A Phase 1/2 Multicenter Study to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of BION-1301 in Healthy Volunteers and Adults with IgA Nephropathy

Jonathan Barratt[1], Bess Sorensen[2], Jerlyn C. Tolentino[2], Brian S. Schwartz[2], AndrewJ. King[2], Charlotte Jones-Burton[2]

1. University of Leicester, Leicester, Leicestershire, United Kingdom; 2. Chinook Therapeutics Inc, Seattle, WA, United States

IgAN and APRIL

Immunoglobulin A 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]

APRIL, A PRoliferation Inducing Ligand:

- Is a TNF superfamily cytokine that drives IgA class switching and survival of IgA-secreting plasma cells in IgAN[8]
- Higher APRIL levels in patients with IgAN are correlated with higher pathogenic galactose-deficient IgA1 (Gd-IgA1), proteinuria and lower eGFR[9-10]

Reference

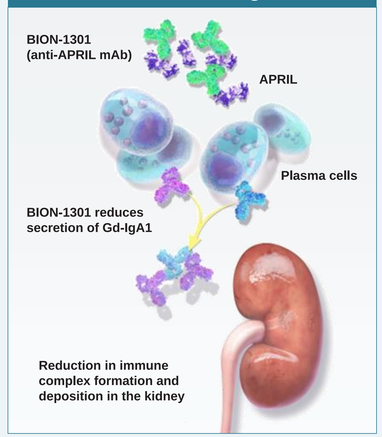
1. Mcgrogan et al, 2011, NDT; 2. Reich et al, 2007, JASN; 3. Moriyama et al, 2014, PLOS ONE; 4. Rauen et al, 2020, Kidney Int; 5. Hastings et al, 2018, Kidney Int Rep; 6. Thompson et al, 2019, CJASN; 7. Barbour et al, 2019, JAMA Int Med; 8. Suzuki et al, 2021, Sem Immun; 9. Zhai et al, 2016, Medicine; 10. McCarthy et al, 2011, J Clin Invest; 11. Barratt et al, 2022, ERA; 12. Lo et al, 2020 ERA-EDTA

BION-1301*

BION-1301 is a novel humanized monoclonal antibody that binds and blocks APRIL

- Blocking APRIL with BION-1301 is a potentially disease-modifying mechanism to deplete Gd-IgA1 and prevent pathogenic immune complex formation
- 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[11]
- Phase 1 bioavailability study in healthy volunteers (HV) supports SC dosing[12]

BION-1301 in IgAN



In a 3-part phase 1/2 study (ADU-CL-19; NCT03945318), the completed Parts 1 and 2 were blinded, placebo-controlled single and multiple ascending (SAD, MAD) dose designs in HVs.

Part 1	SAD in healthy volunteers (up to 1350 mg)	**Completed**
Part 2	MAD in healthy volunteers (up to 450 mg)	**Completed**

Objectives of Parts 1 and 2 included:

- Safety, tolerability, pharmacokinetics, immunogenicity and biomarker effects in healthy volunteers and IgAN patients
- Proof of mechanism (free APRIL, IgA and Gd-IgA1)
- Explore dose/schedule (exposure) necessary to achieve reduction in IgA and Gd-IgA1

BION-1301 Phase 1/2 Study Ongoing Part 3

ADU-CL-19 Phase 1/2 study Part 3 (NCT03945318) is a multicenter (US, UK, South Korea), multicohort, open-label study in up to 40 patients with IgAN

Study Objectives:

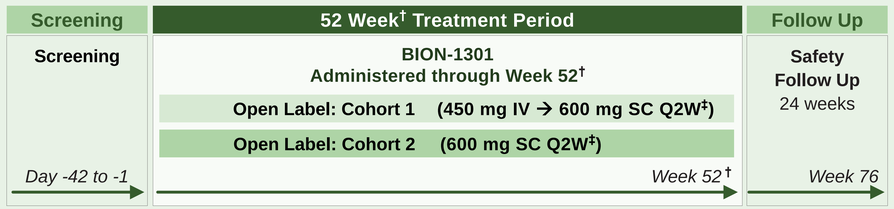
- Safety, tolerability, PK, immunogenicity, biomarker effects and preliminary effect on proteinuria in patients with IgAN
- Proof of mechanism
- Proof of concept
- Explore dose/schedule, intravenous (IV) and subcutaneous (SC) administration

Key Eligibility Criteria, Cohort 2 (Currently Enrolling):

- 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/1.73 m^2
- Stable/optimized dose of RASi for ≥ 3 months prior to screening (or intolerant to RASi)

The current design of the Phase 1/2 study incorporating SC dosing provides improved patient convenience and will enable generation of extended safety, PK, immunogenicity, PD and preliminary efficacy data for the use of BION-1301 in patients with IgAN

Ongoing Part 3 in Patients with IgAN



‡*Patients transitioned to SC after receiving IV BION-1301 for ≥24 weeks*

Cohort 1 (n = 10; enrollment complete)

- 450 mg of BION-1301 IV every 2 weeks (Q2W) for at least 24 weeks; transition to 600 mg of BION-1301 SC Q2W for the remainder of the 1-year study period

Cohort 2 (up to 30 patients; enrollment ongoing)

- 600 mg of BION-1301 SC every 2 weeks for 1 year

†*An optional 1-year treatment extension is available to both cohorts with total treatment duration not to exceed 2 years.*

KIDNEY WEEK 2022 Nov. 3–6 | Orlando, FL

INFO28

*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.