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MO207

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

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Disclosures for Presenting Author

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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**)

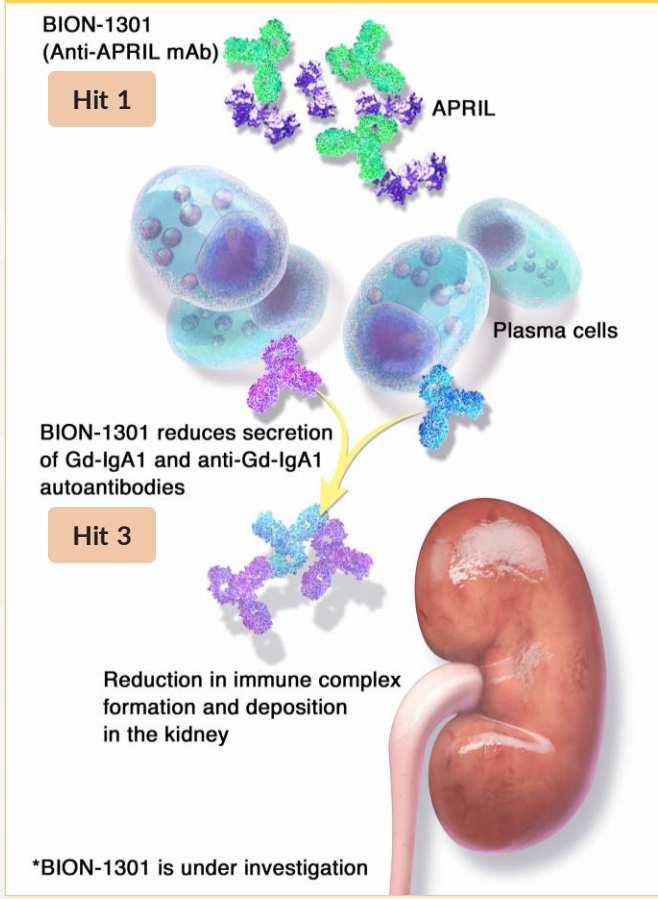
A PRoliferation Inducing Ligand (APRIL) is a signaling molecule that regulates B-cell immune responses

- 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**)

BION-1301* in IgA Nephropathy



Schena FP, Nistor I. *Semin Nephrol.* 2018;38(5):435-442. Magistroni R et al. *Kidney Intl.* 2015;88(5):974-89. Ilyas M. Pediatric IgA Nephropathy. *Medscape.* 2017. https://emedicine.medscape.com/article/981516-overview. Accessed Sept 2021.
BCMA, B-cell maturation antigen; TACI, transmembrane activator and calcium-modulator and cyclophilin ligand.

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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.

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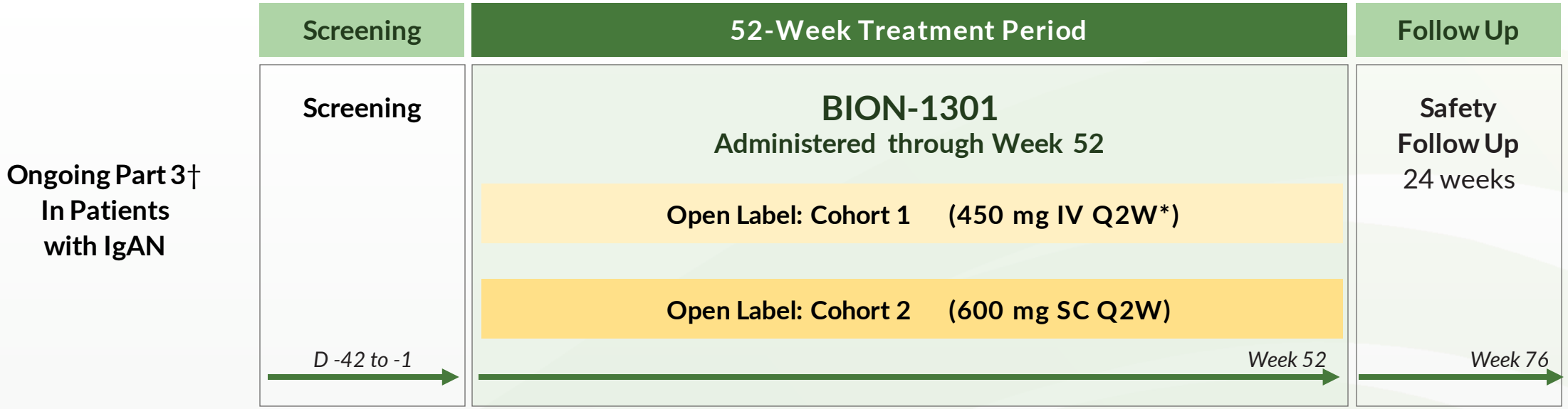
BION-1301 in Patients with IgAN: Study Schema



*Patients transitioned to SC after receiving BION-1301 for ≥24 wks

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

BION-1301 Study Eligibility and Interim Results

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 m^2*
- ✓ 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 m^2 or 30 to 45 mL/min/1.73m^2 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.

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