CHINOOK THERAPEUTICS

FC 040

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 Baratt[1], Billy Hour[2], Brian Schwartz[3], Bess Sorensen[3], Suzanne Roy[3], Colleen Stromatt[3], Margaret MacDonald[3], Aaron Endsley[4], Jeannette Lo[3], Alan Glicklich[3], Andrew King[3]

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

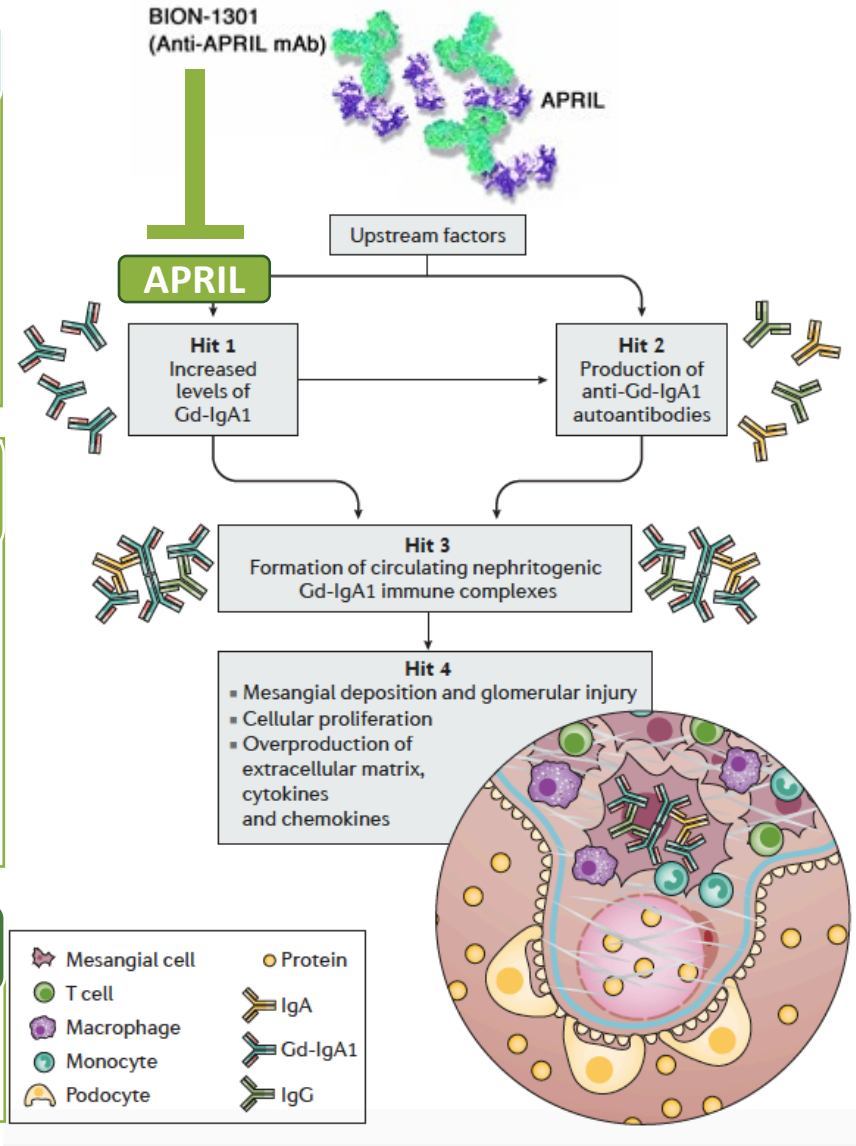
- Excess production of galactose-deficient IgA1 (**Gd-IgA1**) by IgA secreting plasma cells is considered the initiating pathogenic event (**Hit 1**)
- Immune recognition by anti-Gd-IgA1 autoantibodies (**Hit 2**) results in the formation of nephritogenic immune complexes (**Hit 3**) that cause glomerular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



Schena FP, Nistor I, Semin Nephrol 2018, 38(5):435-442; Magistroni et al., Kidney Intl (2015) 88:974-89;
Ilyas M. Pediatric IgA nephropathy. Medscape. 2017. https://emedicine.medscape.com/article/981516-overview

CHINOOK THERAPEUTICS

Updated Phase 1/2 Study Design in Patients with IgAN

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

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 m^2
- Stable on an optimized dose of ACE/ARB for ≥ 3 months prior to screening (or intolerant to ACE/ARB)

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	IgAN Cohort 1 N=5
Age, years	
Median (Min, Max)	41 (35, 59)
Sex, n (%) Male	4 (80%)
Race, n (%)	
White	5 (100%)
Ethnicity, n (%) Hispanic	2 (40%)
Country, n (%) US	5 (100%)

Baseline Characteristics	IgAN Cohort 1 N=5
RASi Use, n (%)	5 (100%)
Time from Bx/Diagnosis (years)	
Median (Min, Max)	2.3 (1.1, 8.6)
Blood Pressure (mmHg)	
Systolic – Median (Min, Max) Diastolic - Median (Min, Max)	123 (113, 128) 82 (69, 88)
eGFR (mL/min/1.73m^2)*	
Median (Min, Max)	72 (55, 107)
24-hour UPCR (mg/g)	
Median (Min, Max)	653 (530, 4551)

*By CKD-EPI

Safety

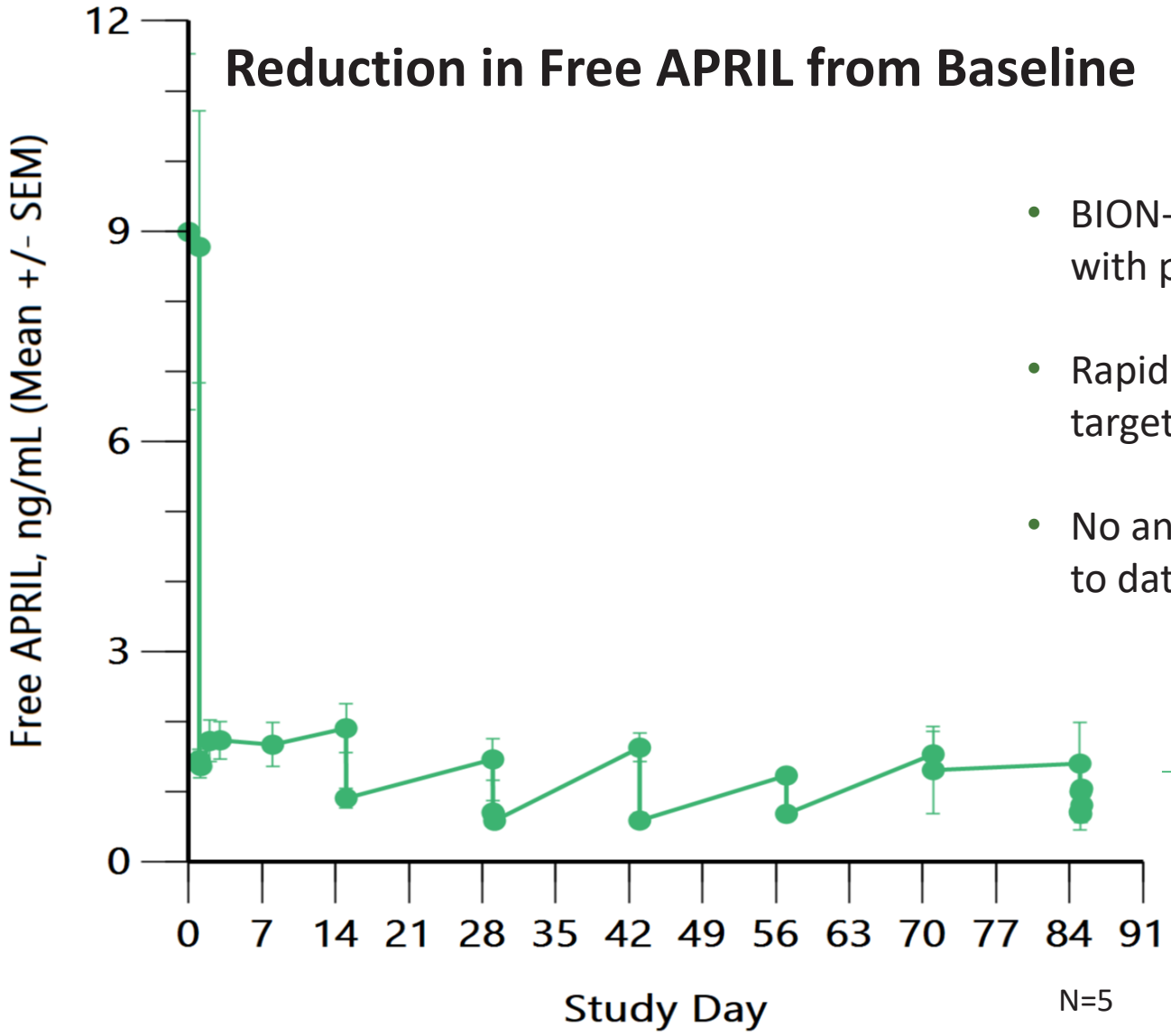
- BION-1301 has been well-tolerated in IgAN patients to date, consistent with previous experience in healthy volunteers (HVs)

AE category	N (%)
Any TEAE	3 (60%)
Any TEAE Occurring in N > 1	0 (0%)
Treatment Related AE	0 (0%)
AE Leading to Discontinuation	0 (0%)
SAE	0 (0%)
Infusion Related Reactions	0 (0%)

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

TEAE = Treatment Emergent Adverse Event; AE = Adverse Event; SAE = Serious Adverse Event

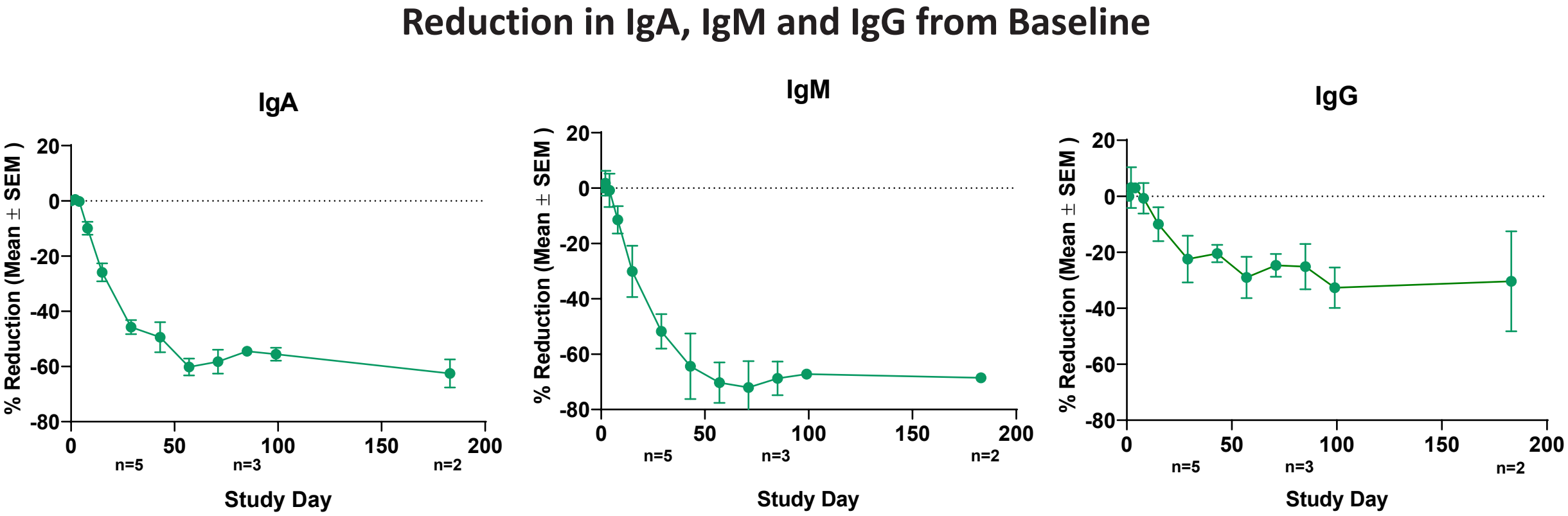
Free APRIL



- 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

CHINOOK THERAPEUTICS

Serum Immunoglobulin Profiles

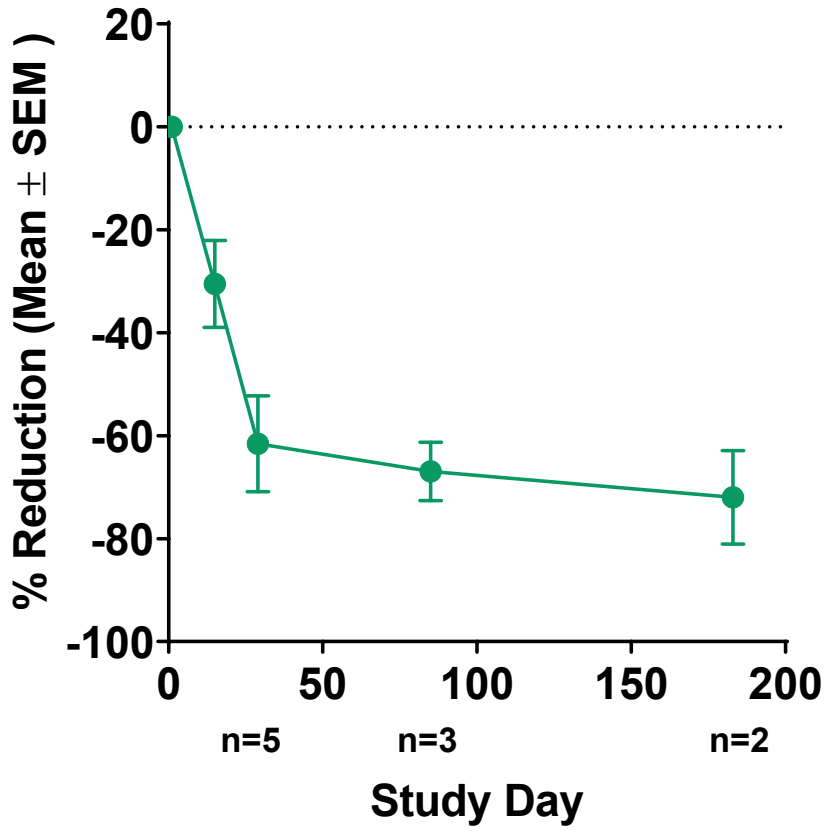


- BION-1301 durably reduces IgA and IgM and to a lesser extent, IgG, in patients with IgAN, with similar kinetics and magnitude as previously observed with BION-1301 in HVs

CHINOOK THERAPEUTICS

Gd-IgA1

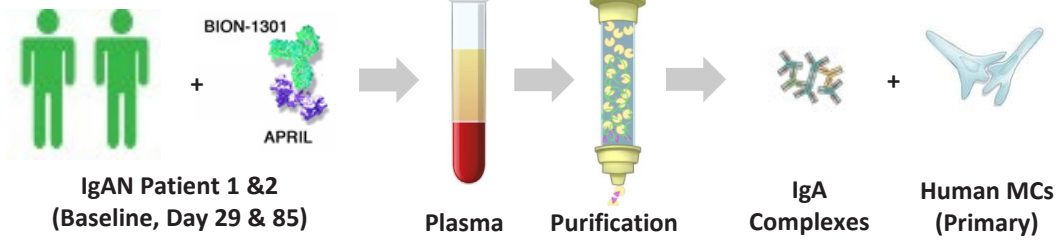
Reduction in Gd-IgA1 from Baseline



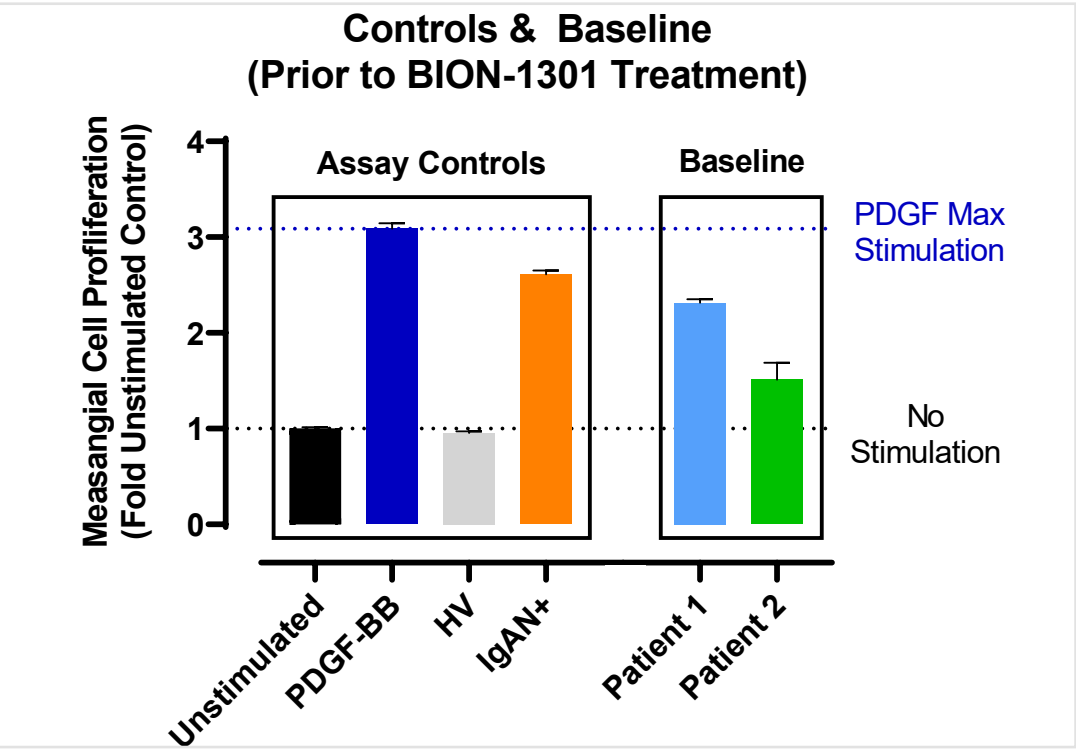
- BION-1301 produces sustained reductions in serum Gd-IgA1
- The depletion of this pathogenic IgA isoform (Hit 1) in patients with IgAN demonstrates the potential disease modifying mechanism of BION-1301
- The kinetics and magnitude of Gd-IgA1 reductions are consistent with previous observations reported with BION-1301 in HVs

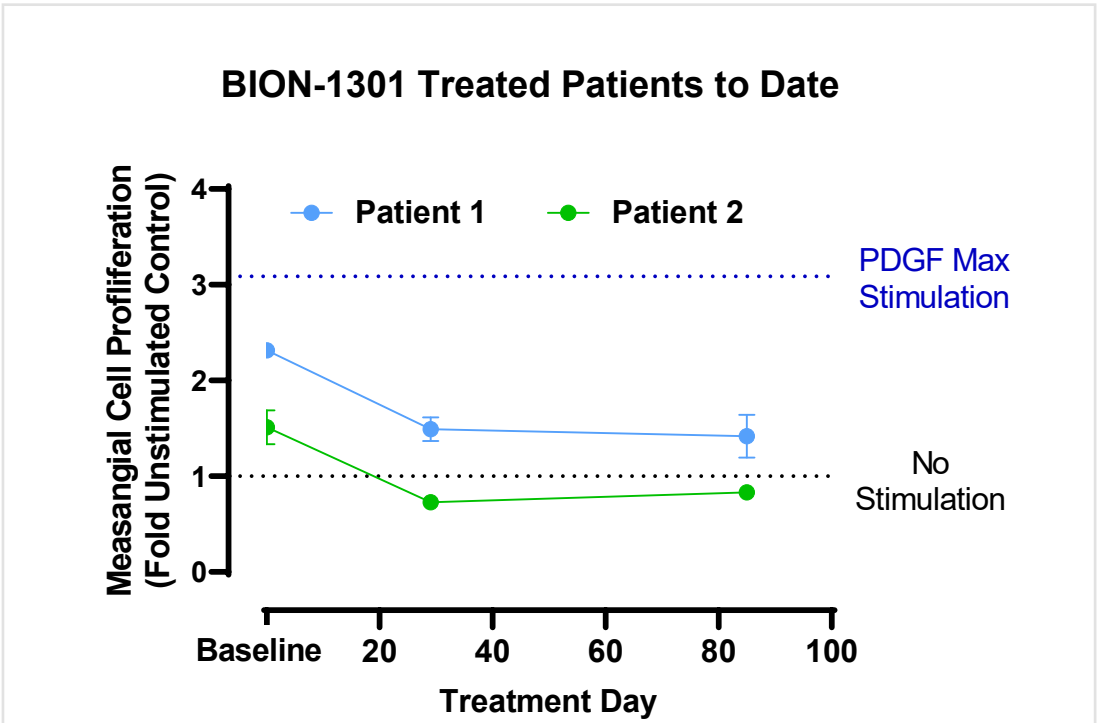
CHINOOK THERAPEUTICS

Ex vivo Mesangial Cell Activation



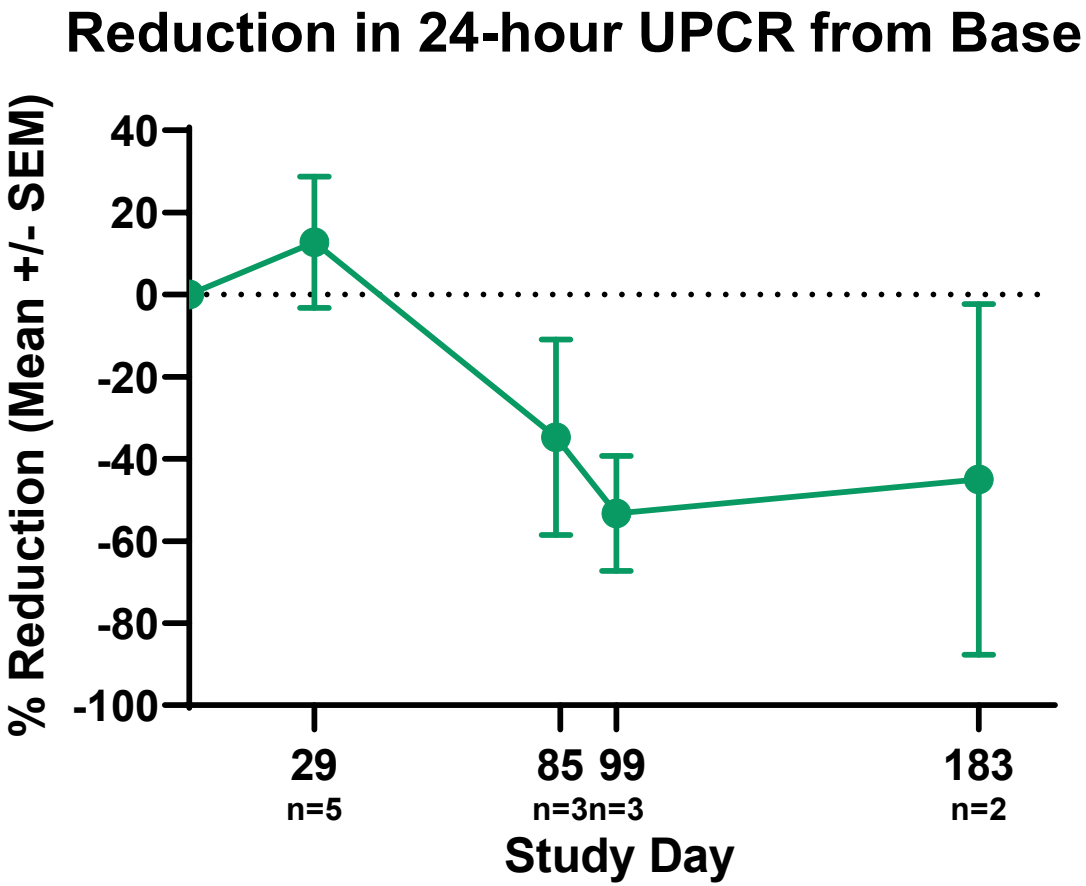
- IgA-complexes from patient 1 and 2 produced mesangial cell hyperproliferation at baseline, which was attenuated following BION-1301 treatment





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

Proteinuria & eGFR

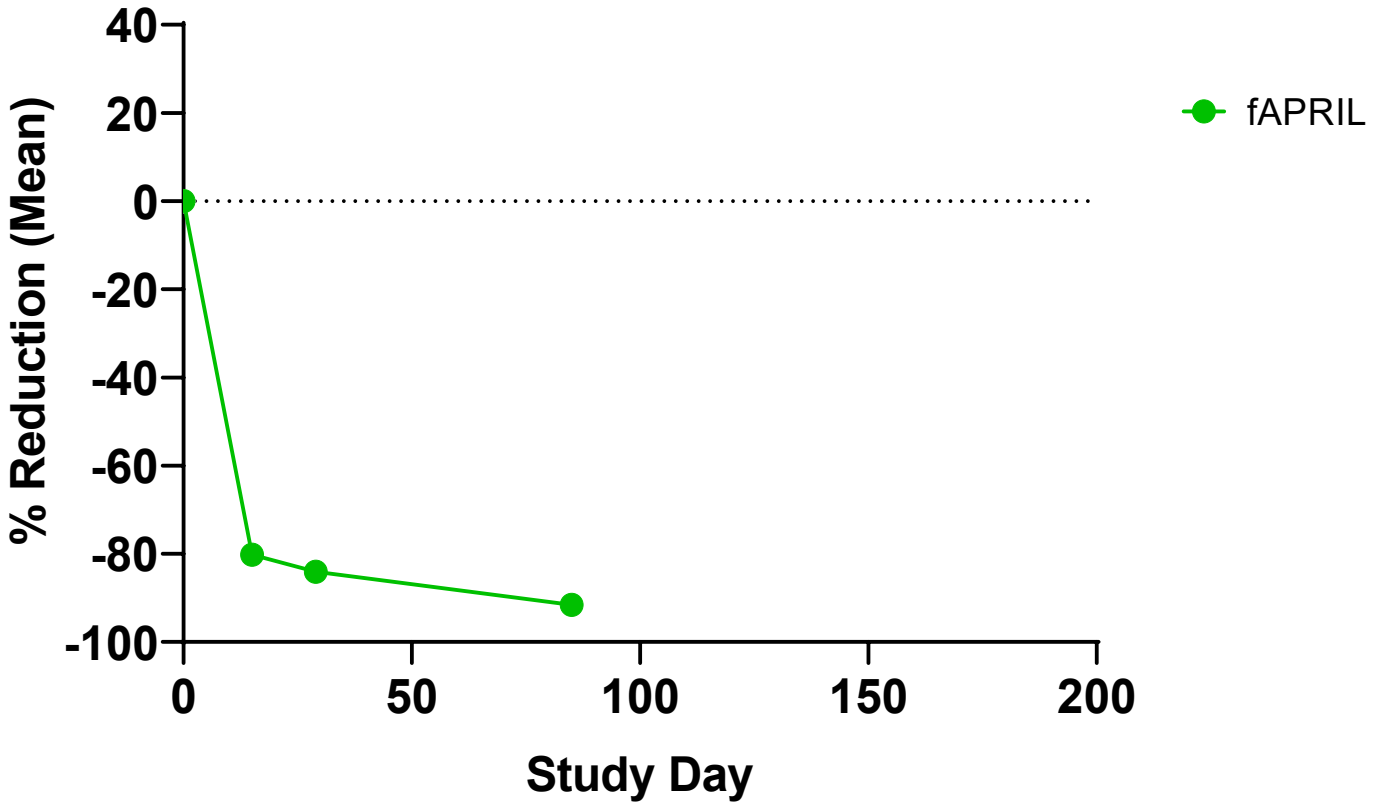


- Baseline 24-hour UPCR (24-hr collections*) ranged from 530 - 4551 mg/g
- Preliminary proteinuria reductions observed in patients with IgAN, across a wide range of baseline UPCR Levels, provide initial clinical proof-of-concept for BION-1301
- No significant change in eGFR was noted for any patient through 183 days of treatment

*1/5 patients missed 24-hr collection; morning void used

BION-1301 Response Kinetics

Reduction in Free APRIL

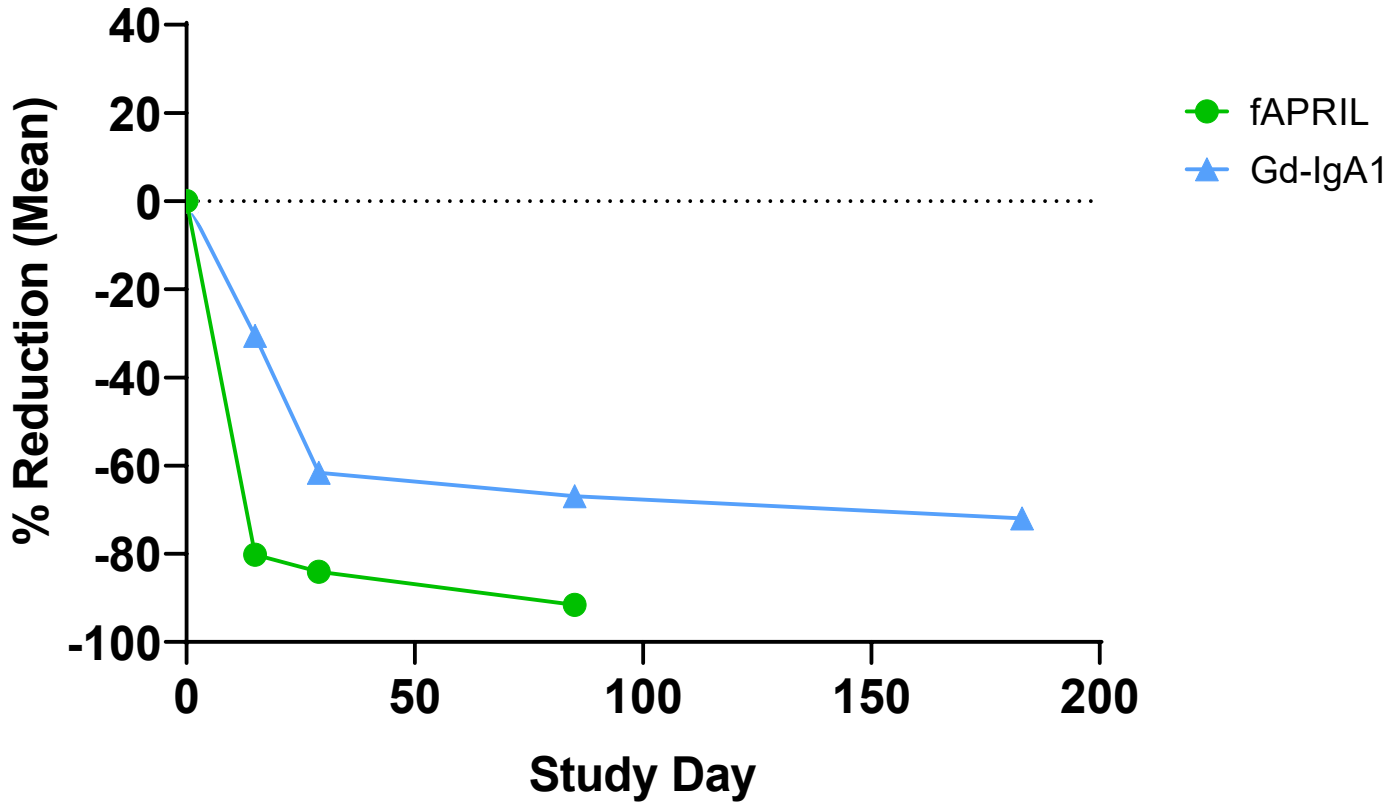


- In patients with IgAN treated to date, BION-1301 resulted in:
  - rapid APRIL neutralization

Mean only shown for clarity

BION-1301 Response Kinetics

Reduction in Free APRIL, Gd-IgA1

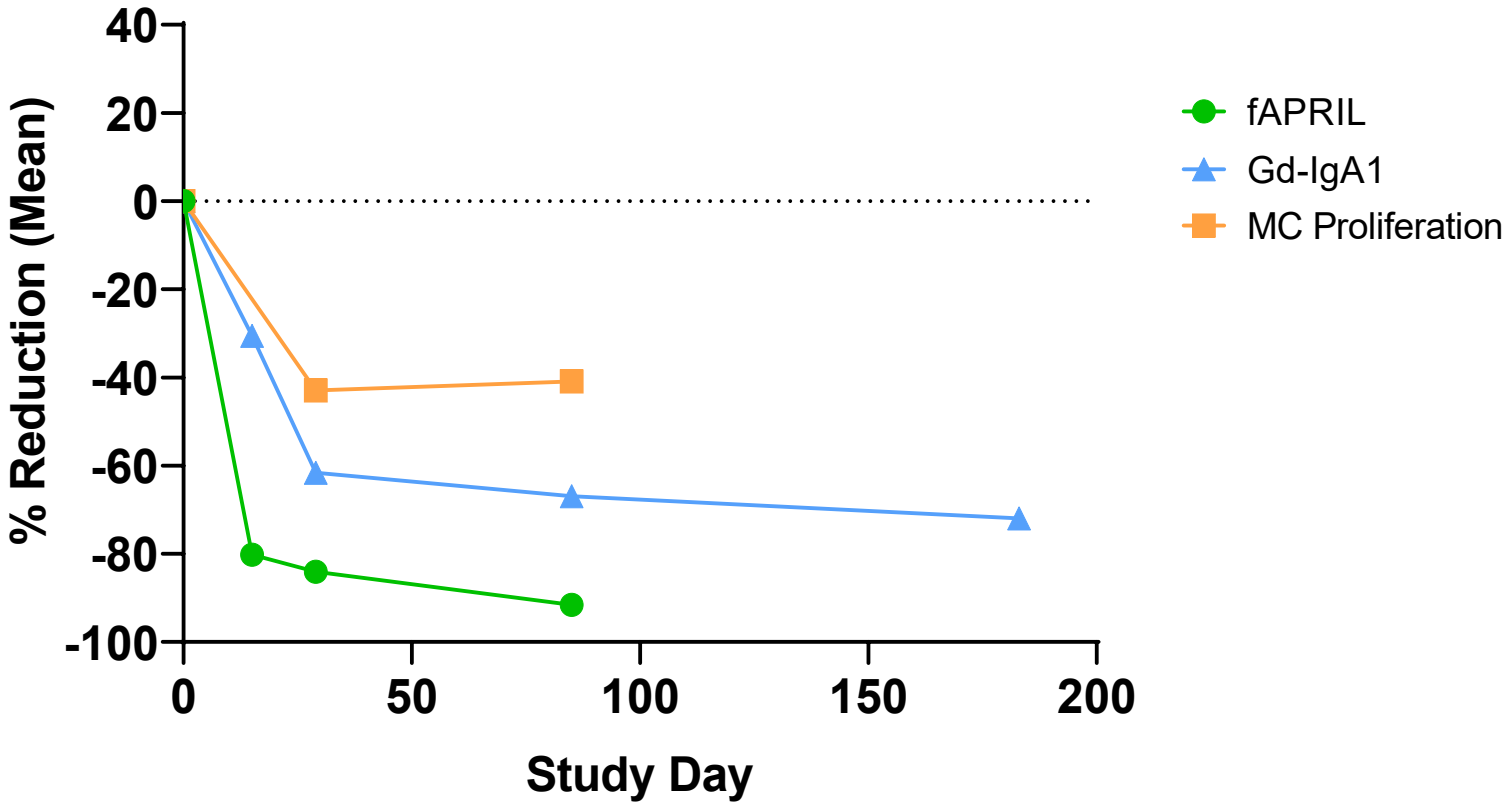


- In patients with IgAN treated to date, BION-1301 resulted in:
  - rapid APRIL neutralization
- Followed by:
  - Gd-IgA1 depletion

Mean only shown for clarity

BION-1301 Response Kinetics

Reduction in Free APRIL, Gd-IgA1, MC Activation



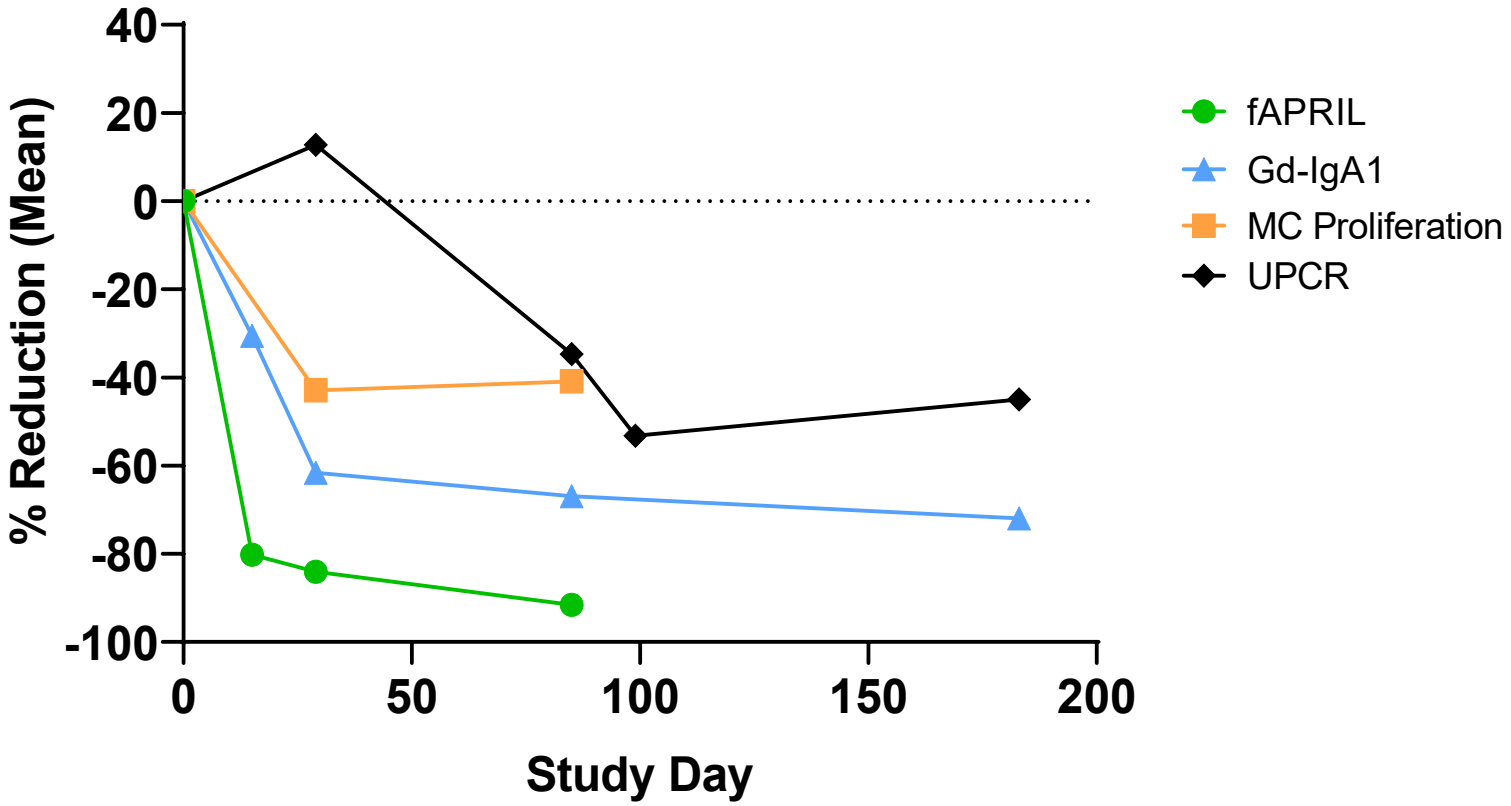
- In patients with IgAN treated to date, BION-1301 resulted in:
  - rapid APRIL neutralization
- Followed by:
  - Gd-IgA1 depletion

    And
  - Reduced mesangial cell activation (*ex vivo*)

Mean only shown for clarity

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

Mean only shown for clarity

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