Interim Results of Phase 1 and 2 Trials to Investigate the Safety, Tolerability, Pharmacodynamics and Clinical Activity of BION-1301 in Patients with IgA Nephropathy

Jonathan Baratt¹, Billy Hour², Brian Schwartz³, Bess Sorensen³, Suzanne Roy³, Colleen Stromatt³, Margaret MacDonald³, Aaron Endsley⁴, Jeannette Lo³, Alan Glicklich³, Andrew King³

1. University of Leicester; Leicester, UK
2. Amicis Research Center, CA, USA
3. Chinook Therapeutics; Seattle, WA, USA
4. Certara; Princeton, NJ, USA
Mechanism of APRIL and BION-1301 in IgA Nephropathy (IgAN)

Multi-Hit Pathogenesis of IgAN, an immune-mediated primary glomerular disease

- Excess production of galactose-deficient IgA1 (Gd-IgA1) by IgA secreting plasma cells is considered the initiating pathogenic event (Hit 1)
- Immune recognition by anti-Gd-IgA1 autoantibodies (Hit 2) results in the formation of nephritogenic immune complexes (Hit 3) that cause glomerular injury following mesangial deposition (Hit 4)

A Proliferation Inducing Ligand (APRIL) is a TNF-family cytokine involved in B-cell signaling via TACI and BCMA receptor activation

- Drives IgA class-switching and survival of IgA-secreting plasma cells
- Stimulates Gd-IgA1 secretion
- Higher APRIL levels in IgAN patients is correlated with higher Gd-IgA1 and proteinuria and lower eGFR
- APRIL gene variants confer increased risk of IgAN

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

- Potentially disease modifying mechanism to deplete Gd-IgA1 (Hit 1) and prevent pathogenic immune complex formation (Hit 3)
Updated Phase 1/2 Study Design in Patients with IgAN

Objectives
- Safety, PK, biomarker effects and preliminary proteinuria
- Proof of mechanism
- Proof of Concept
- Explore dose/schedule - IV and subcutaneous administration

Key Eligibility Criteria
- Biopsy-proven IgAN within past 10 years
- UPCR ≥ 0.5 g/24h OR UPCR ≥ 0.5 g/g
- eGFR over 45 mL/min per 1.73 m²
- Stable on an optimized dose of ACE/ARB for ≥ 3 months prior to screening (or intolerant to ACE/ARB)

ADU-CL-19, Part 3 in Patients with IgAN

Cohort 1
450 mg q2wk IV, up to 52 wks - Enrolling

Cohort 2
Dose/Schedule TBD, SC, up to 52 wks - Enrollment to begin Q3 2021

Optional Cohort 3
Dose/Schedule TBD, SC, up to 52 wks - Enrollment TBD

Results from the Phase 1 Parts 1 & 2 in Healthy Volunteers (HVs) were presented at the 2020 ERA-EDTA mtg, Poster #P0500
Demographics and Baseline Characteristics
ADU-CL-19 Study in Patients with IgAN

### Baseline Demographics

<table>
<thead>
<tr>
<th>Baseline Demographics</th>
<th>IgAN Cohort 1 N=5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
</tr>
<tr>
<td>Median (Min, Max)</td>
<td>41 (35, 59)</td>
</tr>
<tr>
<td>Sex, n (%) Male</td>
<td>4 (80%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Ethnicity, n (%) Hispanic</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Country, n (%) US</td>
<td>5 (100%)</td>
</tr>
</tbody>
</table>

### Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>IgAN Cohort 1 N=5</th>
</tr>
</thead>
<tbody>
<tr>
<td>RASi Use, n (%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Time from Bx/Diagnosis (years)</td>
<td></td>
</tr>
<tr>
<td>Median (Min, Max)</td>
<td>2.3 (1.1, 8.6)</td>
</tr>
<tr>
<td>Blood Pressure (mmHg)</td>
<td></td>
</tr>
<tr>
<td>Systolic – Median (Min, Max)</td>
<td>123 (113, 128)</td>
</tr>
<tr>
<td>Diastolic - Median (Min, Max)</td>
<td>82 (69, 88)</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)*</td>
<td></td>
</tr>
<tr>
<td>Median (Min, Max)</td>
<td>72 (55, 107)</td>
</tr>
<tr>
<td>24-hour UPCR (mg/g)</td>
<td></td>
</tr>
<tr>
<td>Median (Min, Max)</td>
<td>653 (530, 4551)</td>
</tr>
</tbody>
</table>

*By CKD-EPI
Safety

- BION-1301 has been well-tolerated in IgAN patients to date, consistent with previous experience in healthy volunteers (HVs)

<table>
<thead>
<tr>
<th>AE category</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>3 (60%)</td>
</tr>
<tr>
<td>Any TEAE Occurring in N &gt; 1</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Treatment Related AE</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>AE Leading to Discontinuation</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>SAE</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Infusion Related Reactions</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

- All patients continuously treated with biweekly dosing to date; No patients had missed any doses as of the data cutoff date = April 27th, 2021
Free APRIL

- BION-1301 pharmacokinetics in patients with IgAN is consistent with previous experience in HVs
- Rapid and durable reductions in free APRIL confirm effective target neutralization, consistent with previous experience in HVs
- No anti-drug antibodies (ADAs) observed in patients with IgAN to date

Cohort 1 in IgAN pts – 450mg IV Q2W

Reduction in Free APRIL from Baseline

Free APRIL, ng/mL (Mean +/- SEM)

Study Day

N=5
• BION-1301 durably reduces IgA and IgM and to a lesser extent, IgG, in patients with IgAN, with similar kinetics and magnitude as previously observed with BION-1301 in HVs.
Gd-IgA1

Reduction in Gd-IgA1 from Baseline

• BION-1301 produces sustained reductions in serum Gd-IgA1

• The depletion of this pathogenic IgA isoform (Hit 1) in patients with IgAN demonstrates the potential disease modifying mechanism of BION-1301

• The kinetics and magnitude of Gd-IgA1 reductions are consistent with previous observations reported with BION-1301 in HVs
Ex vivo Mesangial Cell Activation

- IgA-complexes from patient 1 and 2 produced mesangial cell hyperproliferation at baseline, which was attenuated following BION-1301 treatment.

**IgA-complexes from patient 1 and 2 produced mesangial cell hyperproliferation at baseline, which was attenuated following BION-1301 treatment.**

Unstimulated = media only, PDGF-BB = Platelet Derived Growth Factor BB, 10 ng/mL, HV = Healthy Volunteer, IgAN+ = IgAN patient positive control
Proteinuria & eGFR

Reduction in 24-hour UPCR from Baseline

• Baseline 24-hour UPCR (24-hr collections*) ranged from 530 - 4551 mg/g

• Preliminary proteinuria reductions observed in patients with IgAN, across a wide range of baseline UPCR Levels, provide initial clinical proof-of-concept for BION-1301

• No significant change in eGFR was noted for any patient through 183 days of treatment

---

*1/5 patients missed 24-hr collection; morning void used
In patients with IgAN treated to date, BION-1301 resulted in:
- rapid APRIL neutralization
BION-1301 Response Kinetics

Reduction in Free APRIL, Gd-IgA1

- In patients with IgAN treated to date, BION-1301 resulted in:
  - rapid APRIL neutralization
- Followed by:
  - Gd-IgA1 depletion

Mean only shown for clarity
BION-1301 Response Kinetics

Reduction in Free APRIL, Gd-IgA1, MC Activation

- In patients with IgAN treated to date, BION-1301 resulted in:
  - rapid APRIL neutralization
- Followed by:
  - Gd-IgA1 depletion
  - Reduced mesangial cell activation (*ex vivo*)
BION-1301 Response Kinetics

Reduction in Free APRIL Gd-IgA1, MC Activation and Proteinuria

- In patients with IgAN treated to date, BION-1301 resulted in:
  - rapid APRIL neutralization
- Followed by:
  - Gd-IgA1 depletion
  And
  - Reduced mesangial cell activation (ex vivo)
- And subsequently:
  - Proteinuria reduction
BION-1301 in Patients with IgAN - Interim Data Observations

Interim BION-1301 IgAN patient data observed to date:

- Well-tolerated, with no early terminations due to adverse events and no SAEs
- Rapid and sustained free APRIL reductions
- Durable reductions in Gd-IgA1, IgA and IgM, and smaller reductions in IgG
- Clinically meaningful reductions in proteinuria (24-hr UPCR)

This preliminary analysis provides early proof-of-concept for the disease modifying potential of BION-1301 to deplete pathogenic Gd-IgA1 and reduce proteinuria in patients with IgAN that remain at risk for progression with residual proteinuria despite optimized SOC treatment

Next Steps

- Enrollment of patients with IgAN in Cohort 2 utilizing subcutaneous injection initiates soon