BION-1301 Trial in Progress

ADU-CL-19: a Phase 1/2, Multicenter Trial to Investigate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BION-1301 in Healthy Volunteers and Adults With IgA Nephropathy

Jonathan Barratt,¹ Brian Schwartz,² Bess Sorensen,² Margaret MacDonald,² Jerlyn Lo,² Andrew King,² Jeannette Lo,² Sai Prasad Iyer,² Alan Glicklich²

¹ University of Leicester, Leicester, UK; ² Chinook Therapeutics, Seattle, WA, USA

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 (IgAN)

IgAN is a chronic, autoimmune, inflammatory glomerulopathy

- B cells of patients with IgAN produce galactose-deficient IgA1 (Gd-IgA1; Hit 1 of the multi-hit hypothesis of IgAN)
- In patients with IgAN, Gd-IgA1 gives rise to autoantibody production (Hit 2)
- Gd-IgA1-autoantibody complexes deposit in the kidneys (Hit 3), resulting in complement activation, inflammation and subsequent renal damage (Hit 4)

A Proliferation Inducing Ligand (APRIL) is a signaling molecule that regulates B-cell immune responses

- APRIL binds to receptors BCMA and TACI on B cells to drive IgA class-switching and proliferation/survival of IgA-producing plasma cells
- Patients with IgAN have significantly higher levels of APRIL than normal
- Higher APRIL levels in IgAN patients correlate with poor prognosis
- A polymorphism in the APRIL gene confers IgAN susceptibility

BION-1301

- Novel humanized monoclonal antibody (mAb) that binds and blocks APRIL, a potentially disease-modifying mechanism to deplete Gd-IgA1 (Hit 1) and prevent pathogenic immune complex formation (Hit 3)
Ph 1/2 Trial of BION-1301

**ADU-CL-19**  
NCT03945318

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

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

**Part 3**  
- **Cohort 1** in IgAN patients:  
  450 mg Q2W IV, up to 52 weeks*  
  Completed

*Patients transitioned to SC at ≥24 wks; may receive BION-1301 up to 124 wks

**Part 3**  
- **Cohort 2** in IgAN patients:  
  600 mg Q2W SC, up to 52 weeks  
  Enrolling

**Part 3**  
- **Cohort 3:** Optional additional cohorts in IgAN patients  
  Enrollment TBD

---

**Objectives: Part 1 and 2**

- Safety, 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

**Additional Objectives: Part 3**

- Preliminary assessment of safety and efficacy in patients with IgAN
- Incorporate SC dosing

**Modifications to Part 3:**

- Simplify operational complexity by combining ADU-CL-19 and ADU-CL-24 total duration to 52 weeks
- Add optional cohort of IgAN patients
- Increase sample size (up to 40 patients)
- Now enrolling patients in the United States, the United Kingdom and South Korea

SAD, single ascending dose; MAD, multiple ascending dose; IV, intravenous; Q2W, every 2 weeks; SC, subcutaneous; TBD, to be determined.
BION-1301 in Patients with IgAN: Study Schema

- **Screening**
  - Ongoing Part 3†
  - In Patients with IgAN
  - D -42 to -1

- **52-Week Treatment Period**
  - BION-1301
    - Administered through Week 52
    - Open Label: Cohort 1 (450 mg IV Q2W*)
    - Open Label: Cohort 2 (600 mg SC Q2W)

- **Follow Up**
  - Safety Follow Up
  - 24 weeks

**Patient-Centric Trial**

- Compensation for 24-hour urine collection
- Reimbursement for trial-related expenses
- SC injections in Part 3 allow for less time at site

†Part 3 is capped at N=40

Clinicaltrials.gov: NCT03945318
Key Eligibility Criteria, Cohort 2 (Currently Enrolling)

- Age 18 years and older
- Biopsy-proven IgAN within the 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 m²*
- Stable on an optimized dose of ACE/ARB for ≥3 months prior to screening (or intolerant to ACE/ARB)
- No history of other chronic kidney disease or any transplantation
- No history of secondary forms of IgAN
- No Type 1 or 2 diabetes

ClinicalTrials.gov: NCT03945318

Results

Results from Parts 1 and 2 in healthy volunteers were presented at ERA-EDTA 2020 (P0500)

Initial results from Part 3 in patients with IgAN presented at ASN 2021 (PO1632)

Updated interim results from Part 3 in patients with IgAN to be presented at ERA 2022 (MO212)

*For Cohort 2. For completed Cohort 1, eGFR >45 mL/min/1.73 m² or 30 to 45 mL/min/1.73m² if kidney biopsy performed within 2 years prior to Day 1 does not provide evidence of glomerular fibrosis.

ACE/ARB, angiotensin converting enzyme inhibitors/angiotensin receptor blockers; eGFR, estimated glomerular filtration rate; UPCR, urine protein to creatinine ratio.