CHINOOK THERAPEUTICS

MO212

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

Jonathan Barratt[1], Laura Kooienga[2], Billy Hour[3], Irfan Agha[4], Brian Schwartz[5], Bess Sorensen[5], Jeannette Lo[5], Andrew King[5], Taher Sathaliya[5], Sai Prasad Iyer[5], Aaron Endsley[6], Alan Glicklich[5]

[1]University of Leicester, Leicester, UK; [2]Colorado Kidney Care, USA; [3]Amicis Research Center, USA; [4]Liberty Research Center, USA; [5]Chinook Therapeutics, Inc; and [6]Certara, Inc.

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.

CHINOOK THERAPEUTICS

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)

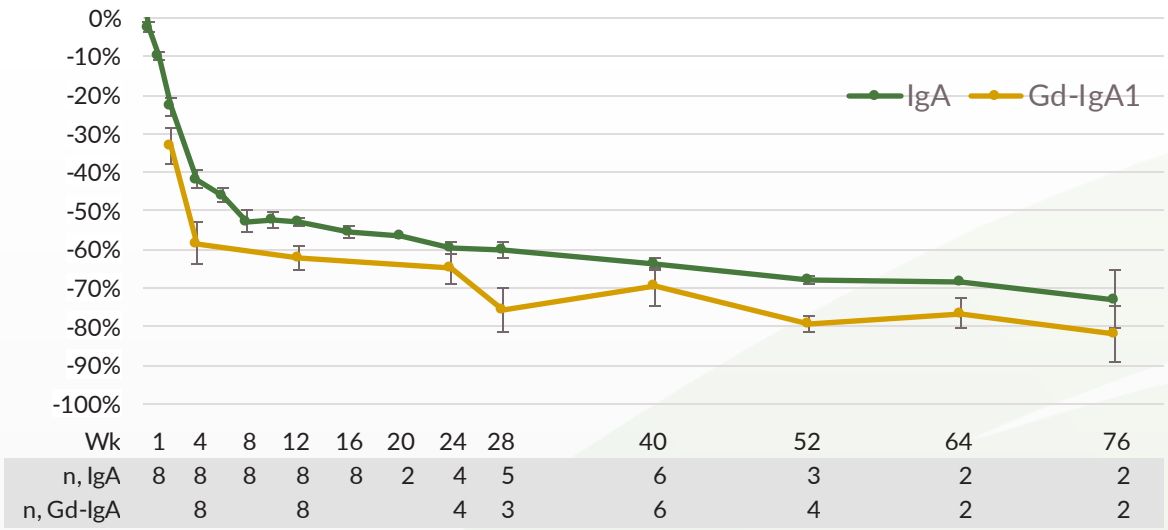
*Data cut-off May 6, 2022, with exception of biomarker data cut-off March 10, 2022. AEs, adverse events

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

BION-1301 Durably Reduces IgA and Gd-IgA1

IgA and Gd-IgA1

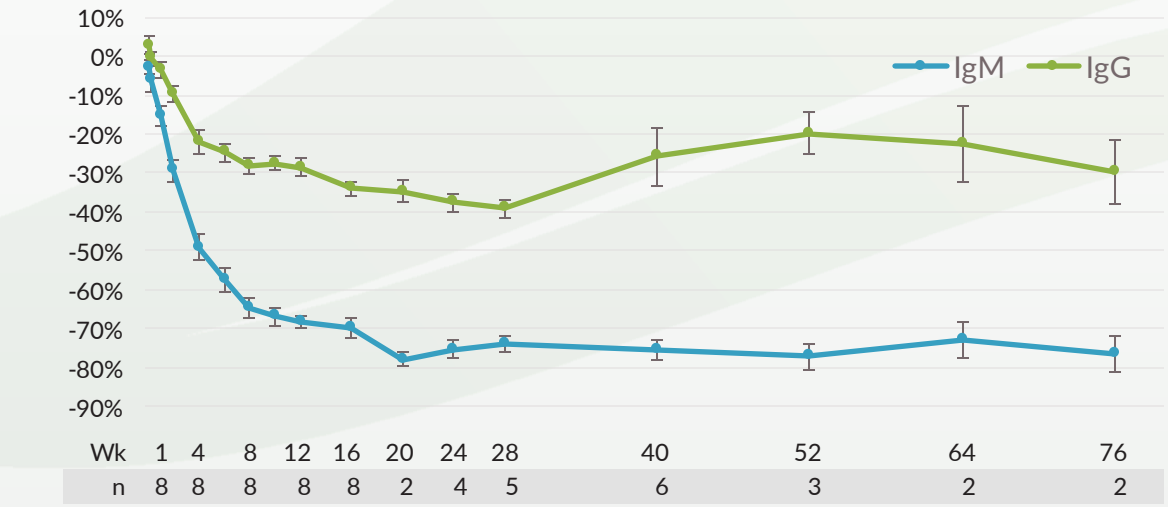
% change from Baseline (Mean ± SEM)



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)

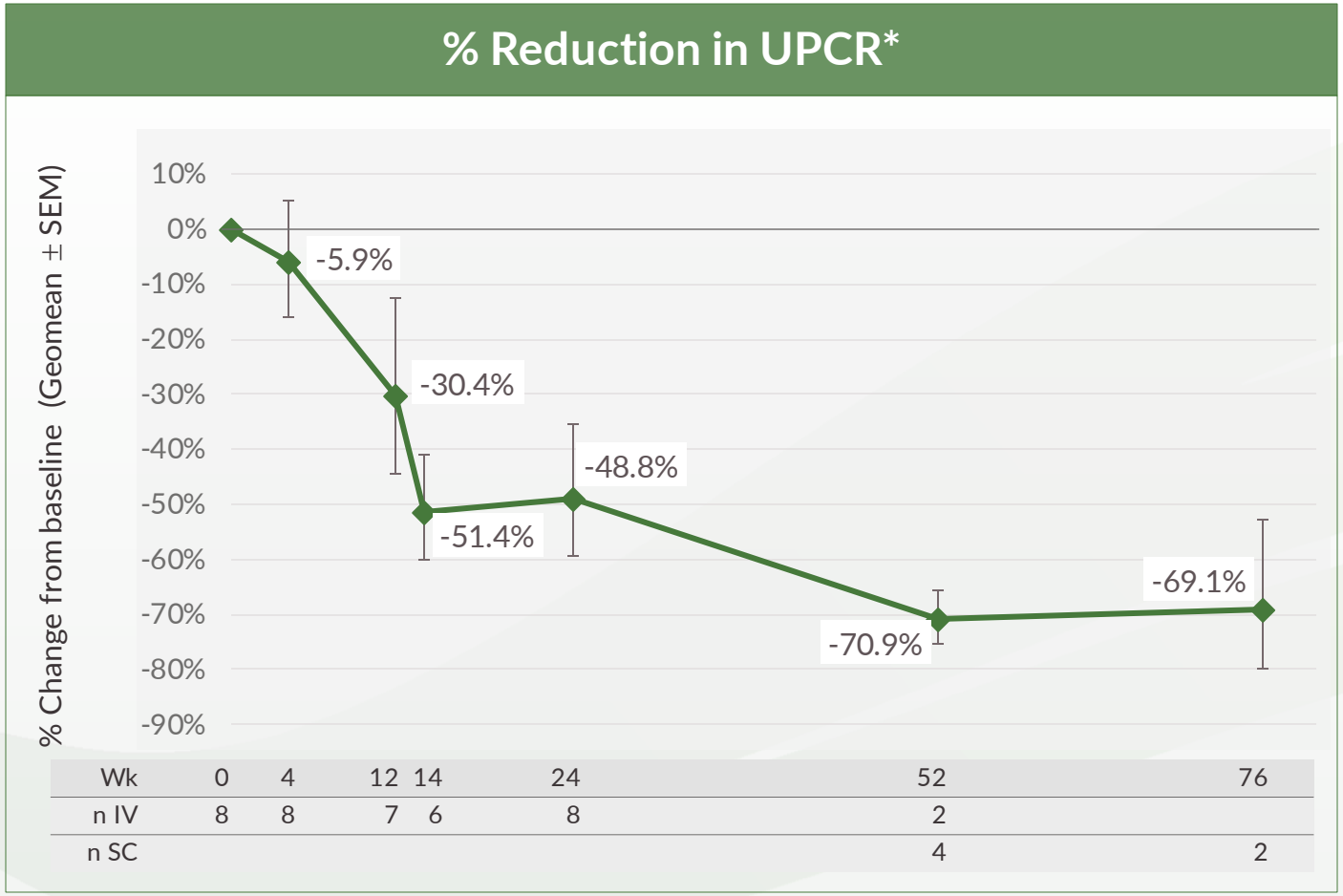


Wk	1	4	8	12	16	20	24	28	40	52	64	76
n	8	8	8	8	8	2	4	5	6	3	2	2

- 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

CHINOOK THERAPEUTICS

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

CHINOOK THERAPEUTICS

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**

CHINOOK THERAPEUTICS