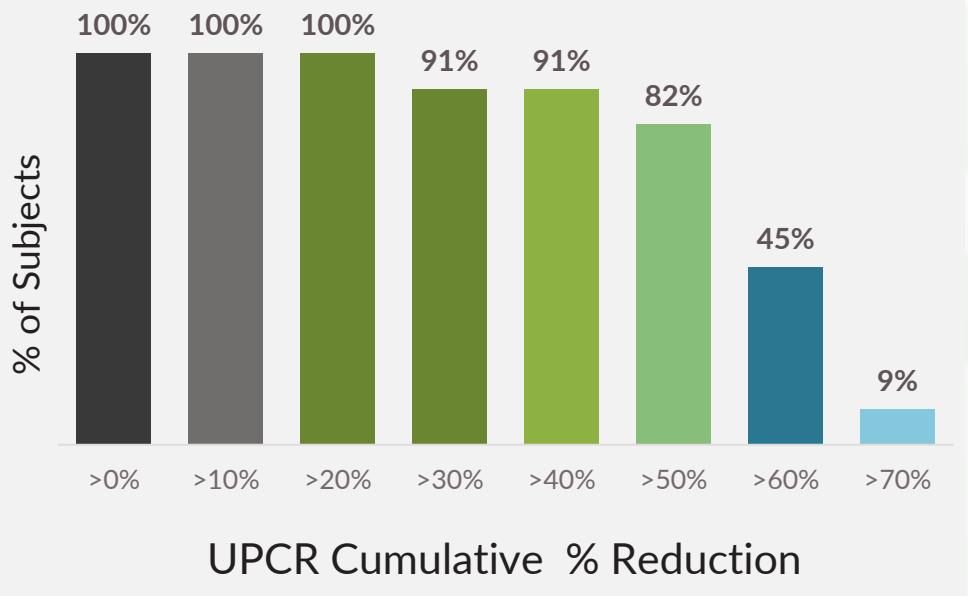
AFFINITY

- **91%** of patients achieved >40% reduction in proteinuria at Week 24

Week 12 (n=18)



Week 24 (n=11)



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Treatment with Atrasentan Provides Clinically Meaningful Proteinuria Reduction and is Well-tolerated in Patients with IgAN

AFFINITY

Interim AFFINITY IgAN data:

- In this Phase II study with 20 patients, 70% of patients had baseline total urine protein >1g/day despite optimized SOC treatment, representing an IgAN population at high risk for 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 and acute eGFR, suggesting proteinuria reductions were not primarily due to hemodynamic effects of atrasentan
- Generally well-tolerated with no treatment-related SAEs
- There was no increase in BNP and mean bodyweight, suggesting minimal fluid retention

This interim analysis demonstrates that atrasentan provides proteinuria reductions in patients with IgAN who remain at risk for progression with residual proteinuria despite optimized standard-of-care treatment.

ALIGN phase 3 trial of atrasentan in patients with IgAN is currently enrolling (NCT04573478)
Inclusion:

- eGFR ≥ 30 mL/min/1.73 m^2
- Total urine protein ≥ 1 g/day based on 24-hour urine collection at screening

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Updated interim results of a phase 1/2 study to investigate the safety, tolerability, PK, PD, and clinical activity of BION-1301 in patients with IgA nephropathy

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Disclosures for Presenting Author

Current Employer:	University of Leicester
Consultancy:	Chinook, EMD Serono, Omeros, Calliditas, Novartis, Retrophin, Visterra, Alnylam, Dimerix, George Clinical, and Astellas
Research Funding:	Novartis, GlaxoSmithKline, Calliditas, Visterra, Chinook, and Retrophin
Honoraria:	AstraZeneca
Scientific Advisor or Membership:	Editorial Board of Kidney International, Clinical Journal of the American Society of Nephrology, and Clinical Science

Role of APRIL and BION-1301 in IgA Nephropathy

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

Potentially disease-modifying mechanism to deplete Gd-IgA1 (**Hit 1**) and prevent pathogenic immune complex formation (**Hit 3**)[1]

A PRoliferation **I**nducing **L**igand (**APRIL**) is a TNF-family cytokine involved in B-cell signaling via TACI and BCMA receptor activation[2]

Higher APRIL levels in IgAN patients is correlated with higher Gd-IgA1 and proteinuria and lower eGFR[2]

APRIL gene variants confer increased risk of IgAN[3]

The ongoing phase 1/2 trial is investigating BION-1301 in patients with IgAN (NCT03945318)

Objectives

- Safety, tolerability, PK, biomarker effects and preliminary effect on proteinuria
- Proof of mechanism
- Proof of concept
- Explore dose/schedule, intravenous (IV) and subcutaneous (SC) administration

Key Eligibility Criteria, Cohort 1

- Biopsy-proven IgAN 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 > 45 mL/min per 1.73 m^{2*}
- Stable on an optimized dose of RASi for ≥ 3 months prior to screening (or intolerant to RASi)

* Or 30 to 45 mL/min/1.73m^2 if kidney biopsy performed within 2 years prior to Day 1 does not provide evidence of glomerular fibrosis

Cohort 1	n=10	450 mg Q2W IV up to 52 wks ‡	Completed
Cohort 2	n=10	600 mg Q2W SC up to 52 wks	Enrolling

‡Patients transitioned to SC at ≥24 wks

1. Suzuki et al. *JASN*. 2011; 22(10), 1795-1803. 2. Zai et al. *Medicine*. 2016; 95(11), e3099. 3. Magistroni et al. *Kidney Int*. 2015; 88(5), 974-89.
BCMA, B-cell maturation antigen; TACI, transmembrane activator and calcium-modulator and cyclophilin ligand.

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Patient Disposition, Interim Safety and PK/PD

Demographics (n=10)		
Age, years	*Median (min, max)*	39 (27, 59)
Sex, male	*n (%)*	9 (90)
Race, white	*n (%)*	10 (100)
Ethnicity, Hispanic	*n (%)*	2 (20)
Country, US	*n (%)*	10 (100)

Baseline Characteristics	*Median (min, max)*
Time from biopsy, years	2.0 (0.2, 3.4)
Blood pressure (mmHg) – Systolic **– Diastolic**	127 (113, 133) 83 (69, 88)
eGFR (mL/min/1.73 m^2)*	69 (30, 122)
24-hour urine protein excretion (g/day)†	1.22 (0.74, 6.47)
24-hour UPCR (g/g)†	0.52 (0.41, 4.55)
Renin-angiotensin system inhibitor use	100 %

Safety

- BION-1301 well tolerated in IgAN patients to date*, with no serious AEs and no treatment discontinuations due to AEs
- 3 patients experienced mild (grade 1) treatment-related AEs, including 1 injection site reaction
- 4 patients experienced mild infections (grade 1), considered not related to treatment
- IgG level below the study defined threshold occurred in one patient, necessitating protocol-mandated withholding of study drug. There have been no infections reported in this patient.

PK/PD

- Rapid reductions in free APRIL confirm durable target neutralization sustained through 1 year
- No anti-drug antibodies observed in patients with IgAN to date
- All patients have transitioned to SC administration for a mean SC treatment duration of 22 weeks (range 5 to 28 weeks)

*Data cut-off May 6, 2022, with exception of biomarker data cut-off March 10, 2022. AEs, adverse events

* eGFR by CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration, n=8; †n=8

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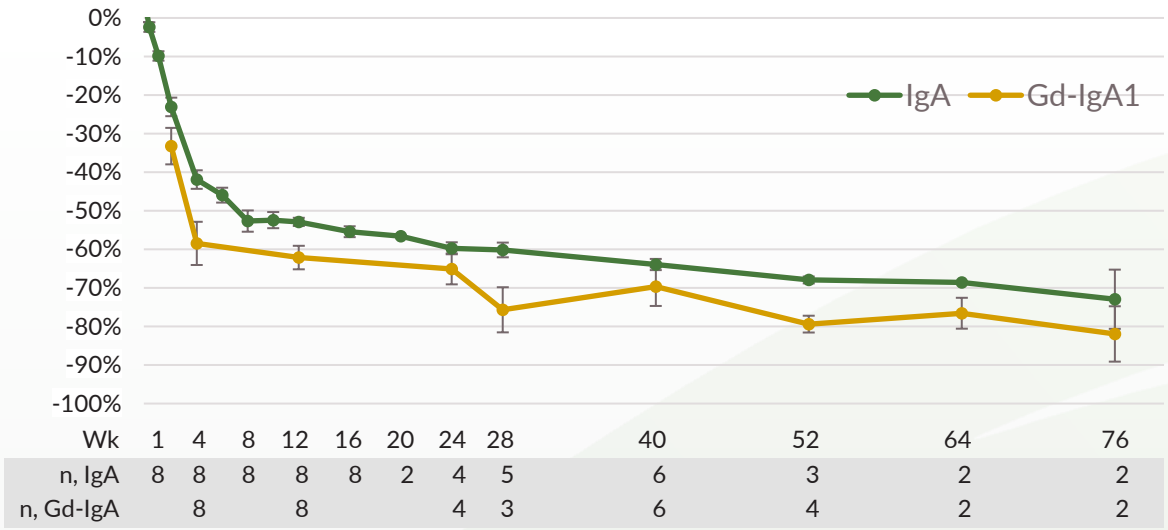
BION-1301 Durably Reduces IgA and Gd-IgA1

IgA and Gd-IgA1

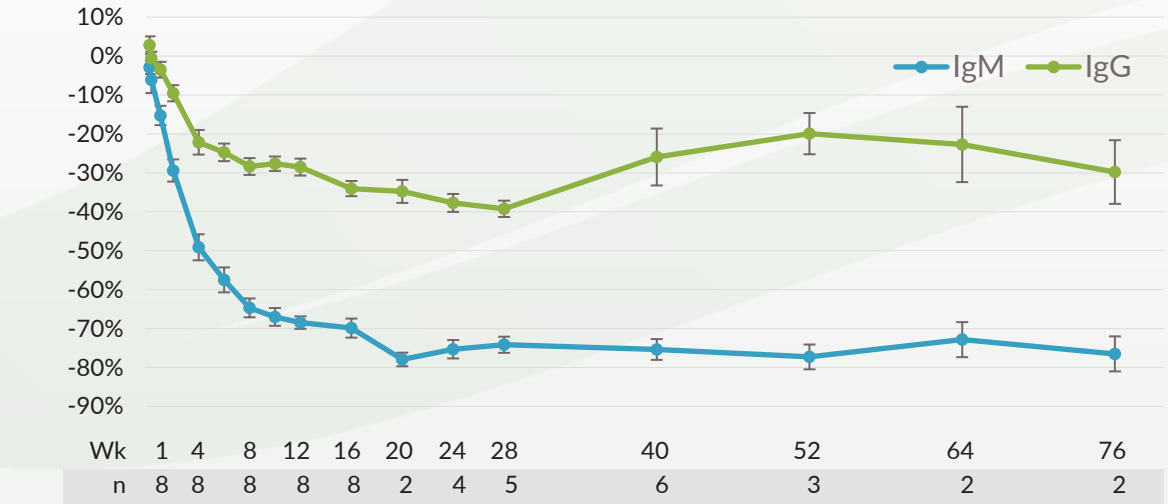
% change from Baseline
(Mean ± SEM)



Wk	1	4	8	12	16	20	24	28	40	52	64	76
n, IgA	8	8	8	8	8	2	4	5	6	3	2	2
n, Gd-IgA		8		8			4	3	6	4	2	2

IgM and IgG

% change from Baseline
(Mean ± SEM)



Wk	1	4	8	12	16	20	24	28	40	52	64	76
n	8	8	8	8	8	2	4	5	6	3	2	2

- BION-1301 durably reduces IgA, IgM, and to a lesser extent, IgG in patients with IgAN
- BION-1301 also produces sustained reductions in Gd-IgA1, the pathogenic IgA variant (Hit 1), demonstrating the potential disease-modifying mechanism of BION-1301
- 6/8 patients have IgA measurements following SC transition; mean SC treatment duration of 15 weeks (range 12-20 weeks) at the most recent IgA measurement

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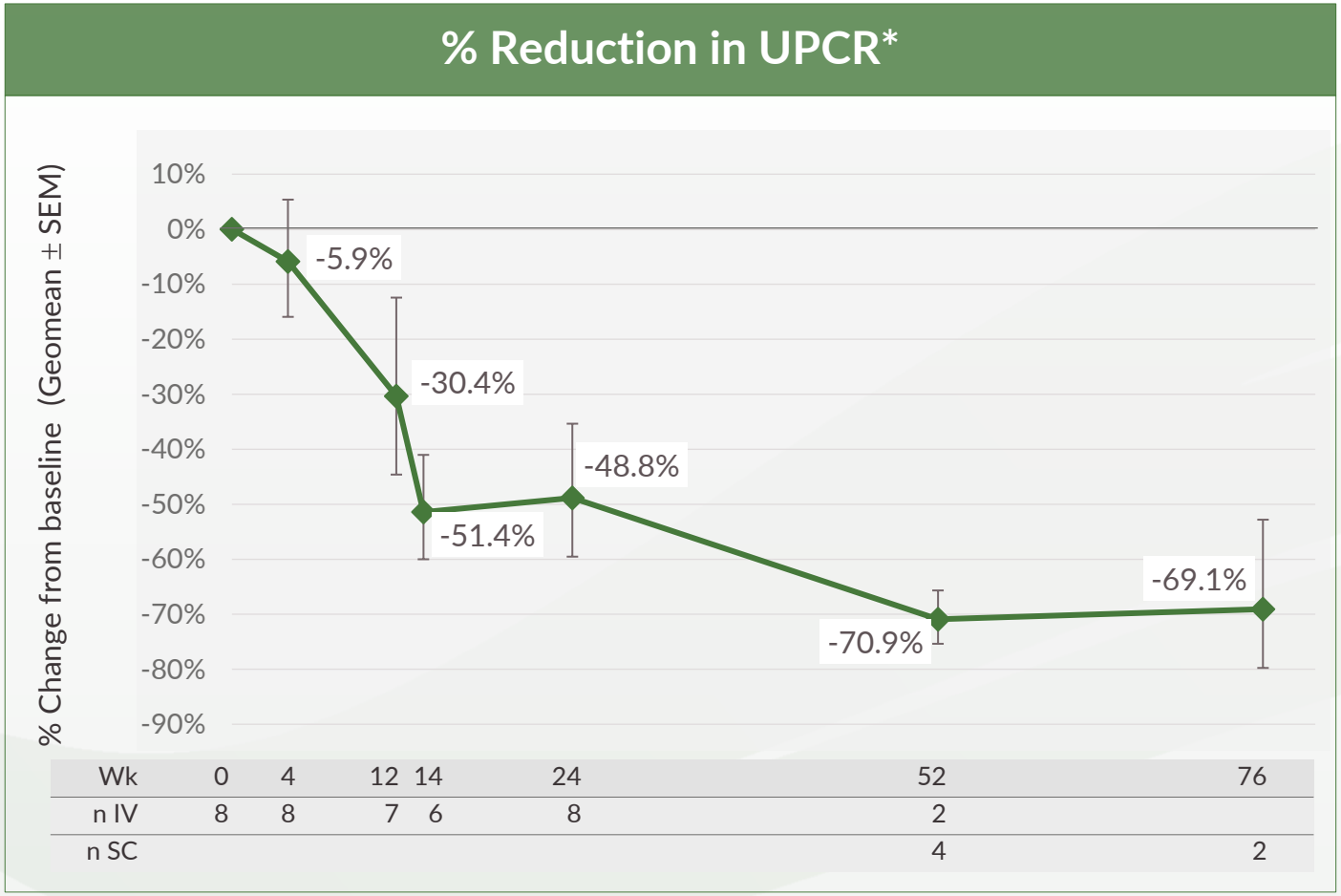
BION-1301 Treatment Results in Sustained, Clinically Meaningful Proteinuria Reductions



Median baseline 24-h urine protein excretion: 1.22 g/day (range: 0.74 - 6.47 g/day)

- BION-1301 treatment results in proteinuria reductions within 3 months, which are sustained and continue to decline through one year in patients across a range of disease severity
- 6/8 patients have proteinuria measurements following SC transition; mean SC treatment duration of 17 weeks (range 5-24 weeks) at the most recent proteinuria measurement
- 4 patients at the week 52 proteinuria measurement had transitioned to SC dosing for 12-24 weeks (mean 20 weeks); 2 patients at week 76 had 5 and 19 weeks of SC dosing, respectively

*Results plotted are based on the least squares mean +/- SE of change from baseline on natural log scale from the MMRM back-transformed to a percent reduction from baseline scale

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

Interim BION-1301 IgAN patient data:

- All patients have transitioned to SC dosing and BION-1301 remains well-tolerated, with no treatment discontinuations due to AEs
- Clinically meaningful sustained reductions in proteinuria (24-hour UPCR) within 3 months
- Rapid and sustained free APRIL reductions
- Durable reductions in Gd-IgA1, IgA and IgM, with smaller reductions in IgG
- No anti-drug antibodies have been observed

These data provide early 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**

➢ **Preliminary response is consistent in patients transitioning from IV to SC**

Next Steps: **Enrollment of patients with IgAN is ongoing for Cohort 2, utilizing subcutaneous injection of BION-1301**

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Selective Endothelin A Receptor Antagonist Atrasentan Attenuates Mesangial Cell Injury, Proteinuria and Intra-Renal Proliferative, Inflammatory and Fibrotic Transcriptional Networks in a Rat Model of Mesangio-proliferative Glomerulonephritis

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All authors: Chinook Therapeutics

Disclosures for Presenting Author

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Consultancy:	None
Research Funding:	None
Honoraria:	None
Scientific Advisor or Membership:	None

Mesangial Cell Activation is the Initiating Intra-Renal Response to Glomerular IgA Immune Complex Deposition in IgA Nephropathy

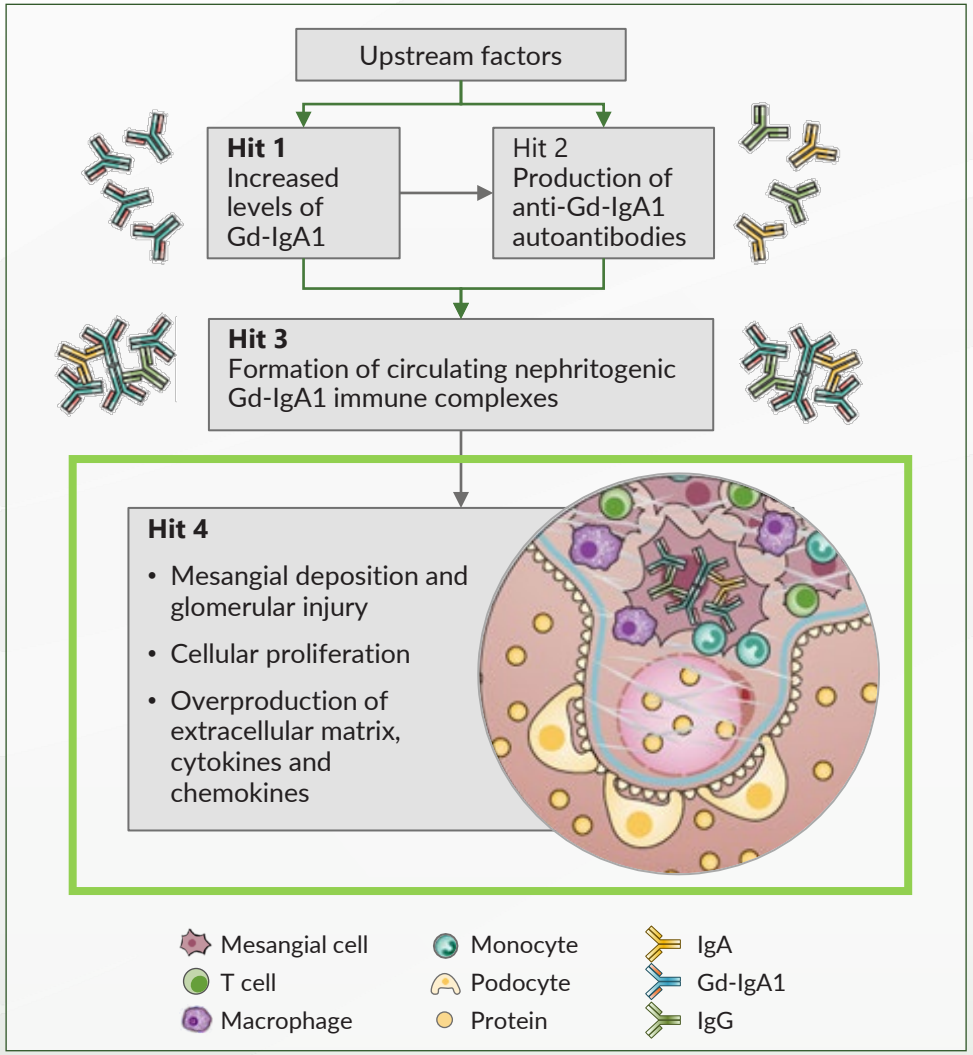
Mesangial cell (MC) activation is characterized by:

- Cellular proliferation
- Overproduction of extracellular matrix and inflammatory cytokines and chemokines

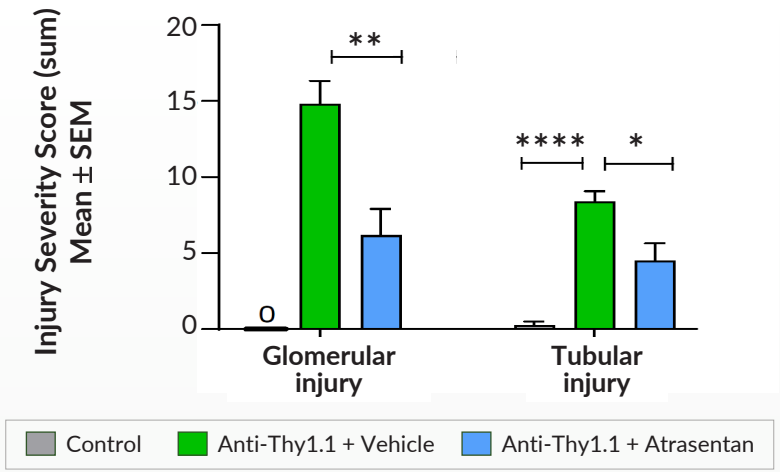
Cellular crosstalk results in podocyte injury and proteinuria, the strongest predictor of IgAN progression

Subsequent tubulointerstitial inflammation and fibrosis leads to progressive kidney function loss

The **molecular pathways** responsible for MC activation and subsequent podocyte injury/proteinuria following glomerular IgA-complex deposition have **not been well-defined**



Effect of Atrasentan in a Rat Model of Mesangio-Proliferative Glomerulonephritis (MPGN)

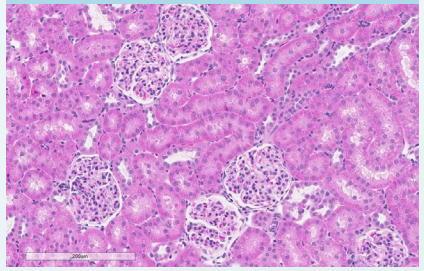


Glomerular injury score includes mesangial hypercellularity and matrix expansion, adhesions, segmental mesangiolysis and glomerulosclerosis

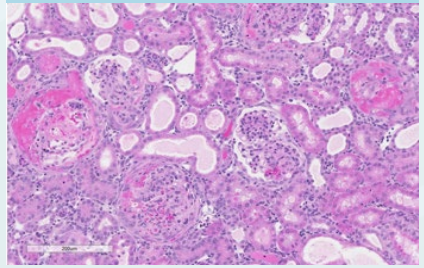
Tubulointerstitial injury score includes protein casts, tubular degeneration, tubular dilation and interstitial fibrosis

Atrasentan attenuated mesangial cell response, glomerular injury and secondary tubulointerstitial injury

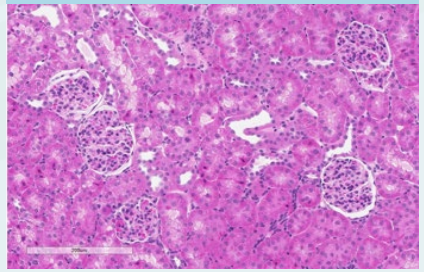
Vehicle + Vehicle



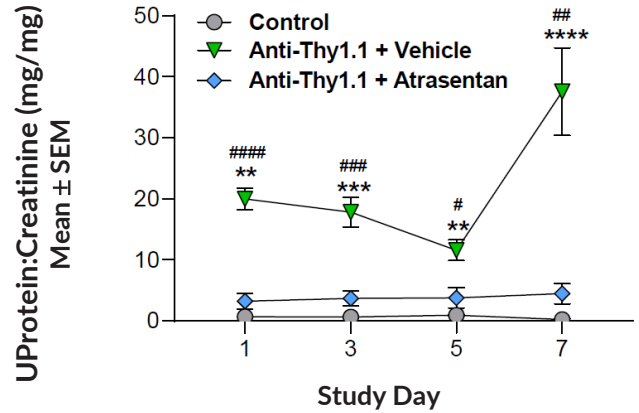
Anti-Thy1.1 + Vehicle



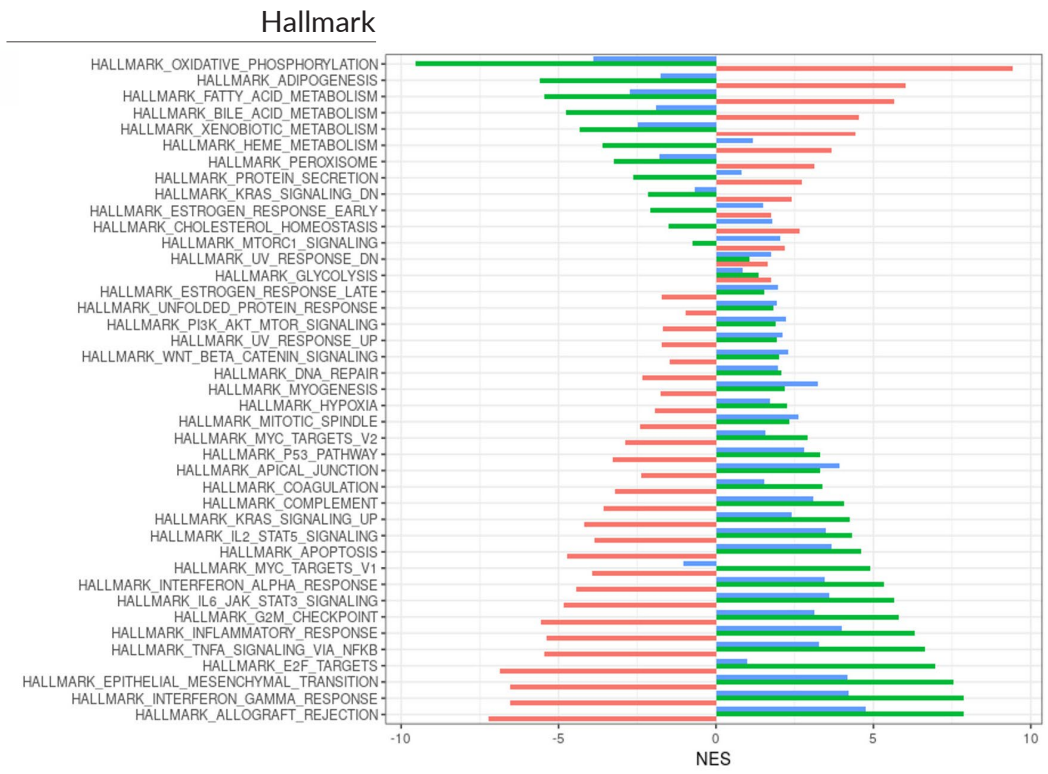
Anti-Thy1.1 + Atrasentan



Atrasentan reduced anti-Thy1.1 induced proteinuria



Atrasentan Reverses Transcriptomic Changes Induced in MPGN Model That are Also Observed in IgAN Patients



Atrasentan reverses Hallmark gene set expression enrichments induced in the anti-Thy1.1 rat model of mesangioproliferative GN, most of which are also observed in the glomerular transcriptome of IgAN patients in the NEPTUNE cohort (GSE104066)

This study suggests an important role of the ET_A receptor in MC activation, subsequent proteinuria and activation of pathogenic proliferative, inflammatory and fibrotic intra-renal transcriptional networks in MPGN

This further supports the therapeutic potential of atrasentan, a selective ET_A receptor antagonist, to attenuate mesangial cell activation, proteinuria and pathogenic intra-renal signaling in MPGNs such as IgAN

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#RESEARCHNEVERSTOPS

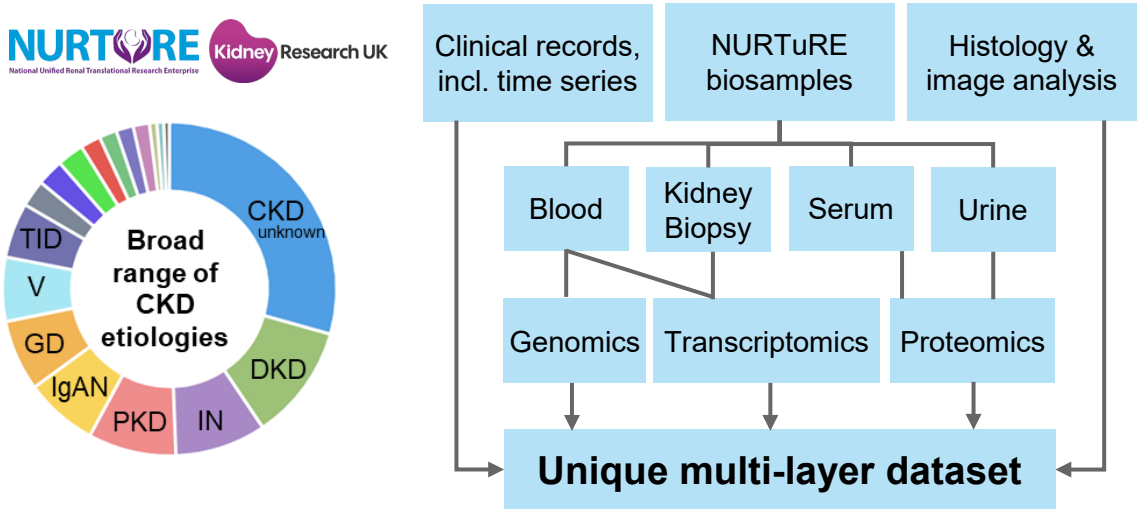
A Systems Nephrology Framework for the Molecular Classification of CKD

Tobias Bohnenpoll, Eric Olson, Mykola Dergai, Jennifer Cox, Simone Romoli, I-Ju Lo, Johannes Pospiech, Krishan Vishnolia, Mark McConnell, Marvin Gunawan, Michaela Bayerlová, Nicolette Honson, Niklas Michel, Nikolas Stroth, Olivier Radresa, Philipp Skroblin, Priyanka Kohli, Seamus Ragan, Shenshen Lai, Steven Bromidge, David Powell, Uwe Andag and Andrew King

Evotec SE and Chinook Therapeutics, 59th ERA Congress, 20.05.2022

A systems nephrology framework for the molecular classification of CKD

Integration of real-world clinical, morphological and molecular data



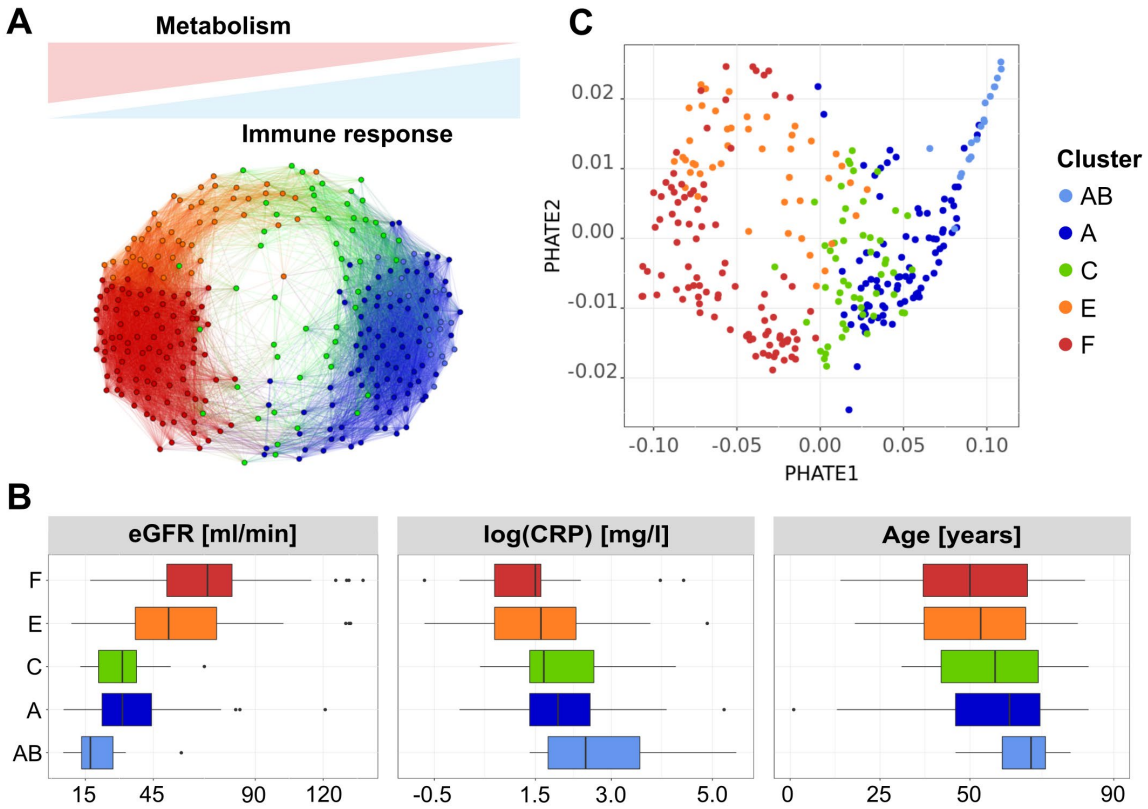
- Conventional stratification by clinical and histopathological phenotypes is insufficient to describe the heterogeneity of chronic kidney diseases (CKD)
- Integration of intra-renal molecular and morphological features with clinical outcomes is required to drive discovery of disease-modifying therapies
- The NURTuRE biobank comprises matched patient samples from a broad range of diagnoses and kidney functional states, that are associated with rich clinical data

We aim to generate mechanistic disease understanding for a patient-centric, integrated target and biomarker discovery that will enable the development of novel precision treatments

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

Unsupervised analysis reveals molecular similarities and transitions that align with disease progression

Definition of molecular clusters and disease trajectories from biopsy transcriptomes



- Unsupervised clustering of kidney transcriptomes via self organizing maps[1] inferred 5 groups with distinct molecular landscapes (F, E, C, A and AB) that were generally consistent with molecular clusters previously described for CKD[2]
- Correlation of metagenes reveals a highly polarized global data structure resulting from strong opposing metabolic and immune signatures (Figure A)
- Molecular stratification aligns with clinical disease progression, but can not be fully explained by conventional parameters (Figure B)
- PHATE[3] dimensionality reduction suggests molecular similarities and transitions that can be interpreted as molecular disease trajectories (Figure C)

Molecular stratification aligns with disease progression irrespective of clinical diagnosis, reflecting common cellular and molecular mechanisms of disease

1) Loeffler-Wirth H, Kalcher M, Binder H (2015). "oposSOM: R-package for high-dimensional portraying of genome-wide expression landscapes on Bioconductor." *Bioinformatics*.
2) Reznichenko A, Nair V, Eddy S et al. (2021). "Molecular Stratification of Chronic Kidney Disease" *medRxiv*. doi.org/10.1101/2021.09.09.21263234
3) Moon K, van Dijk D, Wang Z et al. (2019). "Visualizing structure and transitions in high-dimensional biological data" *Nature Biotechnology*.

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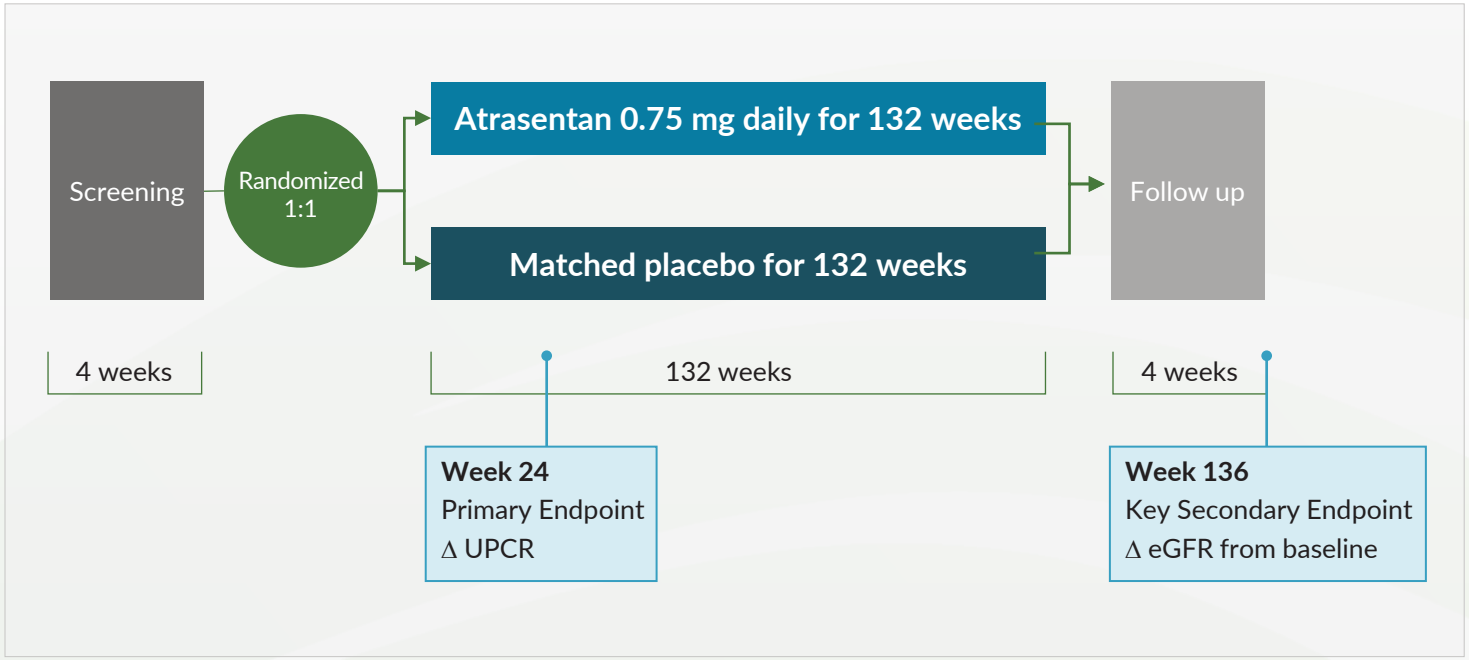
Atrasentan Program Update

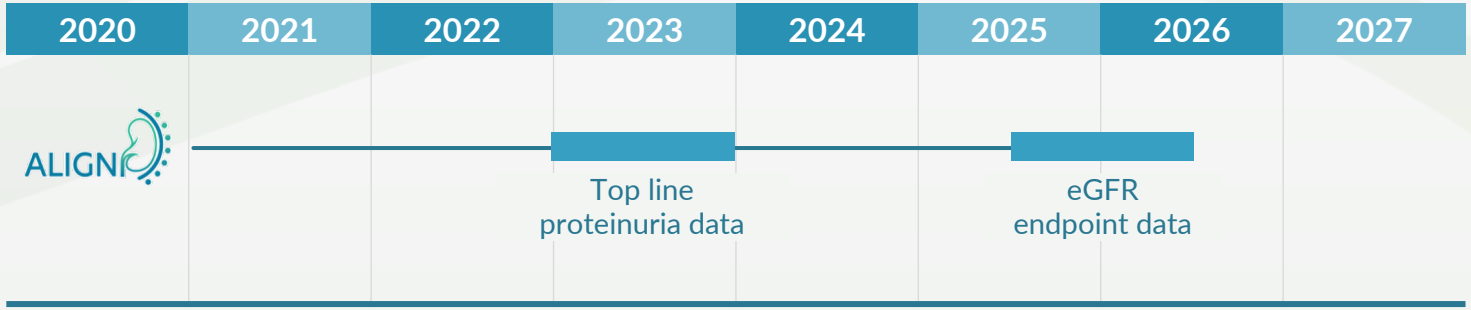
Potent and Selective Endothelin A Receptor (ET_A) Antagonist

Phase 3 ALIGN Trial

Targeting patients with IgAN at high risk for disease progression

- Biopsy-proven IgAN
- Patients on maximally-tolerated, optimized and stable dose of RASi, or RASi intolerant
- Proteinuria >1 g/day and eGFR >30 ml/min
- ~320 pts, 1:1 placebo randomization
- Global study with ~160 – 170 sites
- 6-month proteinuria primary endpoint (accelerated approval)
- 2.5 year eGFR secondary endpoint (full approval)





Phase 2 AFFINITY Trial Update

IgA Nephropathy (UPCR 0.5 to < 1.0g/g)

- Enrollment completed
- H2 2022 update will include additional analysis of IgAN patient cohort

Alport Syndrome (UPCR > 0.5 g/g)

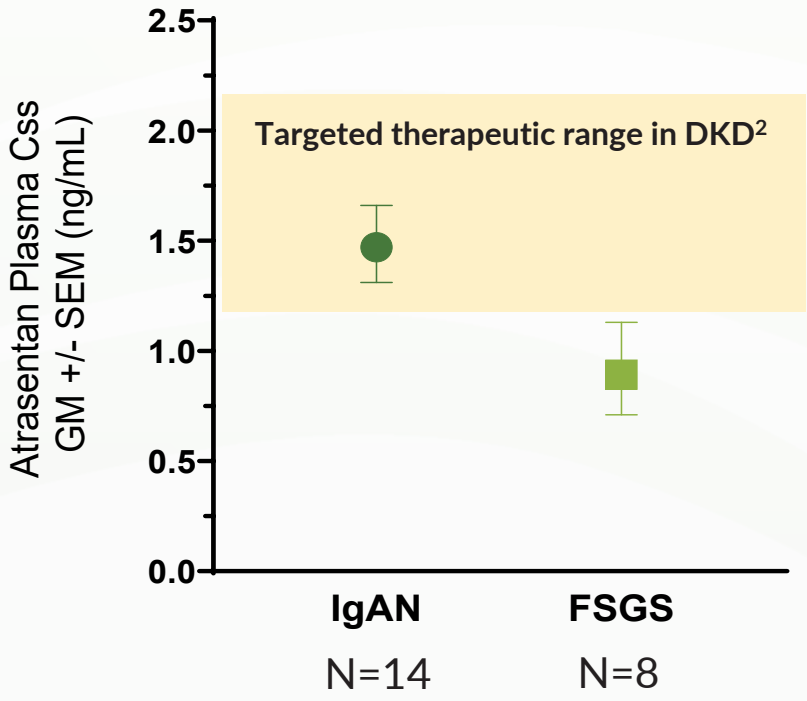
Diabetic Kidney Disease (UACR ≥ 0.5 g/g)

FSGS (UPCR ≥ 1 g/g)

- Enrollment ongoing
- Data in H2 2022 contingent on enrollment and maturity of data at the time of presentation

- Encouraged by observations to date in FSGS patient cohort
- However, exposures in FSGS at 0.75 mg are lower than the therapeutic target achieved in IgAN
- Escalating the dose to 1.5 mg in FSGS is anticipated to achieve exposures in the targeted therapeutic range to optimize proteinuria reductions
- Protocol amendment executed for FSGS cohort to enable dose escalation to 1.5 mg and lowered UPCR inclusion criteria of ≥1 g/g to enroll more patients with secondary FSGS

Atrasentan Phase 2 AFFINITY Preliminary PK: IgAN vs. FSGS[1] (GM ± SEM)



1. Preliminary PK data as of Jan 20, 2022 (last sample analyzed); 2. Koomen, JV, et al., Diabetes Obes Metab. 2018; 20: 2019– 2022.

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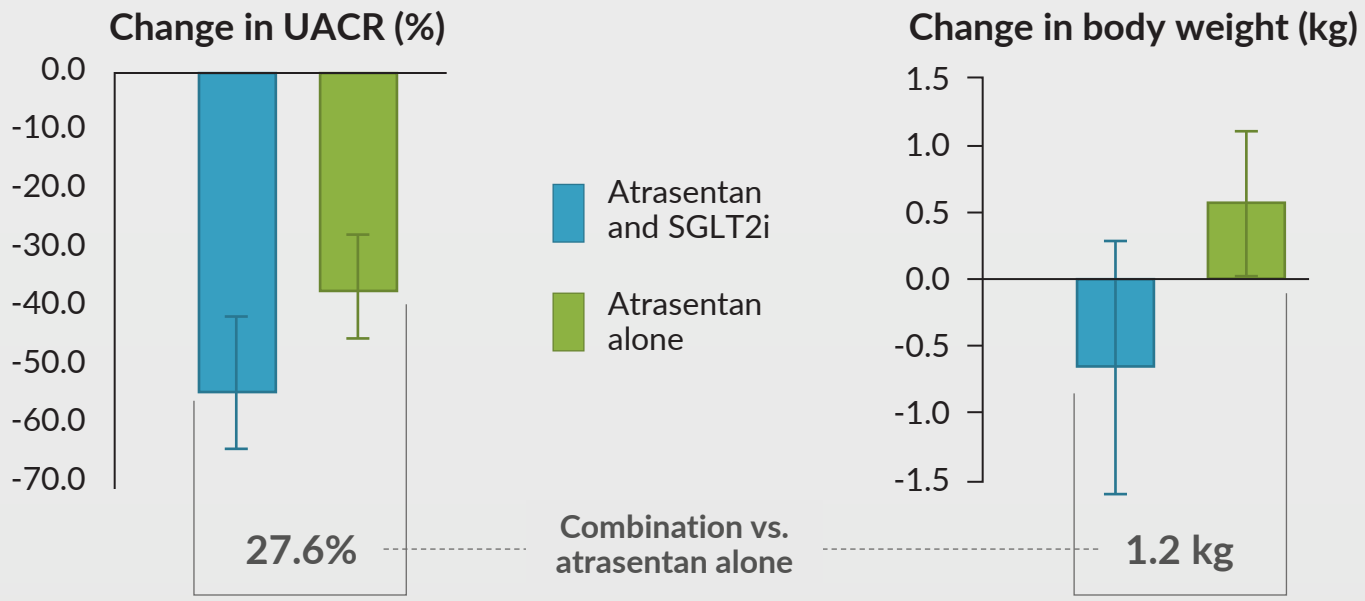
Evaluating Atrasentan + SGLT2i in IgAN Patient Population

SONAR data supports exploration of long-term efficacy of combination in IgAN

Physician uptake of SGLT2i in patients with IgAN is increasing

Proteinuria and kidney protection effects of both drug classes may be complementary due to distinct mechanisms of action, while diuretic effects of SGLT2i may offset potential fluid retention with atrasentan

SONAR post-hoc analysis showed that in patients with DKD, six-weeks of treatment with atrasentan combined with SGLT2i vs. atrasentan alone **further decreased albuminuria** and **decreased body weight**, a surrogate for fluid retention



Atrasentan is well-positioned to be combined with SGLT2i due to:

- ✓ Low hemodynamic effect
- ✓ Non-immunosuppressive

Near-term plans to conduct:

- ✓ ALIGN SGLT2i + atrasentan combination stratum
- ✓ Phase 2 study of SGLT2i + atrasentan in IgAN

Heerspink HJL, et al., Kidney Int. 2021 Feb;99(2):346-349.

Atrasentan + SGLT2i Combination Strategy in IgAN

Establish atrasentan as combination of choice with SGLT2i by evaluating safety and efficacy

Two-pronged approach to evaluate atrasentan in combination with SGLT2i

1 ALIGN SGLT2i + Atrasentan Combination Stratum

- Executed protocol amendment to enable enrollment of stratum of patients on stable dose of SGLT2i
- Allows for safety and efficacy exploratory analysis (UPCR at 24 weeks and eGFR at 136 weeks) with no change to enrollment timelines or primary analysis population

2 Phase 2 Study of SGLT2i + Atrasentan Combination in IgAN

- Data will corroborate exploratory analysis from ALIGN SGLT2i + atrasentan 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 q2w**	**Enrollment Completed**
Cohort 2 in IgAN	**600 mg SC q2w**	10 patients enrolled, with option to enroll up to 20 patients
Optional Cohort 3	Considering optional Cohort 3 at SC dose and schedule TBD; not gating for pivotal trial initiation	

BION-1301

Continues to demonstrate ~50% proteinuria reductions in patients with IgAN after three to six months of treatment, with ~70% reductions observed in six patients at one year and two patients at 1.5 years of treatment

Next Steps

- Determine optimal SC dose and schedule for pivotal trial based on data from phase 1/2 cohorts
- Finalize pivotal trial design and align with regulatory authorities
- Provide additional updates on development strategy in H2 2022
- Initiate pivotal trial in 2023

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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			●
	Glomerular Diseases	Present additional data from AFFINITY		●	●
BION-1301	*IgA Nephropathy*	Present additional phase 1/2 IV/SC data from Cohort 1 in IgAN	✓		
		Present phase 1/2 SC data from Cohort 2 in IgAN		●	●
		Initiate pivotal trial in IgAN			●
CHK-336	*Primary Hyperoxaluria*	Initiate phase 1 study in healthy volunteers	✓		
		Report phase 1 healthy volunteer data and initiate phase 2 POC trial in patients with primary hyperoxaluria			●

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Q&A

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