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
- Approximately 30-40% of IgAN patients progress to end-stage kidney disease (ESRD) over a period of 20-25 years
- Proteinuria is strongly associated with kidney disease progression in IgAN

BION-1301 and the APRIL Pathway
- A Pearson's linear regression (APRIL) is a TNF superfamily cytokine that drives Ig class switching and survival of IgA-secreting plasma cells
- Higher APRIL levels in patients with IgAN are correlated with higher pathogenic:Gd-IgA1, proteinuria, and lower eGFR
- APRIL increases Gd-IgA1 secretion from lymphocytes of patients with IgAN

BION-1301 is a novel humanized monoclonal antibody that binds to and blocks 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
- Phase 1 bioavailability study in healthy volunteers (IV) supports subcutaneous (SC) dosing

Study Design
- ADU-CL-19 (Part 3) is an ongoing phase 1/2 trial investigating BION-1301 in patients with IgAN (NCT03345318)

Cohort 1 (n=30)
- 450 mg Q2W IV → 600 mg Q2W SC, up to 104 weeks

Cohort 2 (n=30)
- 600 mg de novo SC, up to 104 weeks

Objectives
- Safety, tolerability, PK, immunogenicity, biomarker effects, and preliminary effect on proteinuria in patients with IgAN
- Clinical examination of IgA1, the pathogenic variant which drives IgAN pathogenesis

Key Eligibility Criteria, Cohort 2
- Biopsy-proven IgAD diagnoses within past 10 years
- Total protein excretion ≥ 3 g/day OR UPCR ≥ 0.2 g/day for ≥ 24-hour urine collection at screening
- Stable/optimised dose of RAS for ≥3 months prior to screening

References

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

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

Safety and Tolerability

In Cohort 1 and Cohort 2:
- BION-1301 is generally well-tolerated in IgA nephropathy patients, with no reports of deaths, SAEs, or AEs leading to discontinuation of study drug at day 1
- All infections in patients with IgAN have been Grade 1 or 2 and only one infection, which was Grade 1 in severity, assessed as treatment related
- IgA1 secretion from lymphocytes in patients with IgAN who remain at risk for disease progression with residual proteinuria

Pharmacokinetics
- Low inter-individual variability in BION-1301 serum concentrations following IV and SC administrations
- No anti-drug antibody observed in patients with IgAN to date

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 IgA 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 RAS
- 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:
- delay 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 (600 mg Q2W SC) is well-tolerated and results in clinically meaningful proteinuria reductions to be further explored in phase 3