Chinook Therapeutics

Developing Precision Medicines for Kidney Diseases

ASN Kidney Week 2021
Investor Webcast & Conference Call
November 4, 2021

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Today's Presenters

Eric Dobmeier
President & CEO

Andrew King, DVM, PhD
Chief Scientific Officer

Alan Glicklich, MD
Chief Medical Officer

Jonathan Barratt, PhD, FRCP
Mayer Professor of Renal Medicine at
University of Leicester &
Leicester General Hospital, UK

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

Agenda

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PO1593	Precision Medicine Approach Identifies Patients with IgA nephropathy at Risk for Progression Using Endothelin Activation Signatures	
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BION-1301 Program Update		Alan Glicklich, MD
Closing		Eric Dobmeier
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PO1633

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Atrasentan Exhibits a Consistent, Predictable Pharmacokinetic Profile Among Healthy Asian Adults

Anjay Rastogi[1], Jicheng Lv[2], David Catanzaro[3], Vincent Tong[3], Yusuke Suzuki[4]

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2. Peking University First Hospital, Beijing, China
3. Chinook Therapeutics, Seattle, WA, USA
4. Juntendo University Graduate School of Medicine, Tokyo, Japan

Atrasentan Exhibits a Consistent, Predictable Pharmacokinetic Profile Among Healthy Asian Adults

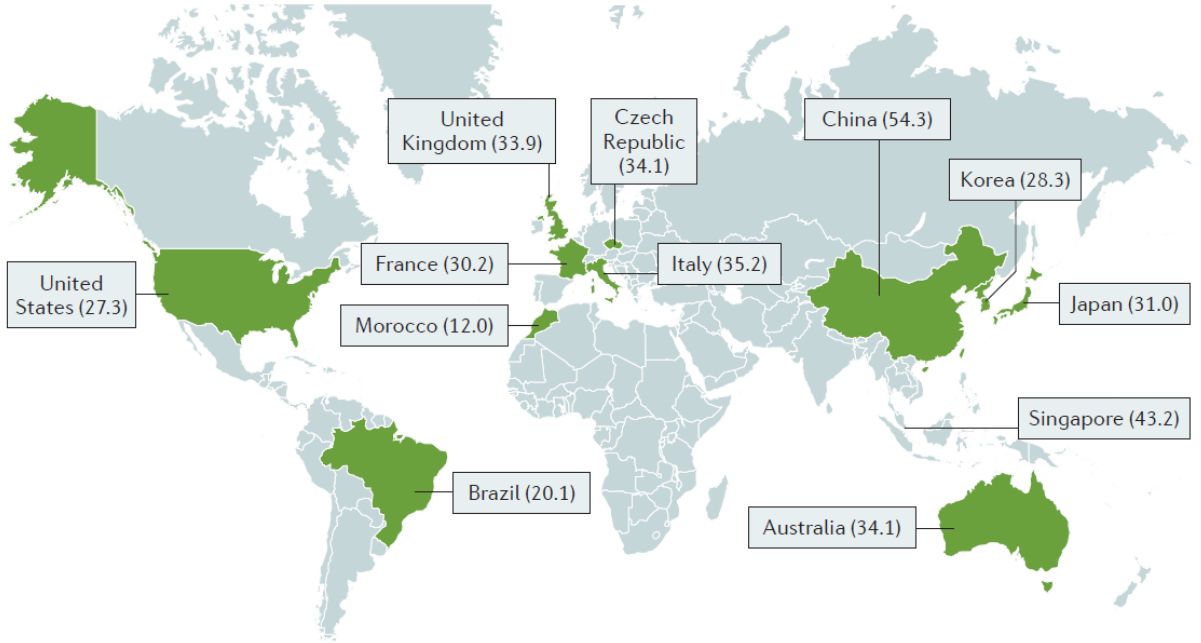
Immunoglobulin A nephropathy (IgAN) is the most common primary glomerulonephritis (GN) globally

Geographical differences in IgAN with a higher prevalence and potentially accelerated progression in Asia

Analysis of three separate single-dose, randomized Phase 1 studies of atrasentan in healthy Chinese, Japanese and North American adults of non-Asian descent demonstrated consistent and predictable:

- Safety and tolerability
- Pharmacokinetic (PK) profiles (C_{max}, T_{max}, AUC)

Global Prevalence of IgAN (% of biopsy-proven primary GN)



The consistent profile of atrasentan across ethnicities and geographic regions, supports the inclusion of patients with IgAN in Asia, in the ongoing global Phase 3 ALIGN study

Lai, K et al. *Nat Rev Dis Primers* 2016; Feb 11;2:16001.

PO1632

Precision Medicine Approach Identifies Patients with IgA Nephropathy at Risk for Progression Using Endothelin Activation Signatures

Viji Nair[1], Eric Olson[2], Sean Eddy[1], Wenjun Ju[1], Marvin Gunawan[2], Joyce Wu[2], Jennifer Cox[2], Andrew King [2], Matthias Kretzler[1]

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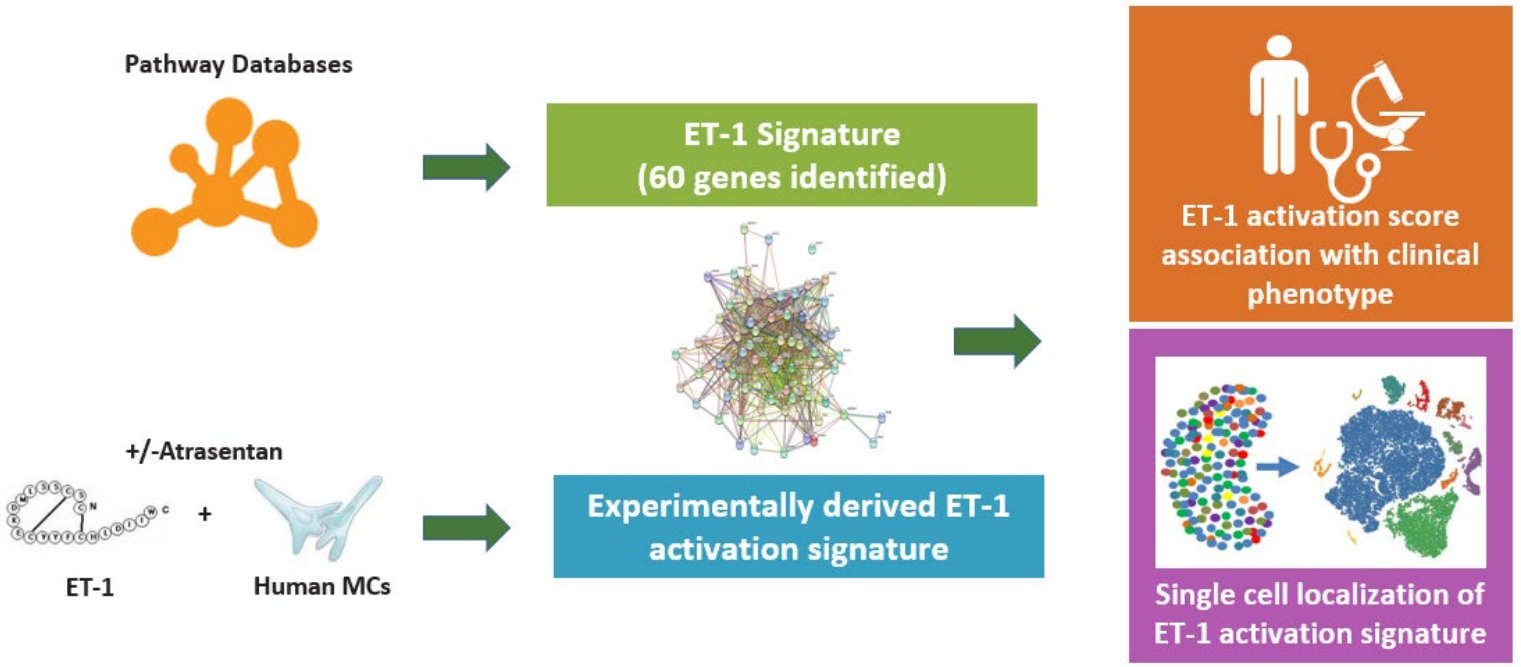
Endothelin Pathway Activation in Kidneys of Patients with IgAN Has a Strong Association with Clinical Progression

Identification of an intra-renal ET-1 transcriptional activation signature



- ET-activation scores strongly associated with clinical progression of IgAN, including increased proteinuria and decreased eGFR
- Analysis of single-cell transcriptional profiles from kidney biopsies of patients with IgAN revealed strong activation of the ET-signature in mesangial cells, which are activated as the initiating intra-renal event to the deposition of IgA-immune complexes in IgAN
- ET-1-induced transcriptional networks in human mesangial cells driving proliferation, inflammation and fibrosis were blocked by atrasentan

Translational research provides additional support for the therapeutic potential of ET_A receptor blockade with atrasentan in IgAN patients at high risk of progression

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Pharmacodynamic and Clinical Responses to BION-1301 in Patients with IgA Nephropathy: Initial Results of a Ph1/2 Trial

Jonathan Barratt[1], Billy Hour[2], Brian Schwartz[3], Bess Sorensen[3], Suzanne Roy[3], Colleen Stromatt[3], Margaret MacDonald[3], Aaron Endsley[4], Jeannette Lo[3], Alan Glicklich[3], Andrew King[3]

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4. Certara, Princeton, NJ, USA

Disclosures for Presenting Author

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Mechanism of APRIL and BION-1301 in IgA Nephropathy

Multi-hit pathogenesis of IgAN, an immune-mediated primary glomerular disease[1-3]

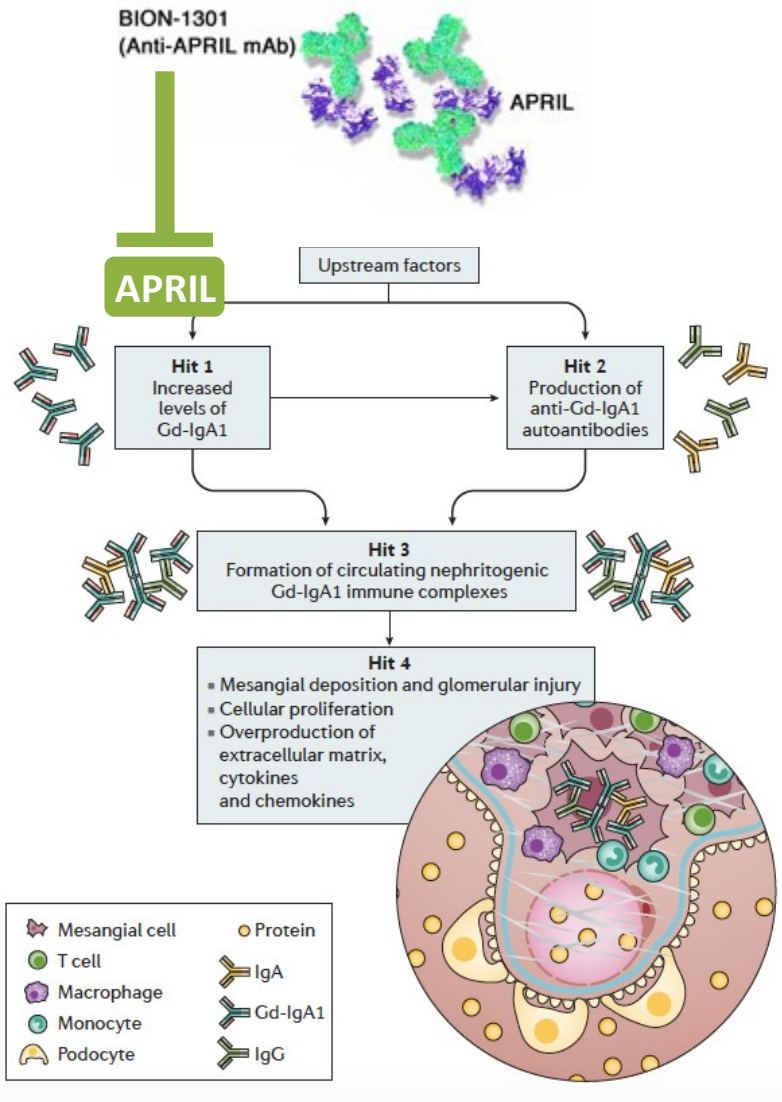
- Excess production of galactose-deficient IgA1 (**Gd-IgA1**) by IgA-secreting plasma cells is considered the initiating pathogenic event (**Hit 1**)
- Immune recognition by anti-Gd-IgA1 autoantibodies (**Hit 2**) results in the formation of nephritogenic immune complexes (**Hit 3**) that cause glomerular injury following mesangial deposition (**Hit 4**)

A PRoliferation Inducing Ligand (APRIL) is a TNF*-family cytokine involved in B-cell signaling via TACI and BCMA receptor activation[1-3]

- Drives **IgA class-switching** and **survival of IgA-secreting plasma cells**
- Stimulates **Gd-IgA1** secretion
- **Higher APRIL** levels in IgAN patients is correlated with higher Gd-IgA1 and proteinuria and lower eGFR
- APRIL gene variants confer increased risk of IgAN

BION-1301, 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**)



*TNF: tumor necrosis factor

1. Schena FP, Nistor I. *Semin Nephrol*. 2018;38(5):435-442 . **2.** Magistroni R et al. *Kidney Intl*. 2015;88(5):974-89. **3.** Ilyas M. Pediatric IgA Nephropathy. *Medscape*. 2017. https://emedicine.medscape.com/article/981516-overview. Accessed September 2021.

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IgAN Phase 1/2 Study Design

Cohort 1
450 mg Q2W IV, up to 52 wks
n=10

Enrollment Completed

Cohort 2
600 mg Q2W SC, up to 52 wks
n=10

Enrolling

Optional Additional Cohorts
SC Dose/Schedule TBD, up to 52 wks

Enrollment TBD

Objectives

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

Key Eligibility Criteria

- Biopsy-proven IgAN within past 10 years
- Urine protein ≥ 0.5 g/24h OR UPCR ≥ 0.5 g/g
- eGFR over 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)

RASi, renin-angiotensin system inhibitors; eGFR, estimated glomerular filtration rate; PK, pharmacokinetics; Q2W, every 2 weeks; UPCR, urine protein/creatinine ratio.

Visit INFO32 for further details about the Phase 1/2 trial

*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, eGFR determined by CKD-EPI.

Demographics & Baseline Characteristics

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	
Renin-angiotensin system inhibitor use %	100
Time from biopsy, years Median (min, max)	2.0 (0.2, 3.4)
Blood pressure (mmHg) Systolic - Median (min, max) Diastolic - Median (min, max)	127 (113, 133) 83 (69, 88)
eGFR (mL/min/1.73 m^2)* Median (min, max)	69 (30, 122)
24-hour urine protein excretion (g/day) Median (min, max)	1.22 (0.74, 6.47)
24-hour UPCR (g/g) Median (min, max)	0.64 (0.41, 4.55)

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

Safety and Tolerability

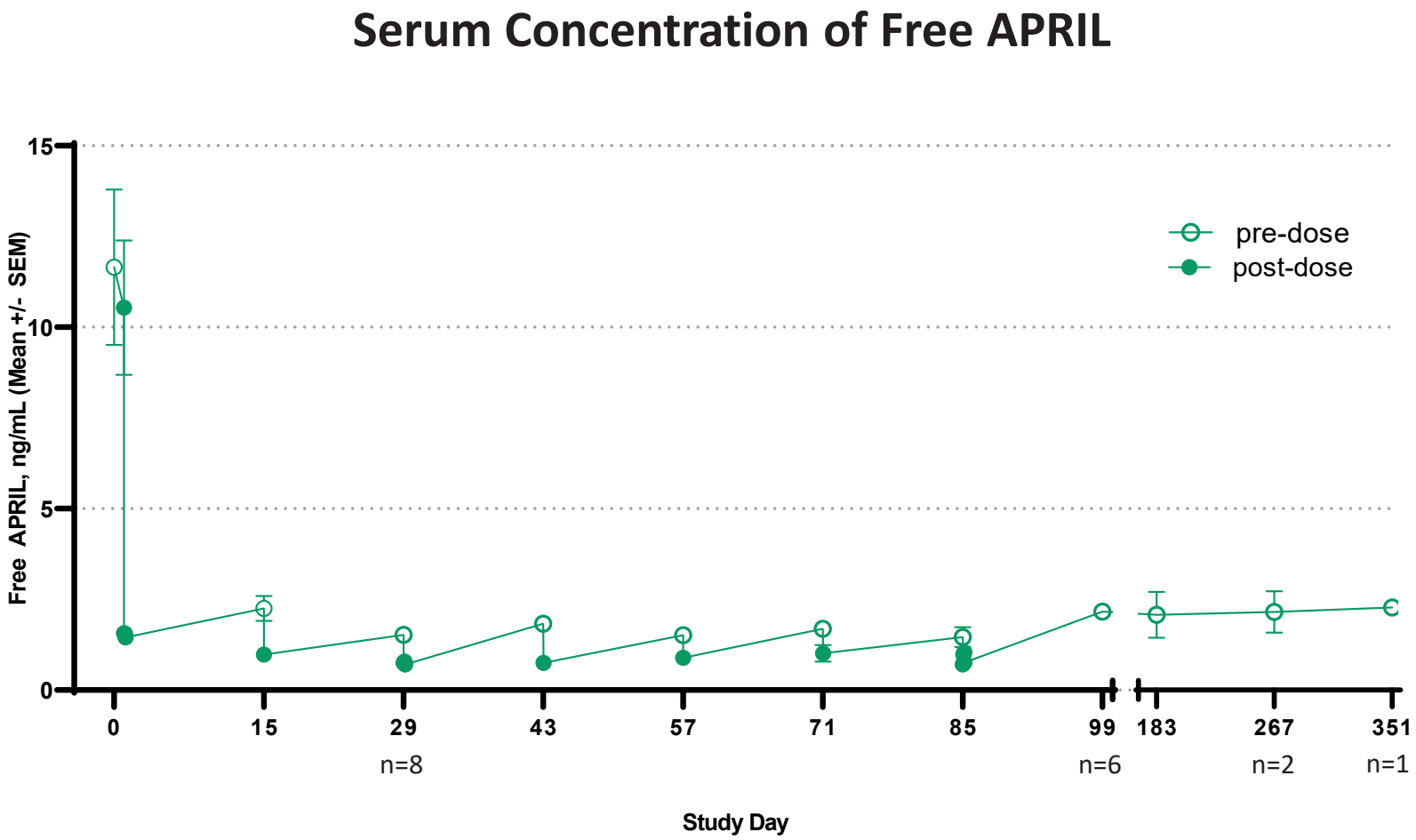
- To date, BION-1301 has been well-tolerated in IgAN patients (n=10)

AE Category	n (%)
Subjects with any TEAE	5 (50)
Any TEAE occurring in N>1 subjects	0 (0)
Treatment-related AE	0 (0)
AE leading to discontinuation	0 (0)
SAE	0 (0)
Infusion-related reactions	0 (0)

- Data cutoff: October 6, 2021
  - IgG concentrations remained above study-defined threshold in all patients
  - No notable changes in frequency of circulating naïve and memory B-cell subsets
  - 8/10 patients remain on treatment, with time on treatment ranging from <1 month to >14 months

AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Changes in Free APRIL Concentrations



- Rapid and durable reductions in free APRIL confirm effective target neutralization sustained through 1 year
- BION-1301 pharmacokinetics in patients with IgAN is consistent with previous experience in healthy volunteers
- No anti-drug antibodies observed in patients with IgAN to date

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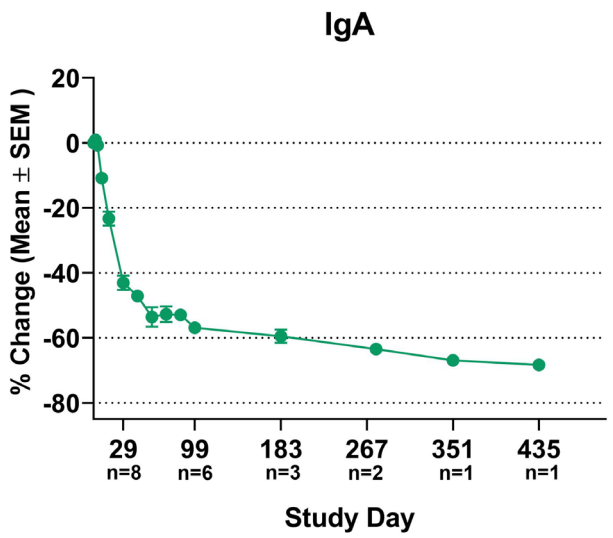
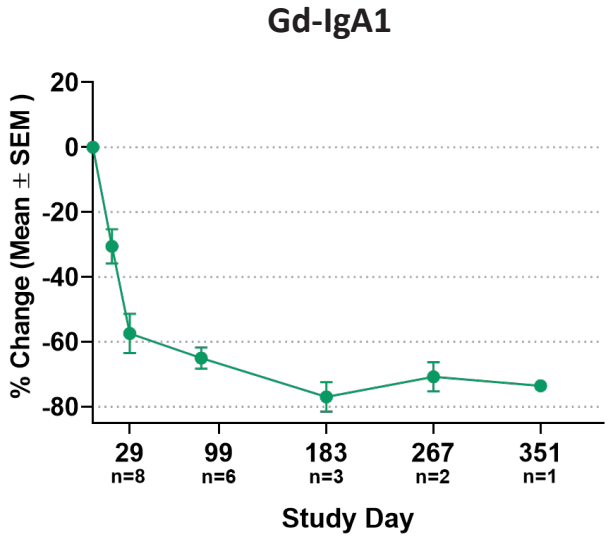
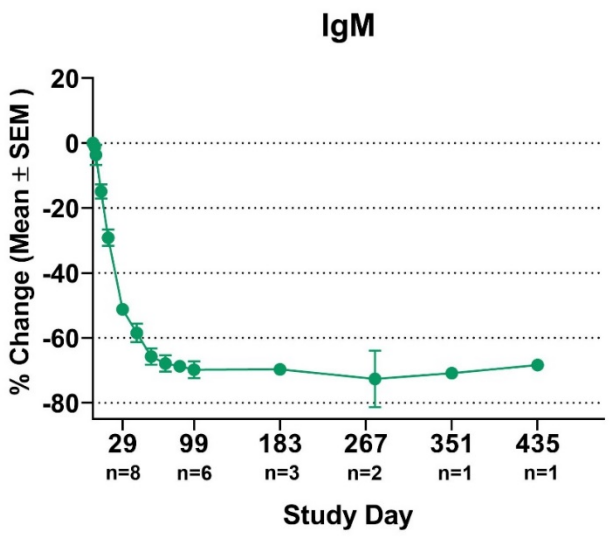
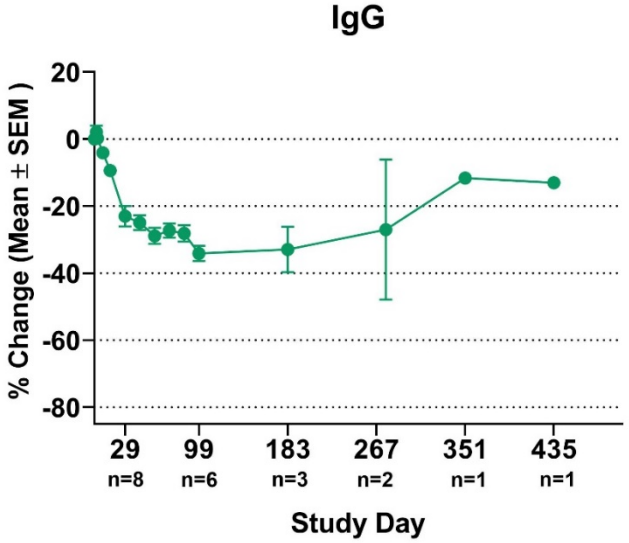
Changes in Serum Ig Concentrations from Baseline









- BION-1301 durably reduces IgA, IgM, and to a lesser extent, IgG in patients with IgAN
- BION-1301 produces sustained reductions in serum Gd-IgA1
  - The depletion of this pathogenic IgA isoform (Hit 1) in patients with IgAN demonstrates the potential disease-modifying mechanism of BION-1301
- IgG concentrations remained above the study-defined threshold in all patients, providing a pharmacodynamic window to deplete IgA while minimizing impact on IgG

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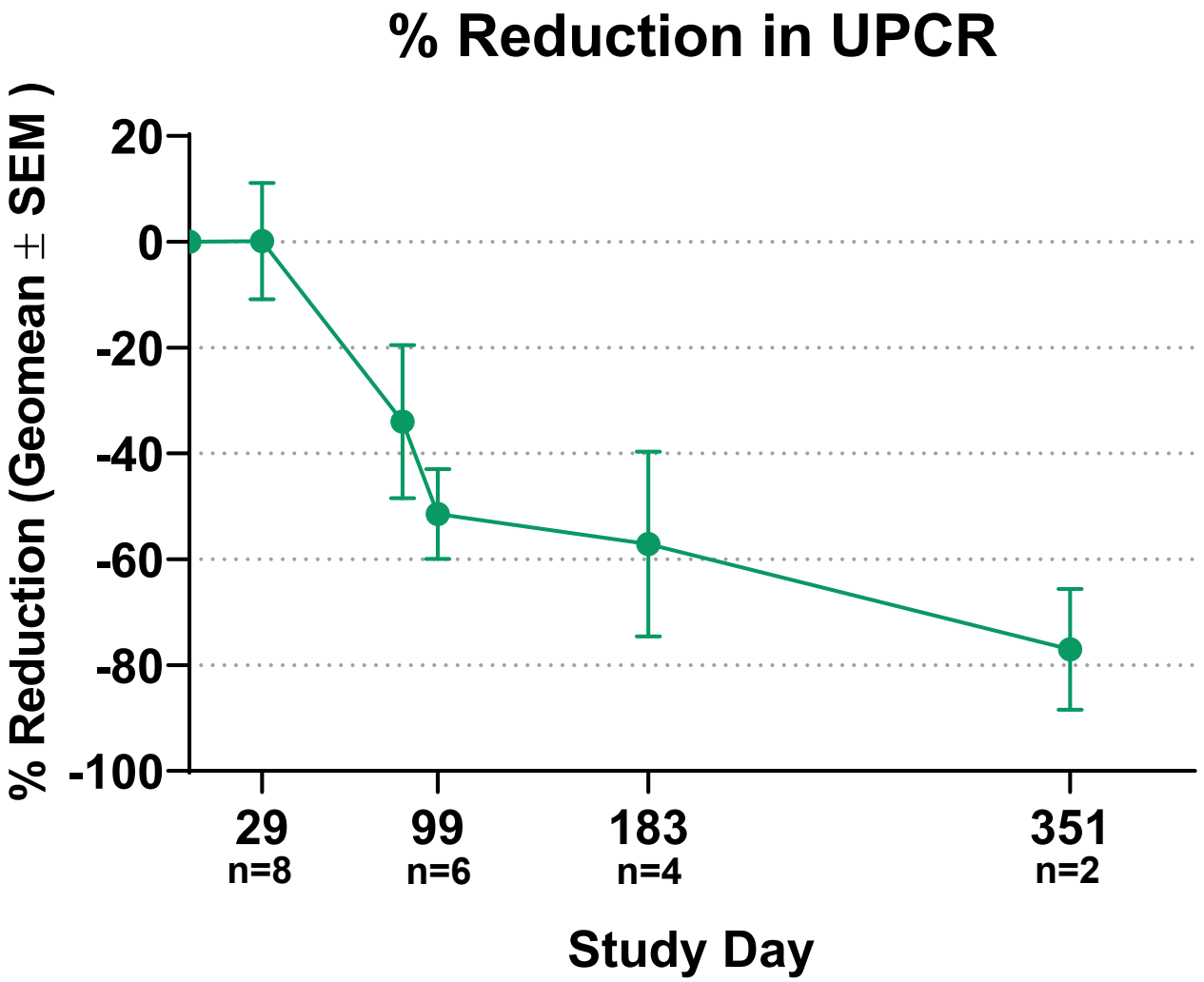
Effects on Proteinuria



- Median baseline 24-h urine protein excretion*: 1.22 g/day (range: 0.74 - 6.47 g/day)
- BION-1301 treatment results in clinically meaningful proteinuria reductions within 3 months in patients across a range of disease severities

*1/10 patients missed 24-hour collection; morning void used.

Conclusions

Interim BION-1301 IgAN patient data:

- ✓ Well-tolerated, with no early terminations due to AEs and no SAEs
- ✓ No anti-drug antibodies have been observed
- ✓ Rapid and sustained free APRIL reductions
- ✓ Durable reductions in Gd-IgA1, IgA and IgM, with smaller reductions in IgG
- ✓ Clinically meaningful reductions in proteinuria (24-hour UPCR) within 3 months

These data provide early proof-of-concept for the disease-modifying potential of BION-1301 to deplete pathogenic Gd-IgA1 and reduce proteinuria in patients with IgAN who remain at risk for progression with residual proteinuria despite optimized standard-of-care treatment

Next Steps:

- Complete enrollment of patients with IgAN in Cohort 2 utilizing subcutaneous injection of BION-1301

Acknowledgments:
Chinook Therapeutics would like to thank Karen Molyneux, Victoria Cotton, and Nadia Nawaz of University of Leicester for their contributions to the Gd-IgA1 data for this study.

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BION-1301 Clinical Experience

Laura Kooienga, MD
Colorado Kidney Care

Clinical Experience with BION-1301

Dr. Kooienga is currently treating four patients with IgAN in the ongoing phase 1/2 trial

Demographics	
Age, years Median (min, max)	45.5 (28, 55)
Sex, male %	100
Race, white %	100
Ethnicity, Hispanic %	0
Country, US %	100

Baseline Characteristics	
Renin-angiotensin system inhibitor use %	100
Time from biopsy, years Median (min, max)	2.0 (0.2, 3.0)
Blood pressure (mmHg) Systolic - Median (min, max) Diastolic - Median (min, max)	128 (118, 133) 84.5 (84, 87)
eGFR (mL/min/1.73 m^2)* Median (min, max)	70 (47, 122)
24-hour urine protein excretion (g/day) Median (min, max)	1.03 (0.74, 3.46)
24-hour UPCR (g/g) Median (min, max)	0.52 (0.41, 0.93)

To date, Dr. Kooienga's patients have been receiving BION-1301 treatment for a range of 1.5 to 5.5 months

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BION-1301 Program Update

Anti-APRIL monoclonal antibody for patients with IgA nephropathy

BION-1301 Moving Forward

Plans to accelerate development given strong clinical data and disease-modifying potential

Status:

- ✓ Enrollment completed for Cohort 1 in IgAN patients dosed with 450 mg IV q2w
- Enrollment ongoing for Cohort 2 in IgAN patients dosed with 600 mg SC q2w
- Optional Cohort 3 at SC dose and schedule TBD

BION-1301 has demonstrated >50% proteinuria reduction in patients with IgAN after three to six months of treatment, with further reductions in two patients through one year of treatment

Next Steps:

- Determine optimal SC dose and schedule based on data from phase 1/2 cohorts
- Finalize late-stage clinical development strategy and pivotal trial design
- Determine combination strategy with other mechanisms, including atrasentan
- Provide updates on development plan in H1 2022

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Closing

Catalysts

Program	Indication	Catalyst	H1 2021	H2 2021	H1 2022	H2 2022
Atrasentan	IgA Nephropathy	Initiate phase 3 ALIGN study	✓			
	Basket of Glomerular Diseases	Initiate phase 2 AFFINITY study	✓			
		Present data from IgAN patient cohort of AFFINITY			●	
		Present data from additional AFFINITY patient cohort(s)				●
BION-1301	IgA Nephropathy	Present additional biomarker data and IV-to-SC bioavailability data in healthy volunteers	✓			
		Present phase 1/2 data in IgAN patients	✓	✓	●	●
		Analyze phase 1/2 data and announce update on later-stage clinical development strategy			●	
CHK-336	Primary Hyperoxaluria	Complete IND-enabling studies		✓		
		Initiate phase 1 study in healthy volunteers			●	

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Q&A

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