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PO1843

Results of a Phase 1 Trial to Investigate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BION-1301 in Healthy Volunteers

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Disclosures

- Current Employer: University of Leicester
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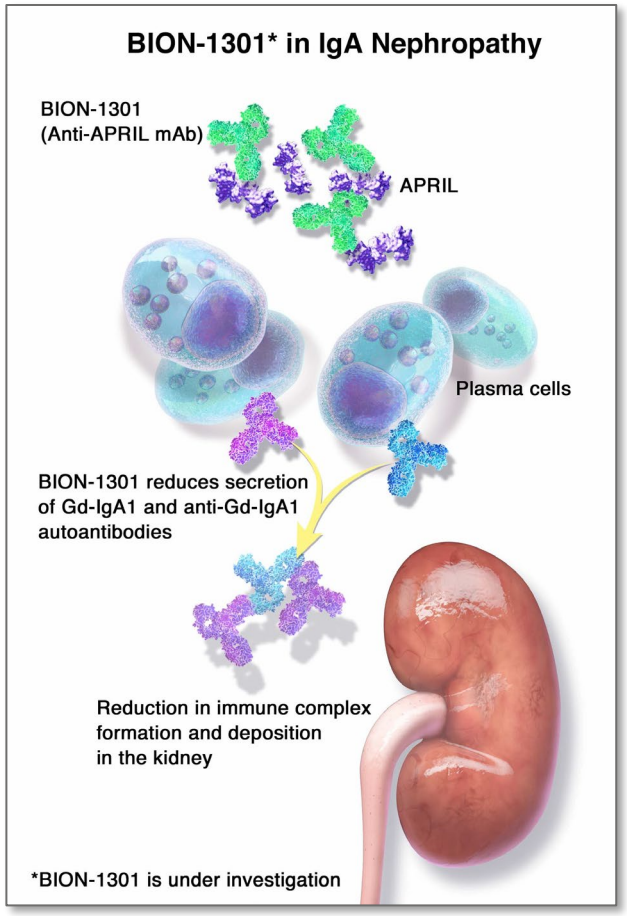
BION-1301 Blocks APRIL, a Critical Factor Driving the Pathophysiology of IgAN

BION-1301: APRIL blockade in IgA Nephropathy

- Novel monoclonal antibody that blocks APRIL binding to B-cell maturation antigen (BCMA) and transmembrane activator and calcium-modulator and cyclophilin ligand interactor (TACI)
- Recombinant, humanized IgG4 monoclonal antibody (mAb)
- Has been evaluated in 2 clinical studies to date (*NCT03340883, NCT03945318)*

APRIL: A PRoliferation Inducing Ligand

- TNF-family ligand implicated in regulation of B-cell mediated immune responses
- Soluble factor that binds to its receptors TACI and BCMA inducing B cell signaling that drives:
  - IgA class switching through TACI
  - Differentiation and survival of IgA-producing plasma cells through BCMA
- Patients with IgAN have higher levels of APRIL compared to healthy controls
- Higher APRIL levels in IgAN patients correlate with poor prognosis
- A polymorphism in the APRIL gene confers IgAN susceptibility



Blocking APRIL is a novel approach to address underlying pathology by reducing circulating levels of IgA, Gd-IgA1, anti-Gd-IgA1 autoantibodies and immune complex formation

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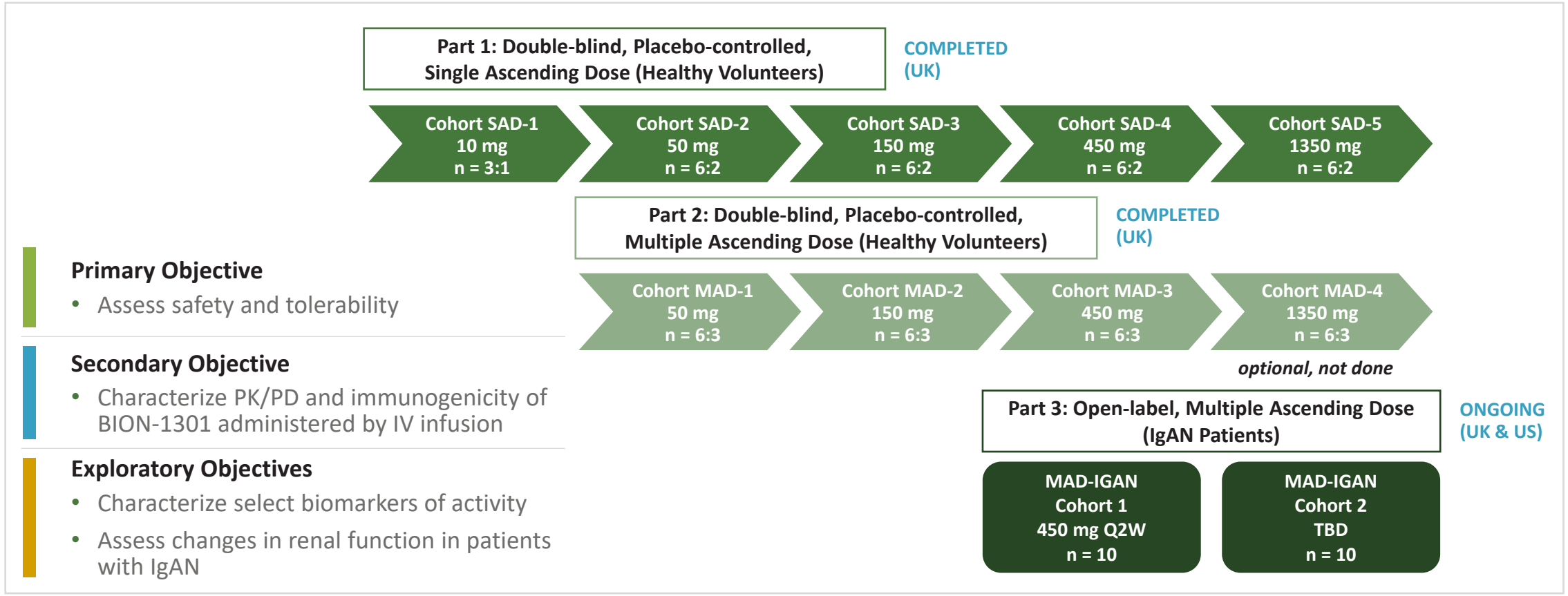
Study Design and Objectives

ADU-CL-19 is a Phase 1 multicenter trial to evaluate the safety, tolerability, PK, and PD of IV administered BION-1301. The study will be conducted in HVs (Parts 1, 2) and in adults with IgA Nephropathy (Part 3)



Data Extract: 22 April 2020
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Baseline Demographics

	SAD BION-1301 (N=27)	SAD Placebo (N=9)	MAD BION-1301 (N=18)	MAD Placebo (N=9)
Age (years)				
Mean (std dev)	36.66 (8.38)	35.0 (8.39)	35.4 (9.01)	36.55 (7.85)
Sex				
Male	27 (100%)	9 (100%)	18 (100%)	9 (100%)
Female	0	0	0	0
Race				
American Indian or Alaskan Native	0	0	0	0
Asian	2 (7.4%)	3 (33.3%)	0	0
Black or African American	6 (22.2%)	1 (11.1%)	3 (16.7%)	2 (22.2%)
White	18 (66.7%)	4 (44.4%)	11 (61.11%)	4 (44.4%)
Native Hawaiian or Pacific Islander	0	0	0	0
Multiple	1 (16.7%)	1 (11.1%)	4 (22.2%)	3 (33.3%)
BMI (kg/m^2)				
Mean (std dev)	25.46 (2.47)	23.73 (2.94)	25.65 (3.00)	25.95 (1.56)

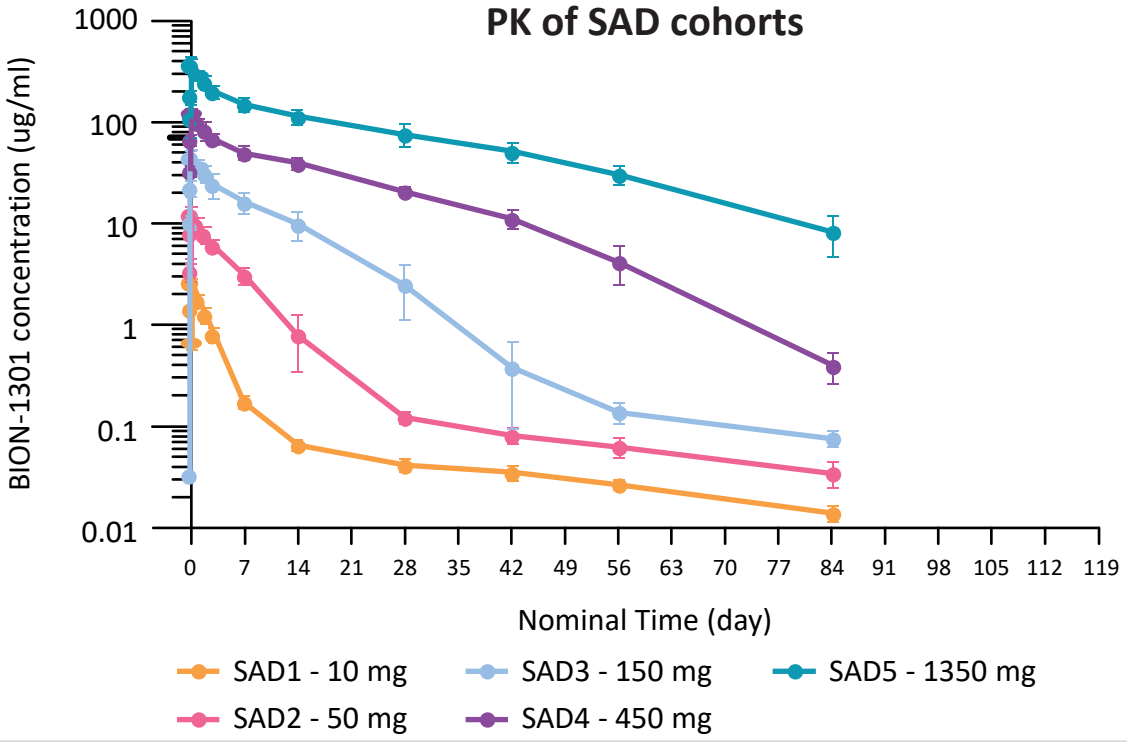
BION-1301 is Well Tolerated in Healthy Volunteers

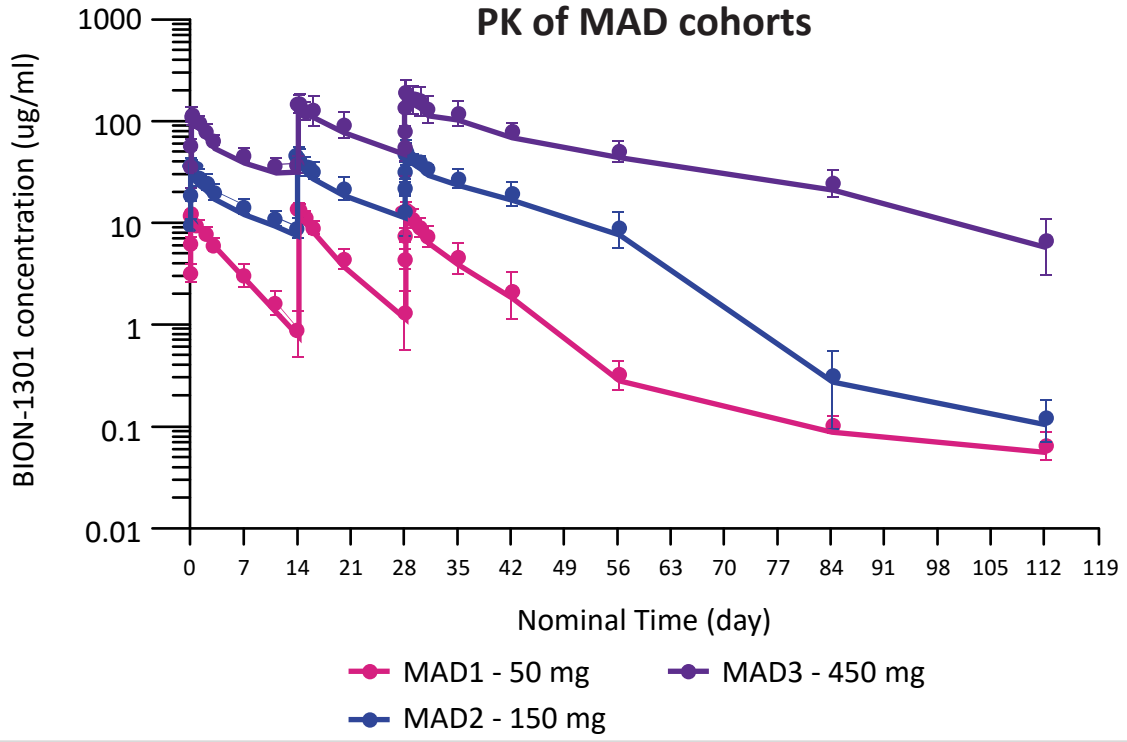
Single Ascending Dose (SAD) 1 Dose (Day 1) Study Duration 13 Weeks	10 mg (N=3)	50 mg (N=6)	150 mg (N=6)	450 mg (N=6)	1350 mg (N=6)	Placebo (N=9)	Total (N=36)
Any TEAEs	2 (66.7%)	3 (50.0%)	3 (50.0%)	4 (66.7%)	3 (50.0%)	7 (77.8%)	22 (61.1%)
Grade 3 or higher TEAEs	0	0	0	0	0	0	0
Treatment-related TEAEs	2 (66.7%)	0	1 (16.7%)	1 (16.7%)	1 (16.7%)	2 (22.2%)	7 (19.4%)
≥ Grade 3 Treatment-related TEAEs	0	0	0	0	0	0	0
Treatment-emergent SAEs	0	0	0	0	0	0	0
Treatment-related treatment-emergent SAEs	0	0	0	0	0	0	0
Infusion-related reactions	0	0	0	0	0	0	0

Multiple Ascending Dose (MAD) 3 Doses (Day 1, 15, 29) Study Duration 17 Weeks	50 mg (N=6)	150 mg (N=6)	450 mg (N=6)	Placebo (N=9)	Total (N=27)
Any TEAEs	2 (33.3%)	6 (100%)	5 (83.3%)	6 (66.7%)	19 (70.4%)
Grade 3 or higher TEAEs	0	1 (16.7%)	0	0	1 (3.7%)
Treatment-related TEAEs	2 (33.3%)	2 (33.3%)	1 (16.7%)	1 (11.1%)	6 (22.2%)
≥ Grade 3 Treatment-related TEAEs	0	0	0	0	0
Treatment-emergent SAEs	0	0	0	0	0
Treatment-related treatment-emergent SAEs	0	0	0	0	0
Infusion-related reactions	0	1 (16.7%)	0	0	1 (3.7%)

No treatment discontinuations or events meeting stopping criteria were reported. The most common AE occurring in ≥ 10% of subjects in the SAD cohorts was nasopharyngitis. The most common AEs occurring in ≥ 10% of subjects in the MAD cohorts were headache, pain in extremity, elevated AST and nasopharyngitis.

BION-1301 Concentration is Generally Dose-Proportional and Estimated Half-Life Suggests Monthly Dosing





	Single Ascending Dose (mg)					Multiple Ascending Dose (mg)		
	10	50	150	450	1350	50	150	450
Summary Statistics	**Mean (CV%)**	**Mean (CV%)**	**Mean (CV%)**	**Mean (CV%)**	**Mean (CV%)**	**Mean (CV%)**	**Mean (CV%)**	**Mean (CV%)**
C_{max} (µg/mL)	2.62 (5.9)	12.5 (19.5)	44.7 (18.5)	120 (9.0)	363 (18.4)	12.8 (5.8)	38.9 (12.7)	123 (18.6)
$AUC_{0\text{-}14\ day}$ (day•µg/mL)	7.3 (12.9)	56.1 (18.8)	264 (22.0)	789 (13.2)	2340 (15.0)	58.9 (15.5)	235 (16.5)	779 (12.8)

Half-life ($t_{1/2}$) was estimated for SAD 1 and SAD 2 cohorts as 31.8 days and 34.0 days, respectively. Low incidence of anti-drug antibodies (ADA) with no correlation to dose. No neutralizing antibodies (NAb) were detected.

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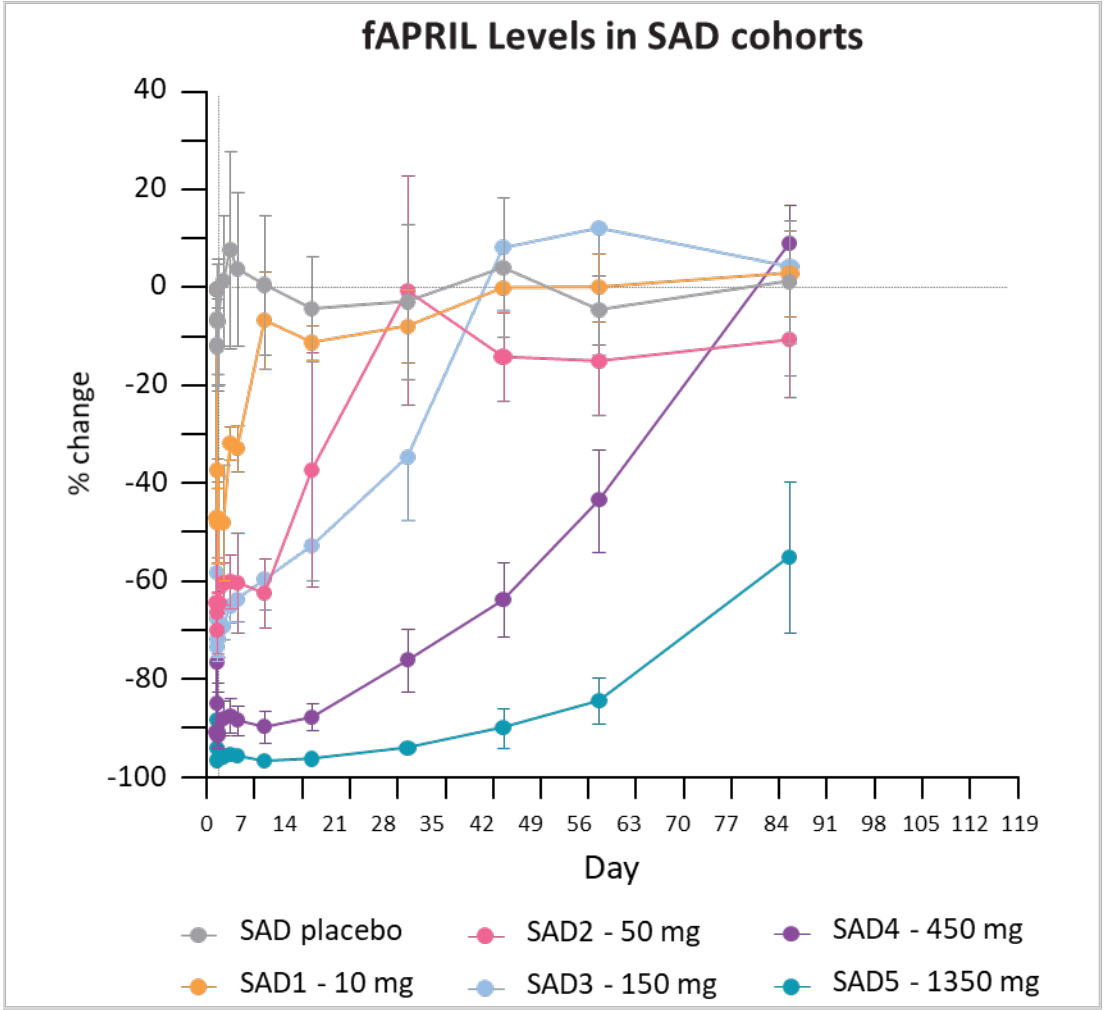
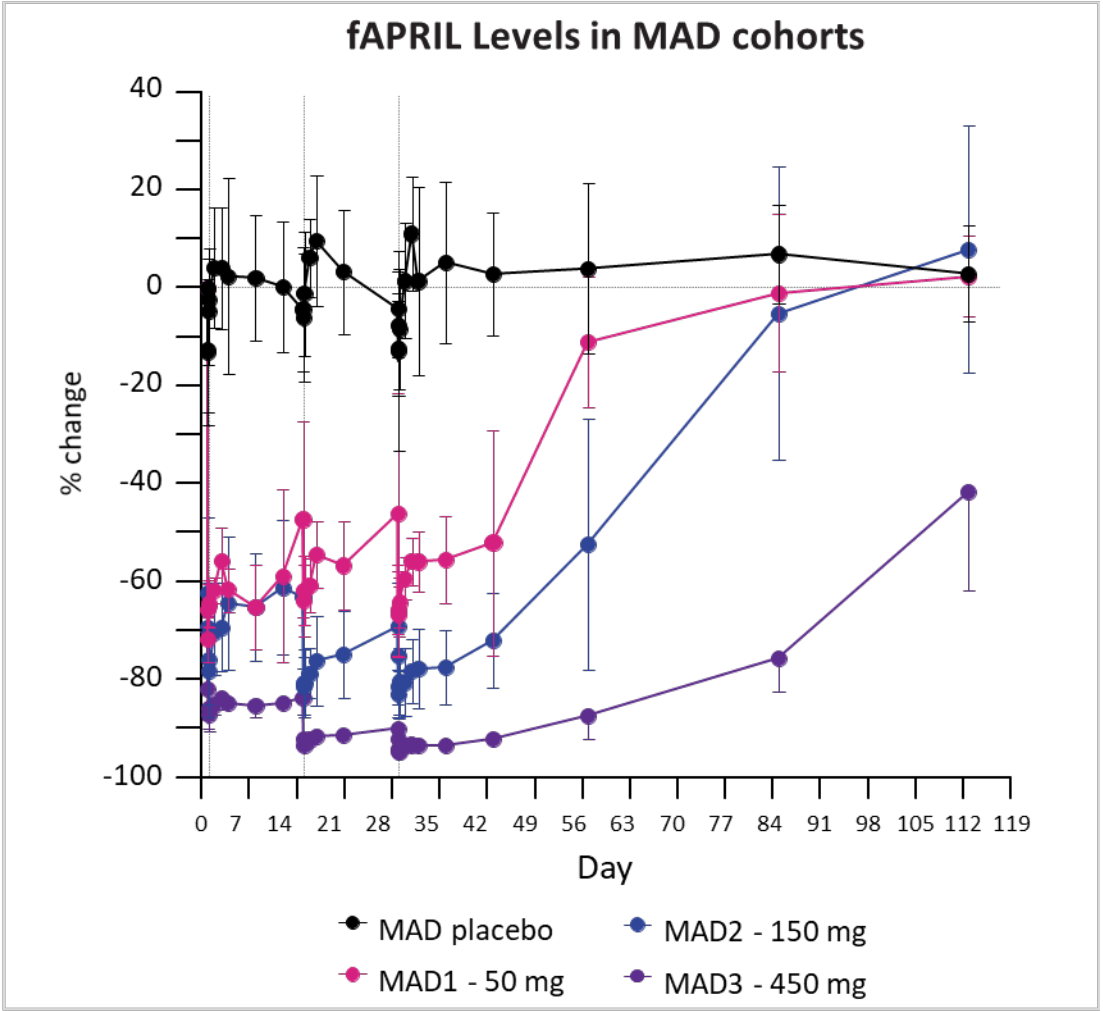
BION-1301 Demonstrates Durable Dose-Dependent Increase in Target Engagement as Measured by Free APRIL (fAPRIL)





Percent change relative to baseline of free APRIL in serum over time (days). Target engagement is sustained for > 1 month at higher doses. Note: APRIL levels in IgAN patients are reported to be higher than in healthy volunteers.

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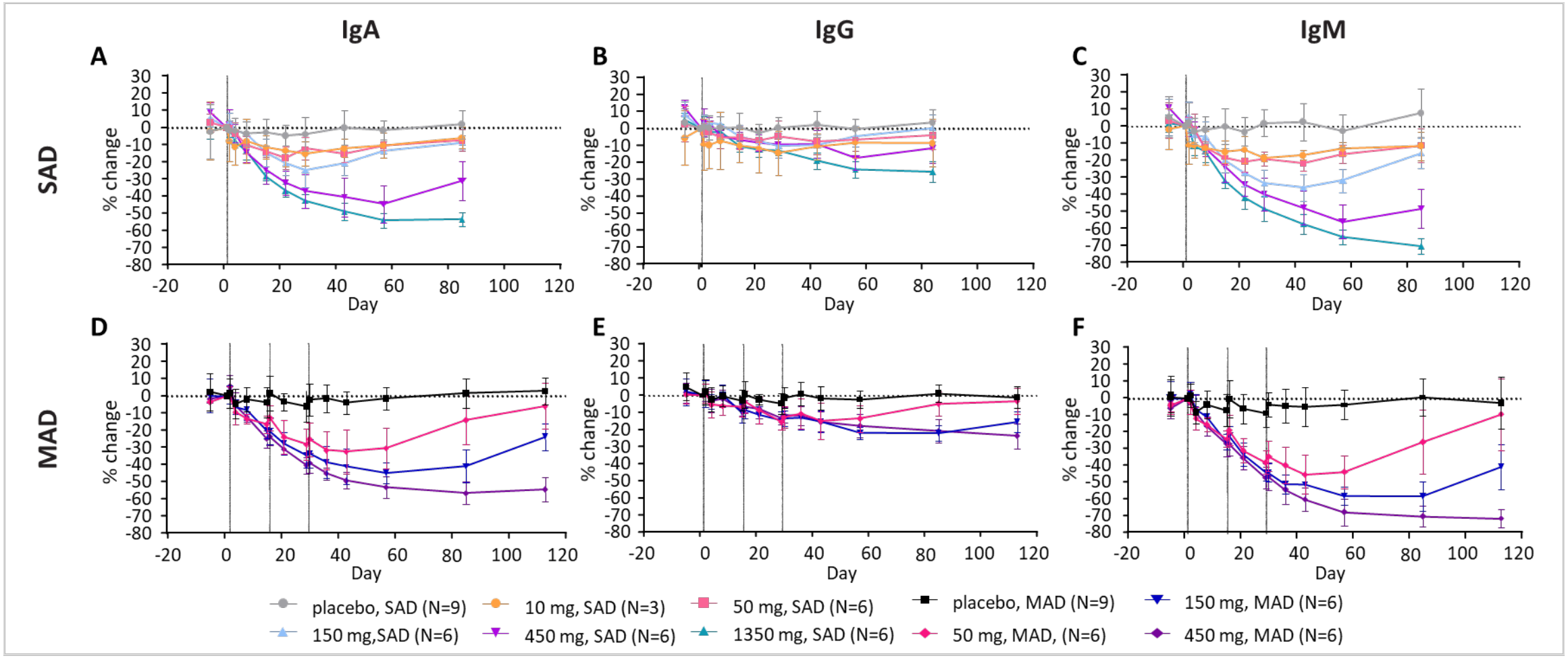
BION-1301 Dose-Dependently and Durably Reduces IgA and IgM, and to a Lesser Extent IgG

Data Consistent with Potential for Monthly Dosing



Mean % change +/- SD of Ig levels in serum relative to baseline. (A-C) Single dose cohorts and (D-F) multiple dose cohorts relative to baseline over time (days). Baseline sample taken on Day 1 pre-dose. IgG values remained in the normal lab range.

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Conclusions and Next Steps

- BION-1301 was well-tolerated in healthy volunteers with no reports of infection associated with treatment
- The PK profile of BION-1301 was well behaved, generally dose-proportional and demonstrated a half-life with the potential to be administered by monthly dosing
  - A low incidence of ADAs; no NAbs were detected
- BION-1301 demonstrates a durable dose-dependent increase in target engagement as measured by fAPRIL
- BION-1301 dose-dependently and durably reduces IgA and IgM, and to a lesser extent IgG
- Next steps include continued enrollment of patients with IgAN into Part 3 of the phase 1 trial (NCT03945318) and development of Gd-IgA1 and other biomarker assays
  - An Open-Label Extension study is available for patients who complete Part 3 of the phase 1 trial
- In preparation for a phase 2 trial, the subcutaneous PK/PD and bioavailability of BION-1301 is being assessed

These data suggests a pharmacodynamic window to maximize durable reductions in IgA while minimizing impact on IgG, thereby supporting the therapeutic utility of BION-1301 for the treatment of patients with IgAN