Results of a Phase 1 Trial to Investigate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BION-1301 in Healthy Volunteers

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Background
IgA nephropathy (IgAN) is the leading cause of primary glomerulonephritis, is an autoimmune disease with no approved treatments. A critical step in IgAN pathogenesis is the production of anti-GBM autoantibodies and immune complexes, formation, and deposition in the glomeruli, which result in kidney damage. A proliferation-inducing ligand (APRIL) promotes B-cell class-switching and survival of IgG-producing plasma cells in a dose-dependent manner. BION-1301, a first-in-class humanized monoclonal antibody targeting APRIL, is a fully human IgG1κ monoclonal antibody with high affinity for APRIL. BION-1301 levels had higher Geometric Mean Concentration (GMC) and lower estimated median BION-1301 levels than those with lower plasma levels of IgAN. BION-1301 is a first-in-class humanized monoclonal antibody targeting APRIL, and has been evaluated in healthy volunteers and patients with IgAN.

BION-1301 Blocks APRIL, a Critical Factor Driving the Etiology / Pathophysiology of IgAN

BION-1301 APRIL blocks in IgAN Nephropathy
From baseline to SAD-1 and MAD-1 cohorts, no reported treatment emergent adverse events (TEAEs). APRIL binding to BION-1301 in healthy volunteers and is known to induce IL-6 and IL-8 which may affect a number of downstream cytokines and growth factors. BION-1301 has been knock-out in mice studies and in IgAN patients and healthy volunteers. BION-1301 does not induce activation of MAPK, PI3K, or JAK2/STAT5 pathways. BION-1301 is well-tolerated in healthy volunteers and patients with IgAN.

BION-1301 Dosing Is Associated With a Low Incidence of Non-Nutrional Antibody-Rated Antibodies (ADA) With No Correlation To Dose

Mean Serum BION-1301 Concentration Is Generally Dose-Proportional but Moderately Greater than Dose-Proportional at Higher Doses

BION-1301 Demonstrates Durable Dose-Dependent Increase in Target Engagement as Measured by APRIL (APRIL)

CONCLUSIONS
• BION-1301 was well-tolerated in healthy volunteers with low incidence of non-neutralizing anti-BION-1301 antibodies.
• The PK profile of BION-1301 w.as used to determine generally dose-proportional and demonstrated a favorable with the potential to be administered by monthly dosing.
• BION-1301 demonstrated a durable dose-dependent increase in target engagement as measured by nonspecific BIL
• BION-1301 dose-dependently and durably reduces IgA and IgG and to a lesser extent IgM. Data consistent with potential for monthly dosing.

References