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

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Background/Methods

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]

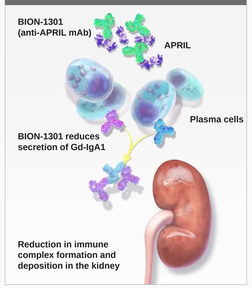
BION-1301* and the APRIL Pathway

- 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]

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 in IgA Nephropathy



Study Design

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**

†Patients transitioned to SC at ≥24 weeks

Cohort 2 (n=30): 600 mg Q2W de novo SC, up to 104 weeks‖ — **Enrolling**

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)

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

References

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

Baseline and Safety

Demographics and Baseline Characteristics

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)

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 m^2)§	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

Safety and Tolerability

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

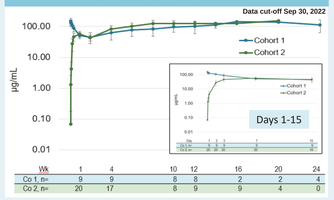
AE Category (N=34)		n (%)
Treatment emergent AEs (TEAEs)	Patients with any TEAE	23 (67.6)
	Patients with Infection TEAE (Grades 1 or 2)	17(50.0)
	Infection TEAE occurring in N>1 patient	
	COVID-19	8 (23.5)
	Upper Respiratory Tract Infection	3 (8.8)
	Asymptomatic COVID-19	2 (5.9)
	Sinusitis	2 (5.9)
	Urinary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

Data cut-off Oct 13, 2022

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



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

Results

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

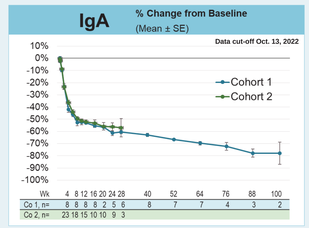
➢ **Following both IV and SC dosing, BION-1301 produced rapid and sustained reductions in IgA and Gd-IgA1, the pathogenic variant**

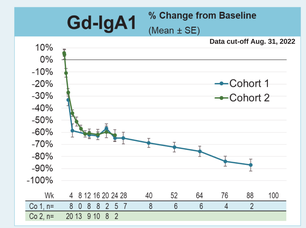
Cohort 1 (IV → SC):

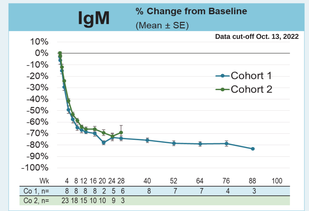
- Patients received 450 mg IV then transitioned to 600 mg SC after at least 24 weeks
- Reductions in IgA and Gd-IgA1 were maintained beyond 52 weeks of treatment
- Reductions in IgM, and to a lesser extent IgG, were also observed
- Reductions in free APRIL confirm durable target neutralization sustained through 1 year (data not shown)

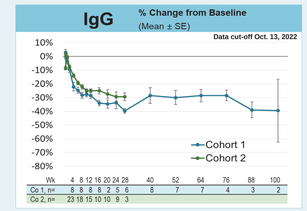
Cohort 2 (de novo SC):

- SC BION-1301 treatment resulted in rapid and sustained reductions in IgA and Gd-IgA1, IgM, and to a lesser extent IgG, through 24 weeks of treatment, consistent with Cohort 1
- Cohort 2 measurements for free APRIL concentrations are in process



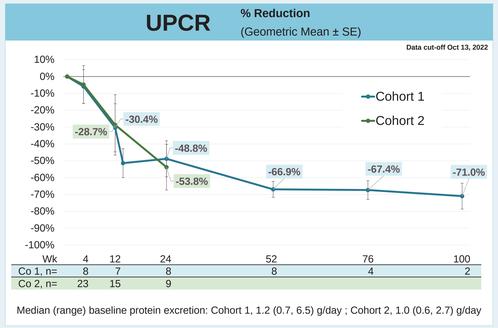






Mean IgM and Gd-IgA1 are not available at week 100

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



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

Conclusions

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 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.