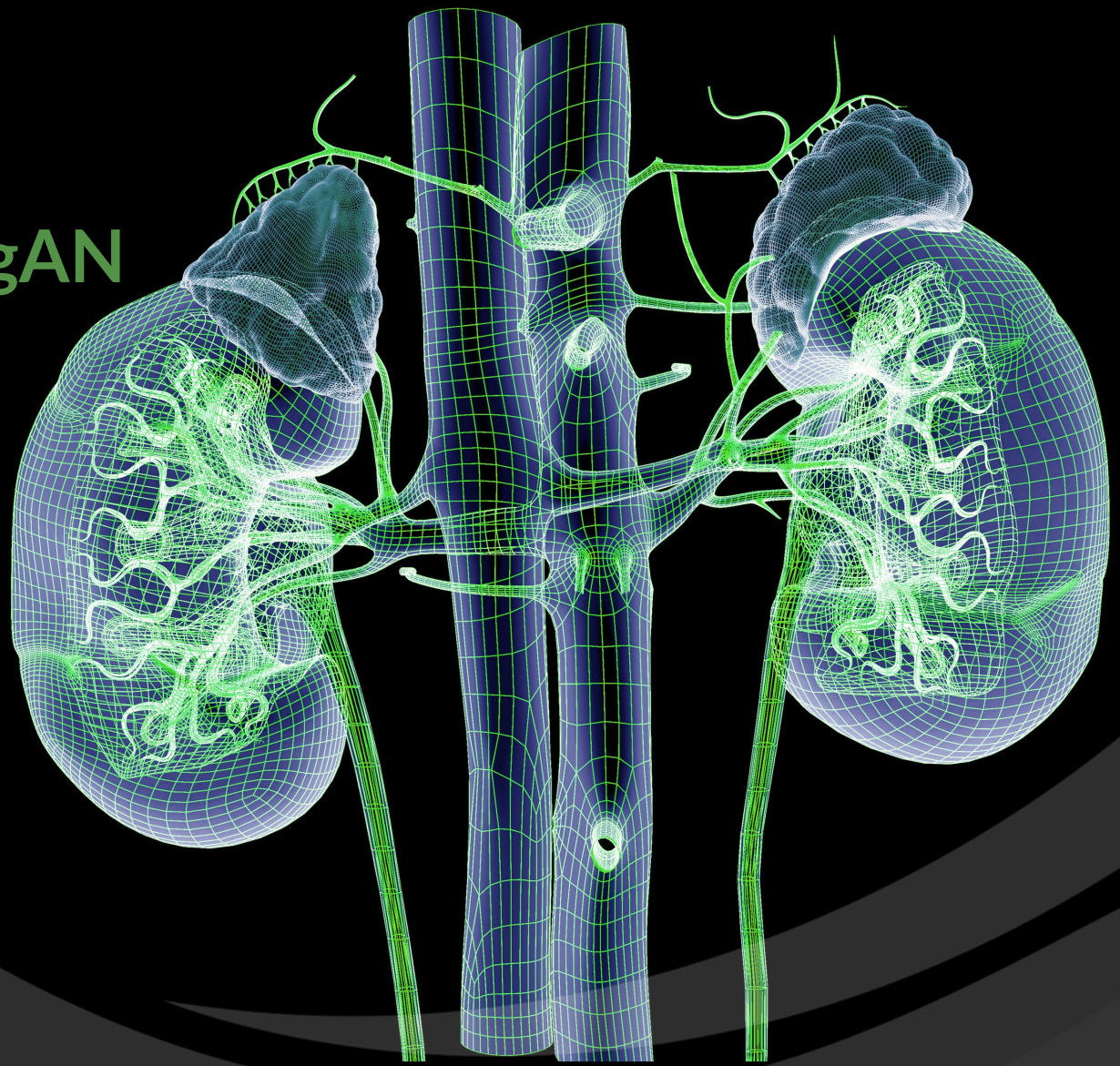
CHINOOK™ THERAPEUTICS

5th CKD Summit
Chronic Kidney Disease Drug Development

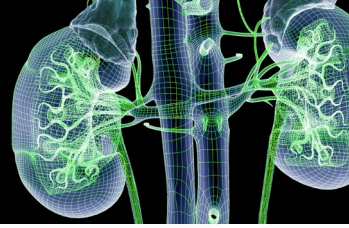
Accelerating the Development of BION-1301 for the Treatment of IgAN

From Proof of Concept to Phase 3

Andrew King
Chief Scientific Officer
March 9, 2023



Outline



The potentially disease modifying MOA of BION-1301* in IgAN

BION-1301 clinical development program to IgAN PoC

BION-1301 Phase 3 key trial design elements

*BION-1301 is an investigational drug that has not been approved by regulatory authorities. Efficacy and safety have not been established. There is no guarantee that it will become commercially available for the use(s) under investigation

IgA NEPHROPATHY HAS A

LARGE UNMET MEDICAL NEED

IgAN is the most common primary glomerular disease globally and requires chronic treatment

~150,000 Biopsy-confirmed IgAN patients in the U.S.[1]

~45% with >1 g/day[1]

~25% with 0.5 – 1 g/day[1]

Patients with persistent proteinuria despite optimized standard of care RAS inhibition (ACEi or ARB)

~100,000 Patients remain at high risk for progression (US)

Clear need for novel strategies to directly target the initiating molecular events in the complex pathogenesis of IgAN

~30-45% of IgAN patients progress to ESKD over 20-25 years[3-6]

ACHIEVING

30% PROTEINURIA REDUCTION

EQUATES TO

>10 YEAR DELAY IN TIME TO ESKD[2]

Greater proteinuria reductions are associated with greater clinical benefit

1. Based on Chinook market research; 2. Carroll KJ, et al. ERA-EDTA Congress 2021, MO246; 3. Reich et al, 2007, JASN; 4. Moriyama et al, 2014, PLOS ONE; 5. Rauen et al, 2020, Kidney Int; 6. Hastings et al, 2018, Kidney Int Rep

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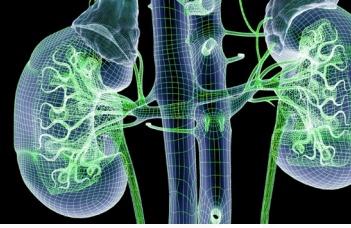
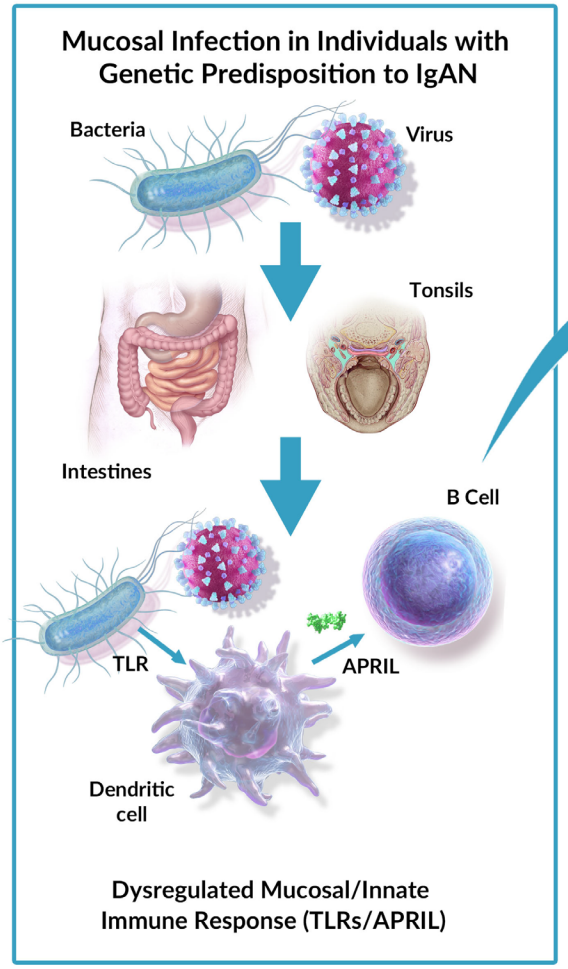
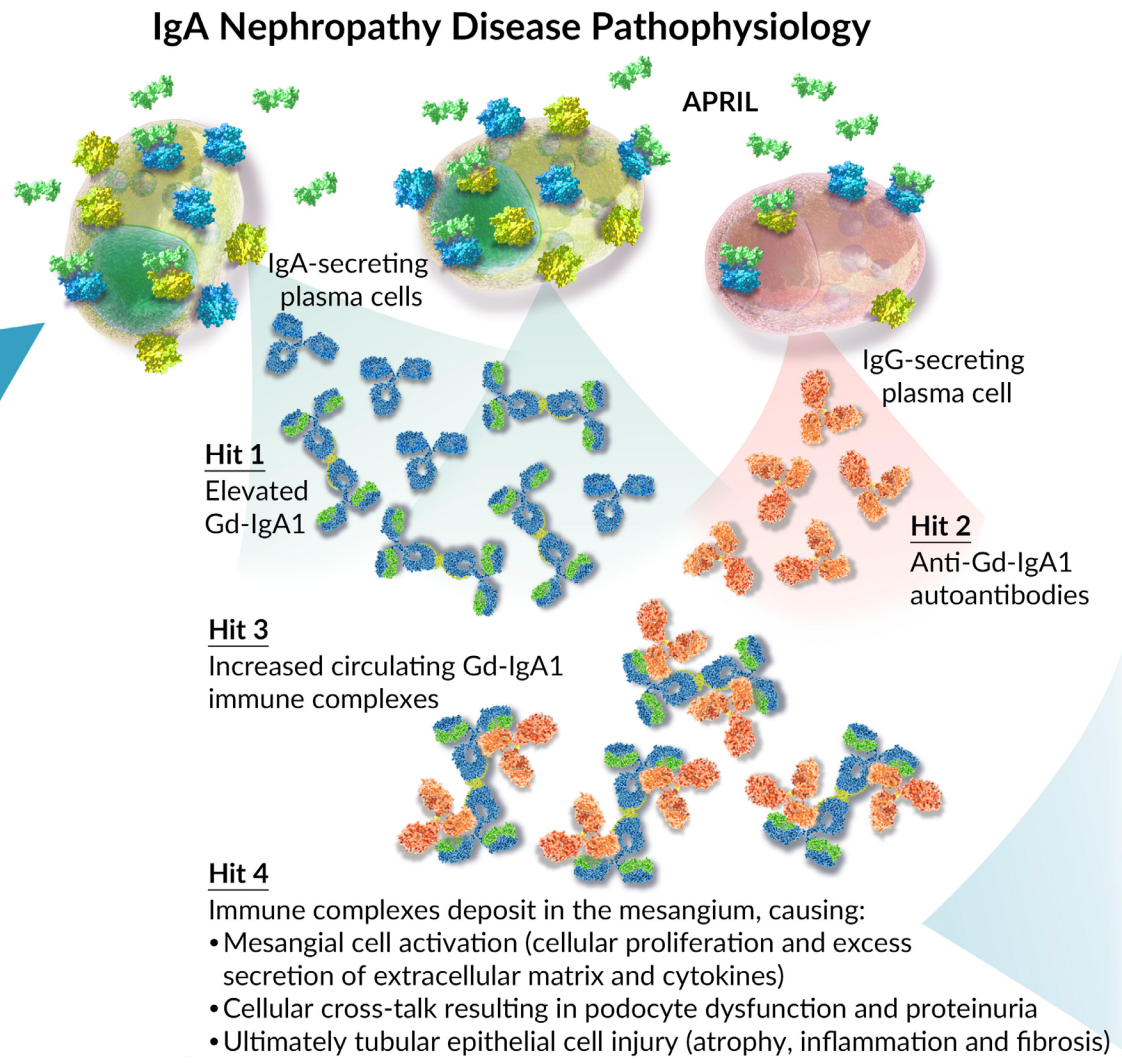
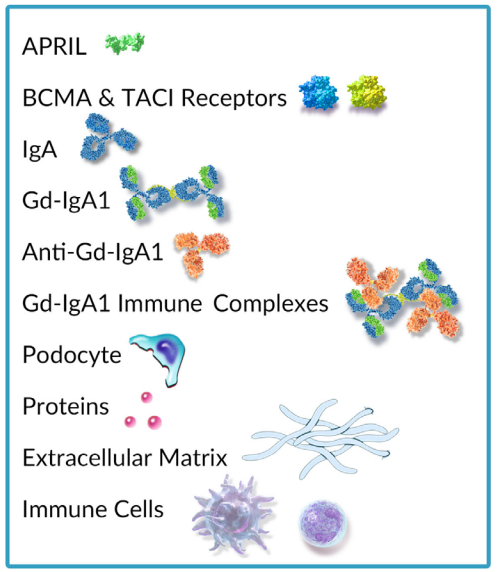
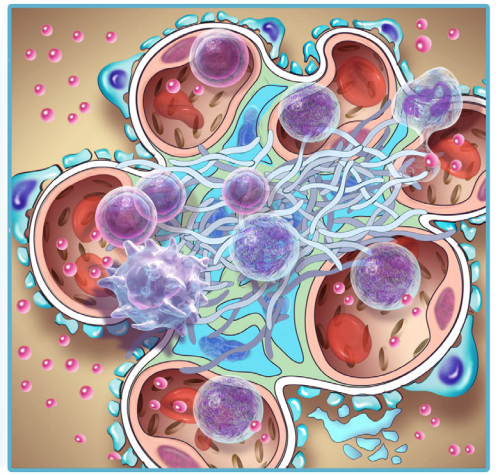
Complex Multi-Hit Pathogenesis of IgAN Provides Potential for Targeted Therapeutic Strategies











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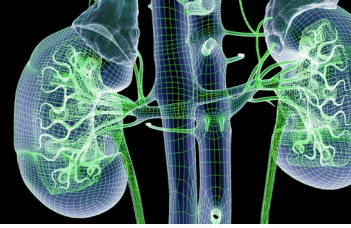
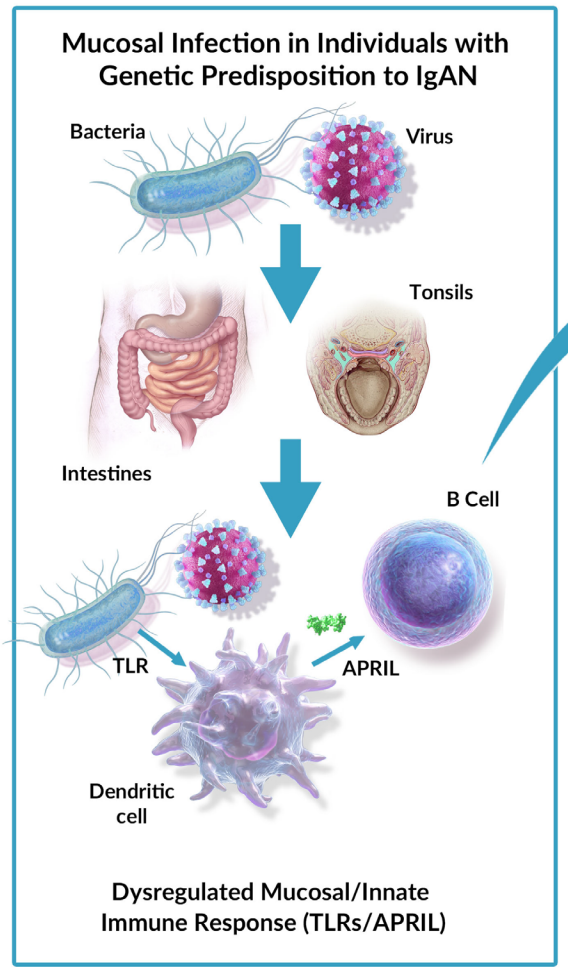
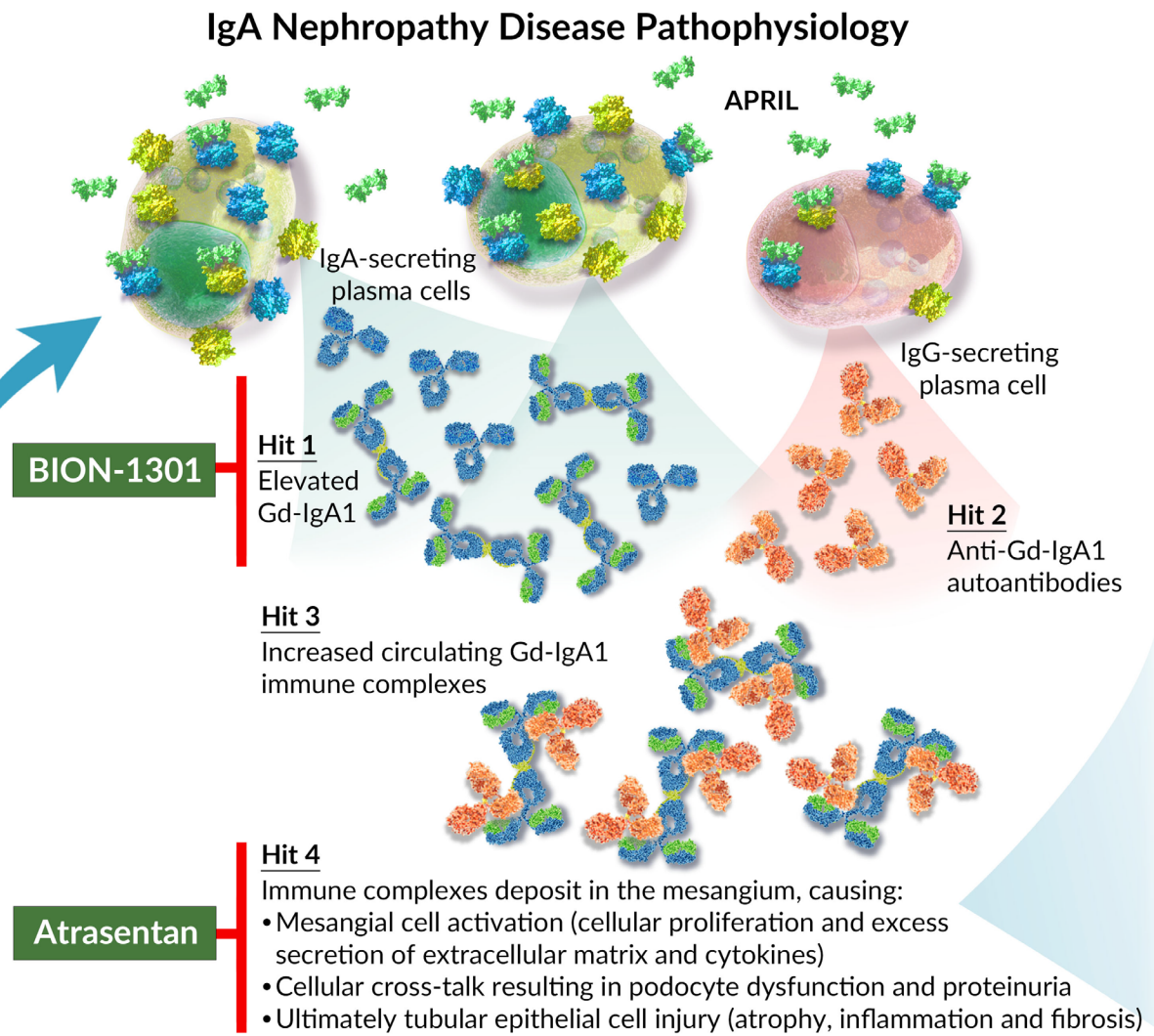
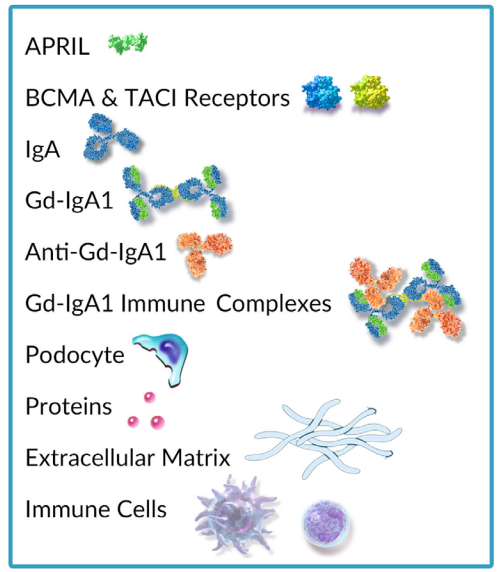
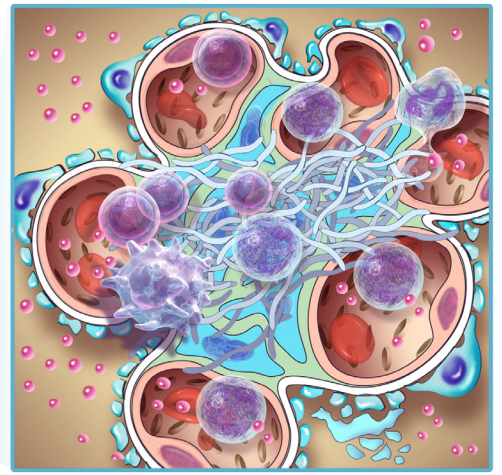
Complex Multi-Hit Pathogenesis of IgAN Provides Potential for Targeted Therapeutic Strategies











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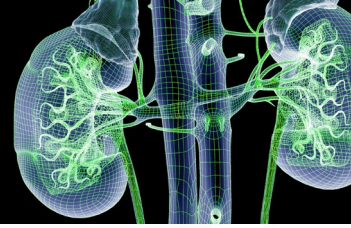
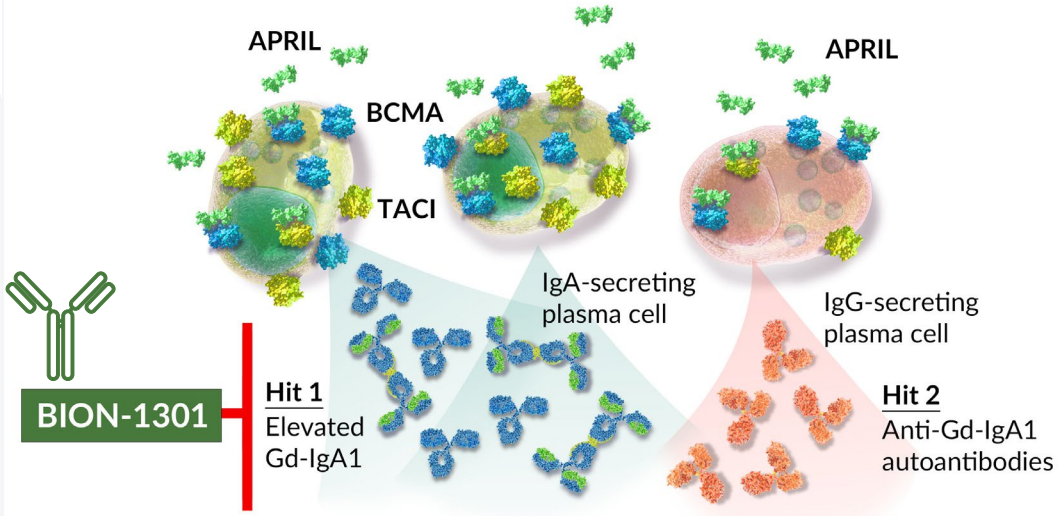
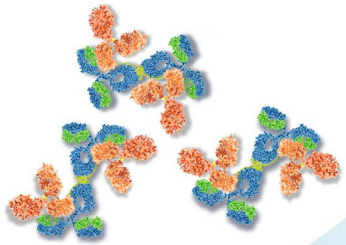
BION-1301: Potentially Disease-Modifying Anti-APRIL mAb in IgAN

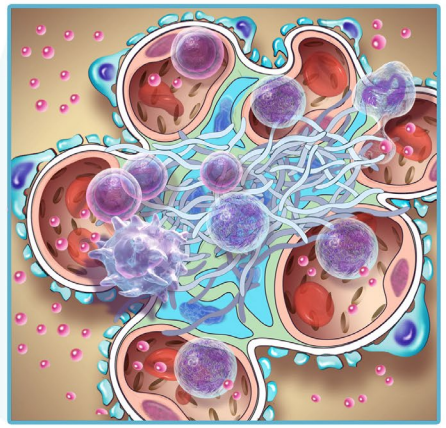




Hit 3
Increased circulating Gd-IgA1 immune complexes



Hit 4
Immune complexes deposit in the mesangium, causing:
- Mesangial cell activation (cellular proliferation and excess secretion of extracellular matrix and cytokines)
- Cellular cross-talk resulting in podocyte dysfunction and proteinuria
- Ultimately tubular epithelial cell injury (atrophy, inflammation and fibrosis)



APRIL
TNF-family cytokine involved in B-cell signaling[1]

- **Drives IgA production** and survival of IgA-secreting plasma cells[2]
- Shown to **increase Gd-IgA1 secretion**[3]
- Higher APRIL levels in IgAN patients correlated with **higher Gd-IgA1 and proteinuria** and **lower eGFR**[3]
- APRIL gene variants confer **increased risk of IgAN**[4]

BION-1301
Humanized IgG4 monoclonal antibody that blocks APRIL binding to its receptors

- **Potently** binds recombinant **human and cynomolgus APRIL** (but does not bind rodent APRIL)
- **Functional blocking** of APRIL at **BCMA** and **TACI** receptors
- **Does not induce cytokine release** in human PBMCs

1. Guadagnoli, M, et al. Blood. 2016. 2. He B, et al. Nat Immunol. 2010; 3. Zhai YL, et al. Medicine (Baltimore). 2016. 4. Yu XQ, et al. Nature Genetics. 2012 Feb;44(2):178-182. 5. Kreijtz J, et al. ERA-EDTA 2020 poster presentation: poster #P0379..

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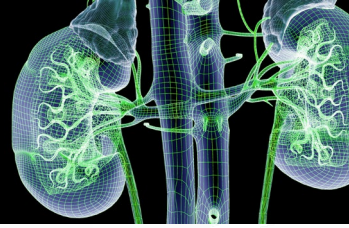
BION-1301 Development Program: HV, POM and POC in IgAN



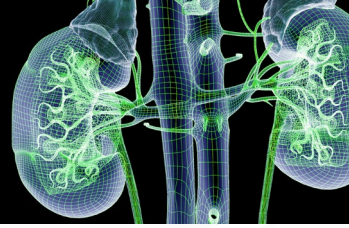
ADU-CL-19 | **Phase 1/2: HV & IgAN Patients**

- **Part 1:** Single Ascending Dose, Healthy Volunteers
- **Part 2:** Multiple Ascending Dose, Healthy Volunteers
- **Part 3:** Proof of Mechanism / Proof of Concept, IgAN Patients

Other | **Additional HV Studies**

- **SC Bioavailability:** Single Dose IV/SC, Healthy Volunteers
- **Japanese HV:** Single Ascending Dose, Healthy Volunteers (in progress)
- **Chinese HV:** Single Ascending Dose, Healthy Volunteers (planned)

Phase 1 Study in Healthy Volunteers (HVs): Study Design, Safety and Pharmacokinetics (PK)



Primary Objective

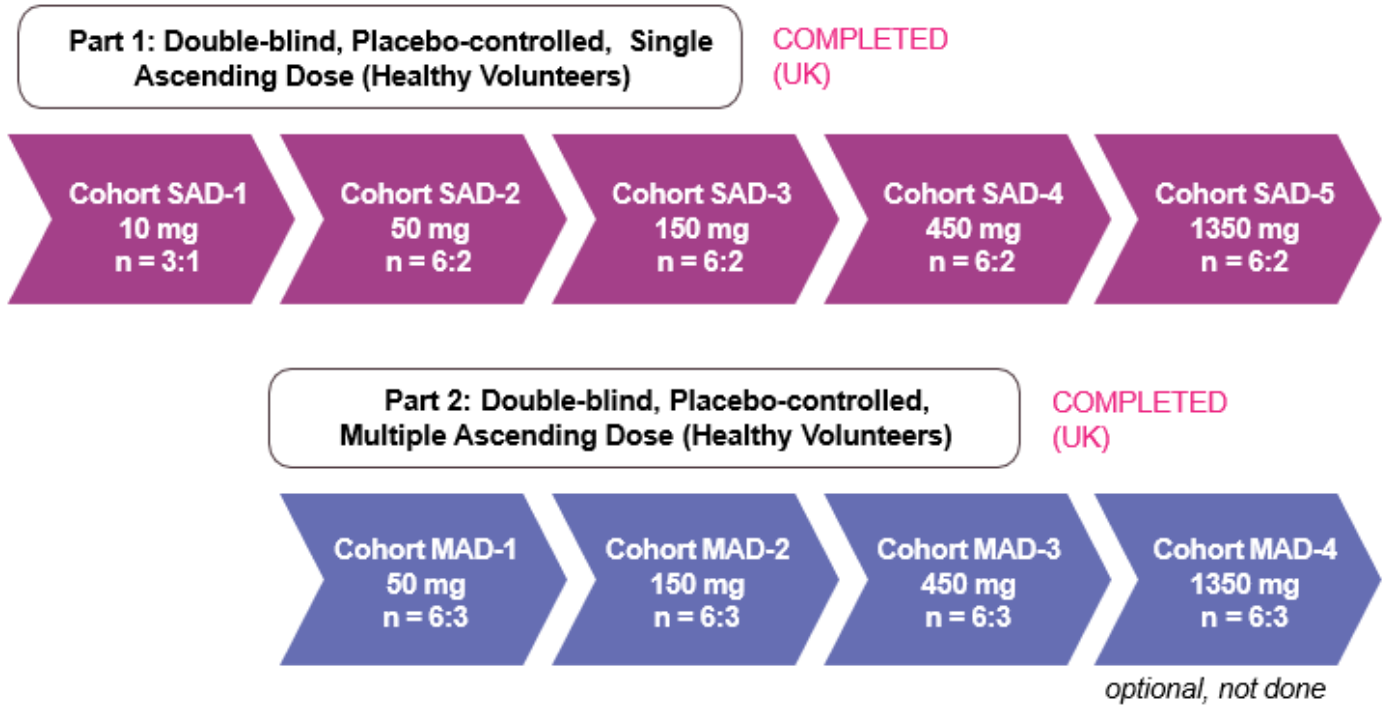
- Assess safety and tolerability

Secondary Objective

- Characterize PK/PD and immunogenicity of BION-1301 administered by IV infusion

Exploratory Objectives

- Characterize select biomarkers of pharmacodynamic (PD) activity



- **BION-1301 was well-tolerated in HVs; no SAEs, treatment discontinuations or events meeting stopping criteria**
- **PK of BION-1301 was well behaved, generally dose-proportional, T ½ ~ 33 days; low incidence of non-neutralizing ADAs**

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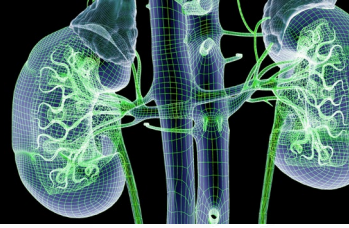
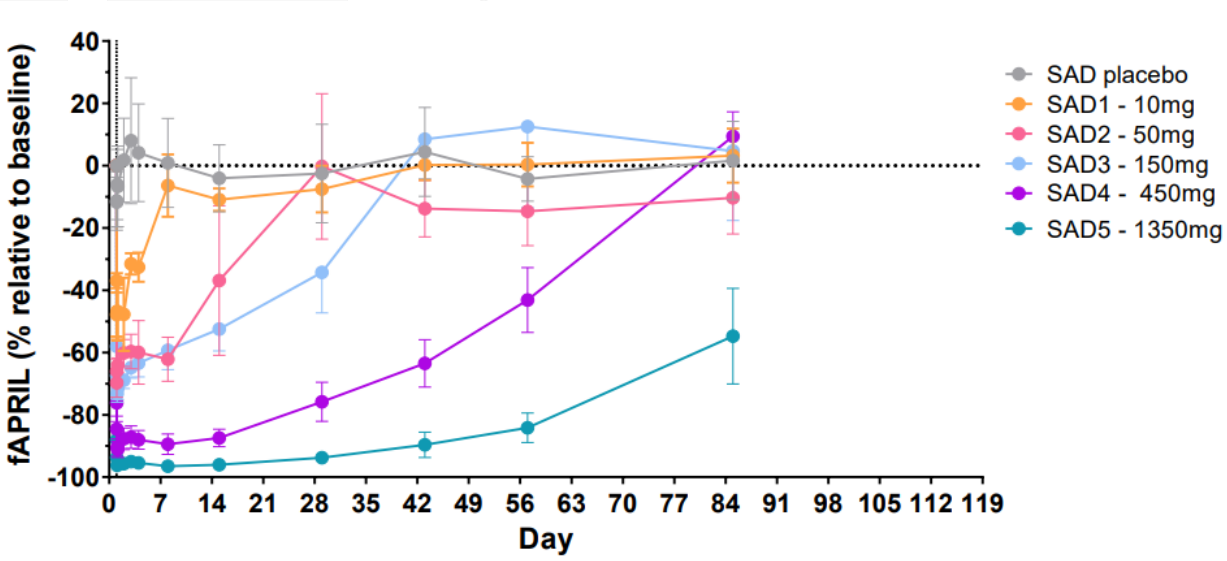
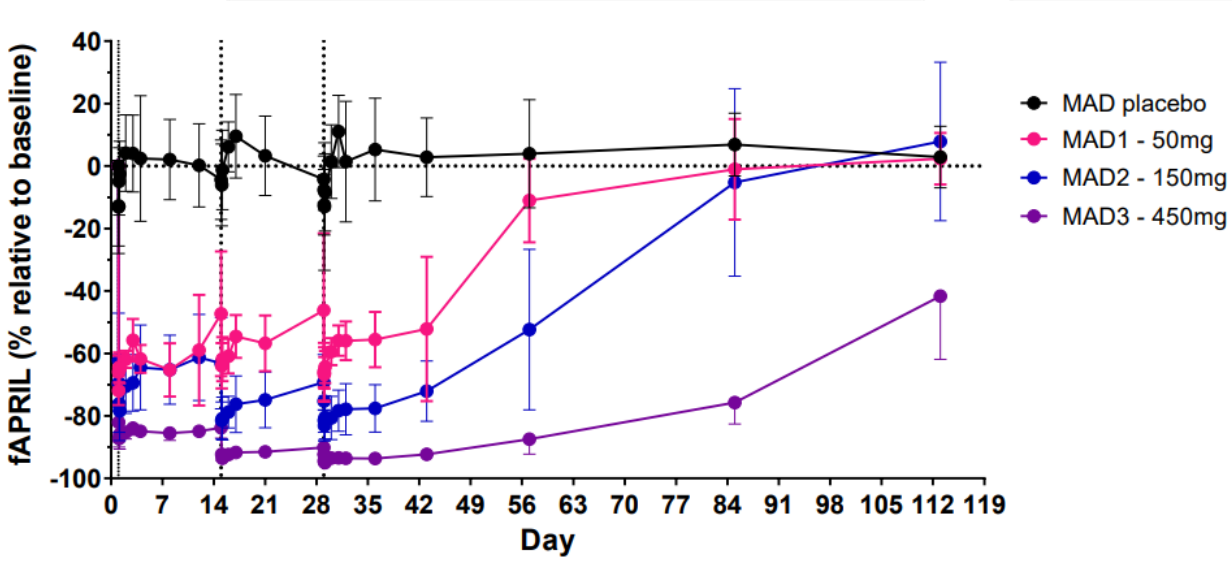
Phase 1 Study in Healthy Volunteers (HVs): Target Engagement



SAD — Free APRIL (fAPRIL) Reduction



MAD — Free APRIL (fAPRIL) Reduction



Immediate, dose-dependent and sustained neutralization of APRIL

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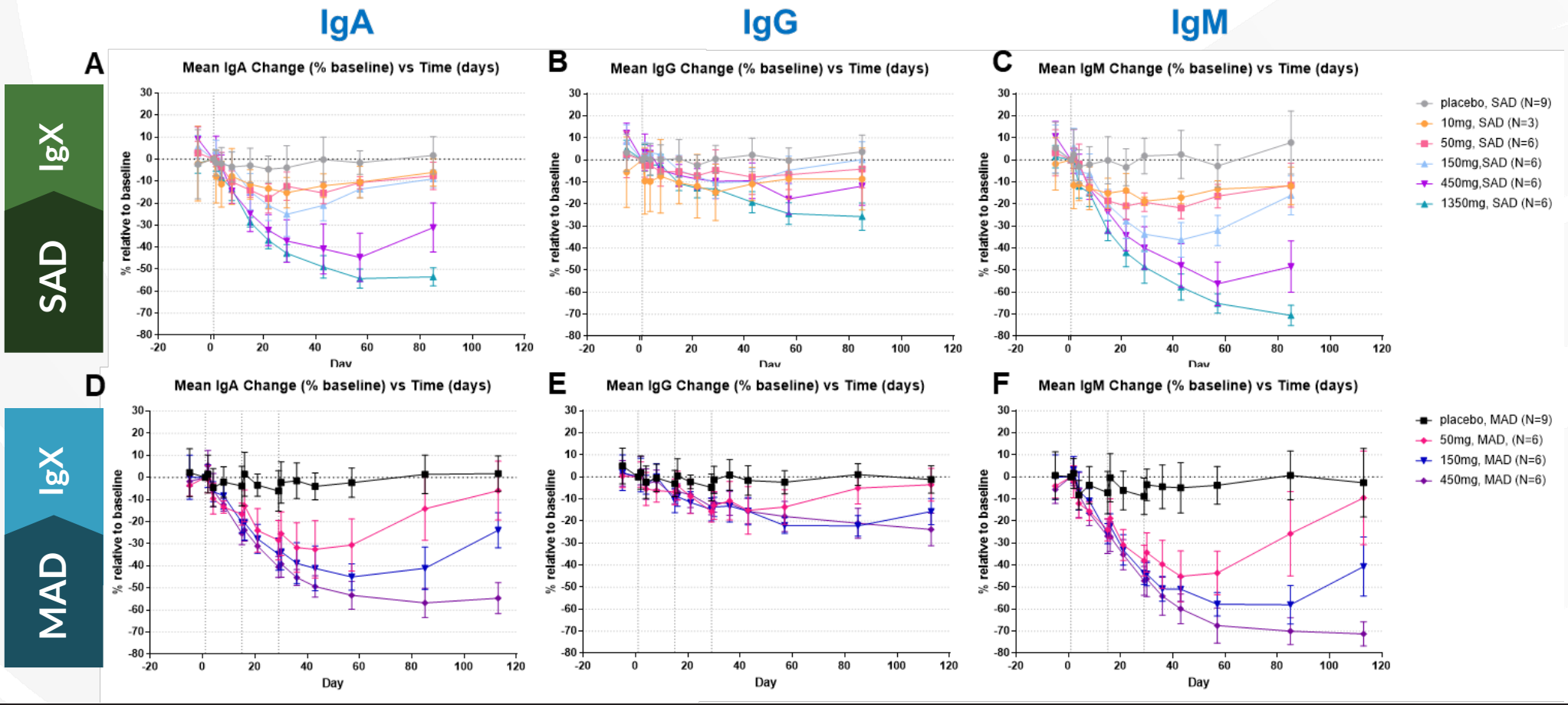
Phase 1 Study in Healthy Volunteers (HVs): PD Responses



- **Dose-dependent and durable reductions in IgA & IgM, with lesser effects on IgG**
- **Offers a pharmacodynamic window to exploit IgA reduction while minimizing impact on IgG**

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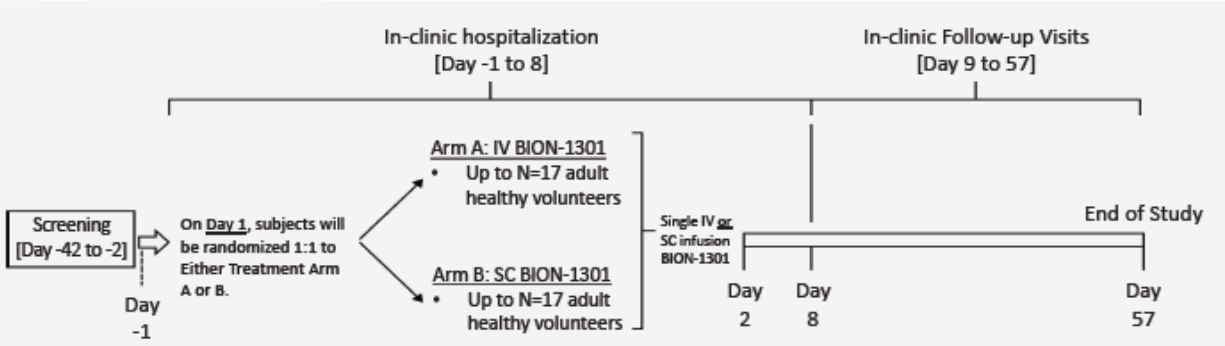
Phase 1 SC Bioavailability Study in HVs: Supports Transition to SC Administration of BION-1301

A Phase 1, Open Label, Randomized, Single Dose, Parallel Group Safety and Bioavailability Study of BION-1301 Administered by Intravenous (IV) and Subcutaneous (SC) Routes



The PK profile of BION-1301 was consistent with previous clinical studies and minimal differences in drug concentration were observed between administration routes after 1 week

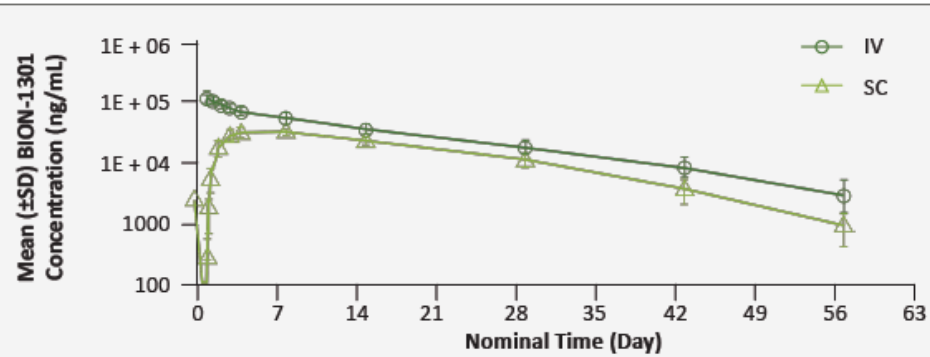


Figure 4: Mean (±SD) Serum Concentrations of BION-1301 in Healthy Volunteers After Single-Dose IV or SC Administration

- **BION-1301 was generally well tolerated:**
  - **No SAES or early terminations**
  - **No ISRs**
  - **No ADAs in the SC cohort**

Comparable reductions in serum fAPRIL

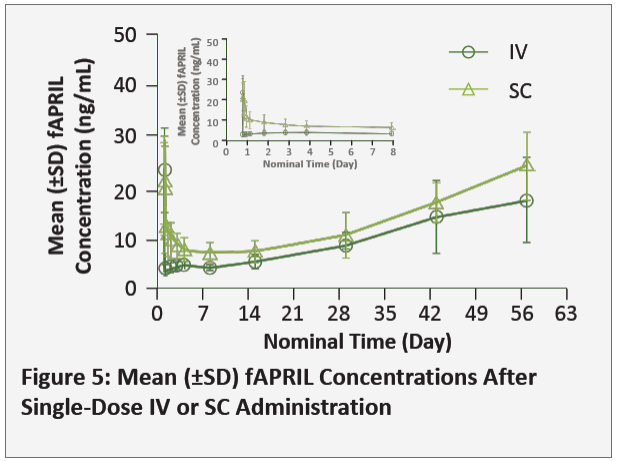


Figure 5: Mean (±SD) fAPRIL Concentrations After Single-Dose IV or SC Administration

A single 300mg SC or IV dose of BION-1301 provides similar reductions in immunoglobulins

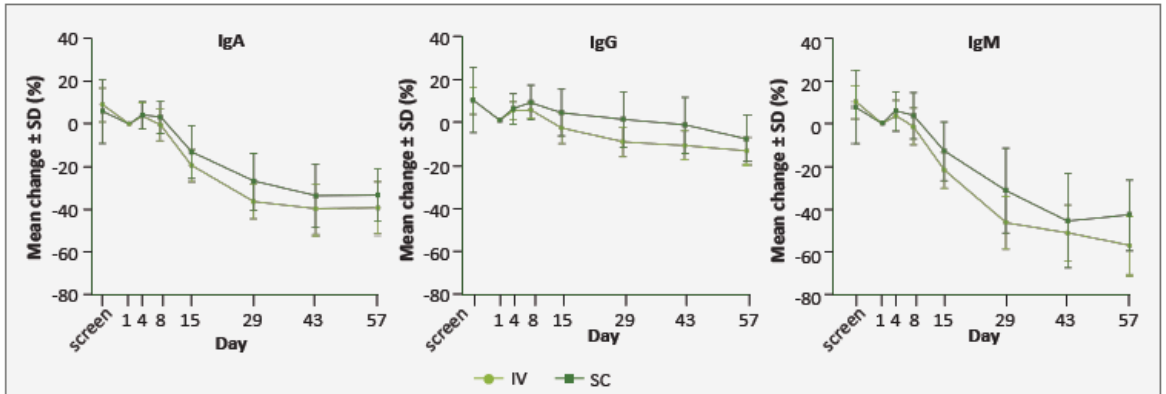


Figure 7. Mean % Change ± SD (Relative to Baseline) in Serum Immunoglobulin Levels Over Time (Days)

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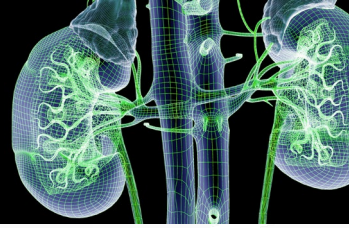
IgAN POC: Study Design



ADU-CL-19 (Part 3) is an ongoing phase 1/2 trial investigating BION-1301 in patients with IgAN (NCT03945318)

Cohort 1 (n=10)	450 mg Q2W IV → 600 mg Q2W SC, up to 104 weeks ‖†	**Ongoing**
Cohort 2 (n=30)	600 mg Q2W de novo SC, up to 104 weeks‖	**Ongoing**

†*Patients transitioned to SC at ≥24 weeks*

‖ *An optional 1-year treatment extension is available to both cohorts*

Objectives

- Safety, tolerability, PK, immunogenicity, biomarker effects, and preliminary effect on proteinuria in patients with IgAN
- Proof of mechanism
- Proof of concept
- Explore dose/schedule, IV and SC administration

Key Eligibility Criteria, Cohort 2

- Biopsy-proven IgAN diagnosis within 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 per 1.73 m^2
- Stable/optimized dose of RASi for ≥ 3 months prior to screening (or intolerant to RASi)

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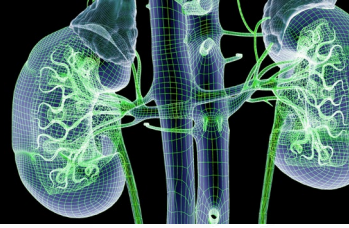
Demographics and Baseline Characteristics



Demographics and Baseline Characteristics

Demographics	Cohort 1 (n=10**) 450 mg IV → 600mg SC	Cohort 2 (n=24) 600 mg de novo SC
Age, years, *mean (min, max)*	42 (27, 59)	40 (21, 74)
Sex, male, *n (%)*	9 (90)	15 (63)
Race, White, *n (%)* **Asian,** *n (%)* **Black,** *n (%)* **Missing,** *n (%)*	10 (100) 0 0 0	11 (46) 11 (46) 1 (4) 1 (4)
Ethnicity, Hispanic, *n (%)*	2 (20)	2 (8)
Country, US, *n (%)*	10 (100)	16 (67)
Baseline characteristics	*Median (min, max)*	*Median (min, max)*
Time from biopsy, years	2.1 (0.3, 7.7)	3.3 (0.1, 7.6)
Blood pressure (mmHg), Systolic **Diastolic**	127 (113, 133) 83 (69, 88)	127 (110, 147) 79 (57, 88)
eGFR (mL/min/1.73 m²)§	69 (30, 122)	75 (37, 131)
24-hour urine protein excretion (g/day)	1.2 (0.7, 6.5)	1.0 (0.6, 2.7)
24-hour UPCR (g/g)	0.5 (0.4, 4.6)	0.8 (0.2, 3.2)
Renin-angiotensin system inhibitor use (%)	100%	100%

§ eGFR by CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration
** Two patients withdrew from study for reasons unrelated to study drug

Cohort 1 enrollment and treatment duration:

- 10 patients enrolled; 8 patients continued to SC
- Mean treatment duration of 64 weeks (range 0.1 to 106 weeks)
  - Mean treatment duration of 450 mg IV prior to transition to SC was 37 weeks
  - Mean treatment duration after transition to 600 mg SC was 40 weeks

Cohort 2 enrollment and treatment duration:

- 24 patients enrolled (enrolling up to 30 patients)
- Mean treatment duration of 17 weeks (range 2 to 30 weeks)

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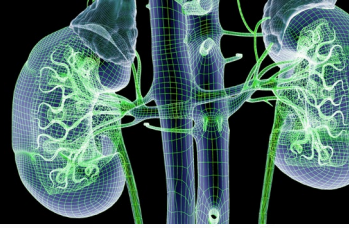
Safety and Tolerability



In Cohort 1 and Cohort 2:

- BION-1301 is generally well tolerated in IgAN patients, with no reported deaths, SAEs, or AEs leading to discontinuation of study drug to date
- All infections in patients with IgAN have been Grade 1 or 2 in severity and only one infection, which was Grade 1 in severity, was assessed as treatment-related
- Injection site reactions have all been Grade 1 or Grade 2 in severity
- IgG level below the study defined threshold (< 3 g/L) occurred in one patient in Cohort 1, requiring protocol-mandated withholding of study drug. There have been no infections reported in this patient

AE Category (N=34)		n (%)
Treatment emergent AEs (TEAEs)	Patients with any TEAE	23 (67.6)
	Patients with Infection TEAE (Grades 1 or 2)	17(50.0)
	Infection TEAE occurring in N>1 patient	
	COVID-19	8 (23.5)
	Upper Respiratory Tract Infection	3 (8.8)
	Asymptomatic COVID-19	2 (5.9)
	Sinusitis	2 (5.9)
	Urinary Tract Infection	2 (5.9)
Treatment-related AEs	Patients with any treatment-related AE	8 (23.5)
	Related AEs occurring in N>1 patient	
	Fatigue	3 (8.8)
	Injection site erythema	3 (8.8)

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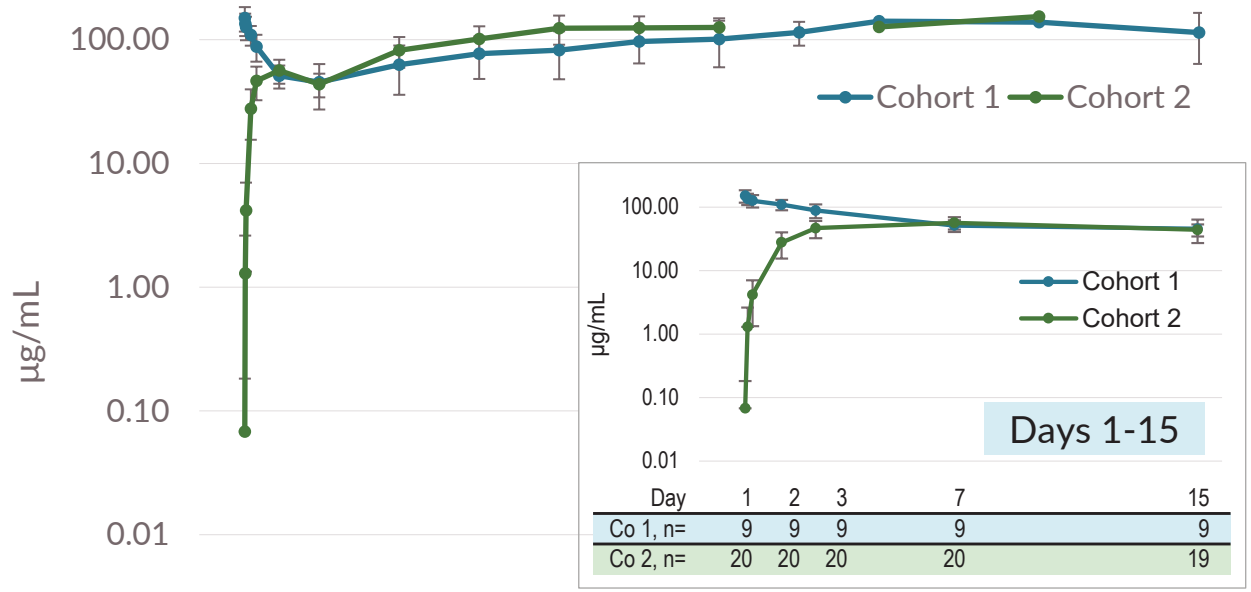
Pharmacokinetics

- Low inter-individual variability in BION-1301 serum concentrations following IV and SC administrations
- Trough concentrations of BION-1301 following 600 mg SC Q2W (Cohort 2) are consistent with trough concentrations observed following 450 mg IV Q2W (Cohort 1)
- No anti-drug antibodies observed in patients with IgAN to date

BION-1301 Serum Concentrations



Wk	1	4	10	12	16	20	24
Co 1, n=	9	9	8	8	2	2	4
Co 2, n=	20	17	8	9	9	4	0

Mean (± SD) BION-1301 serum concentrations following IV (Cohort 1) or SC (Cohort 2) administration Q2W‡. Data points after Day 7 are trough concentrations.

Data cut-off Sep 30, 2022

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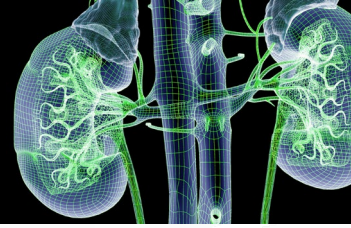
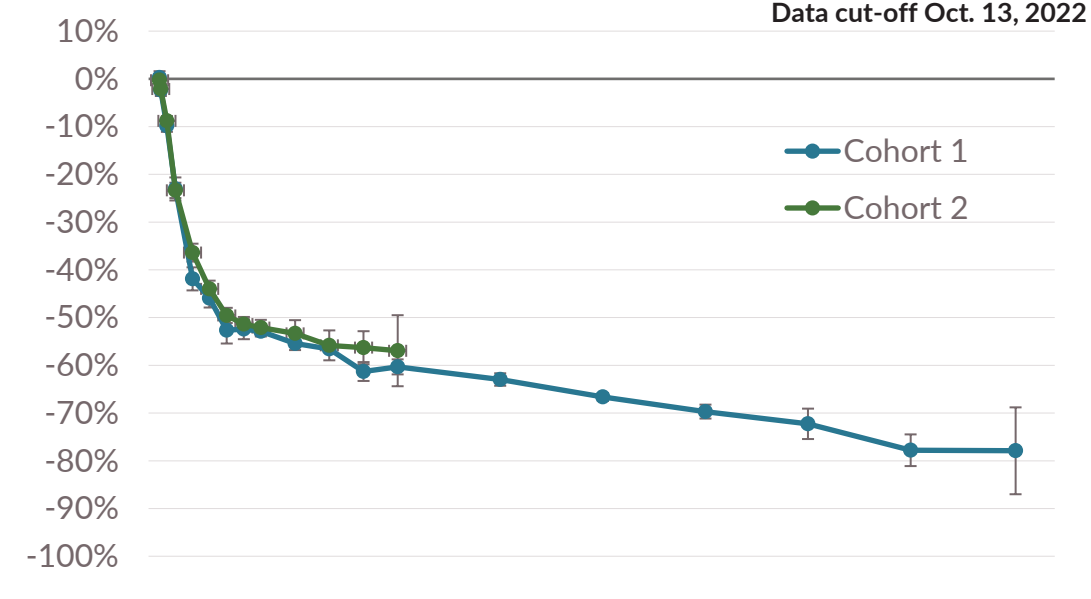
BION-1301 Results in Rapid and Durable Reduction in IgA and Gd-IgA1



IgA % Change from Baseline (Mean ± SE)

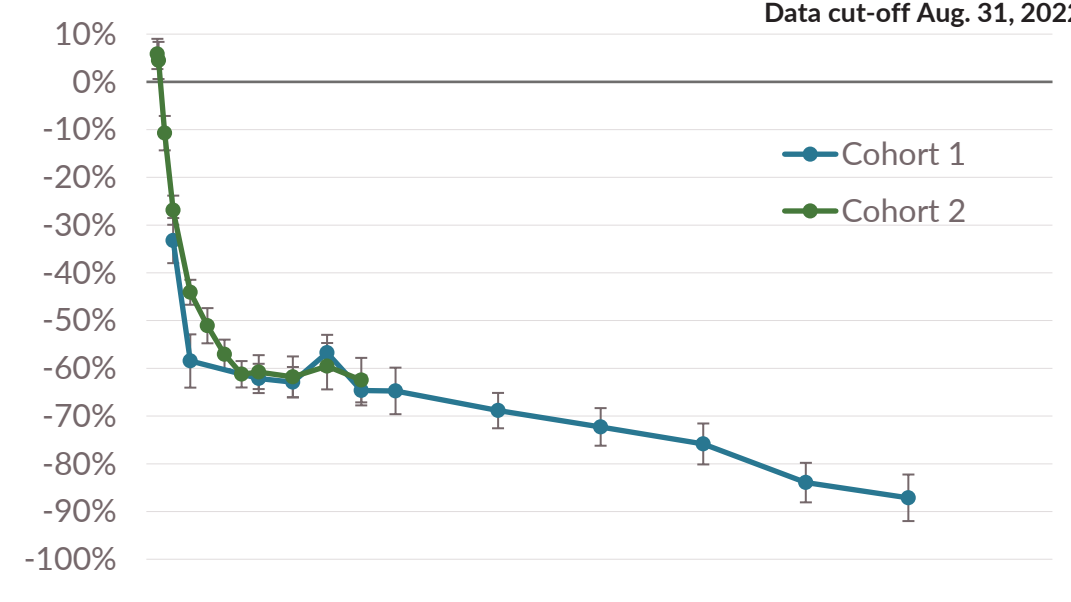
Data cut-off Oct. 13, 2022



Wk	4	8	12	16	20	24	28	40	52	64	76	88	100
Co 1, n=	8	8	8	8	2	5	6	8	7	7	4	3	2
Co 2, n=	23	18	15	10	10	9	3						

Gd-IgA1 % Change from Baseline (Mean ± SE)

Data cut-off Aug. 31, 2022



Wk	4	8	12	16	20	24	28	40	52	64	76	88	100
Co 1, n=	8	0	8	8	2	5	7	8	6	6	4	2	
Co 2, n=	20	13	9	10	8	2							

Mean Gd-IgA1 are not available at week 100

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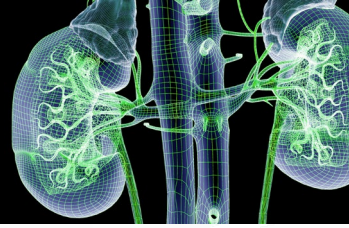
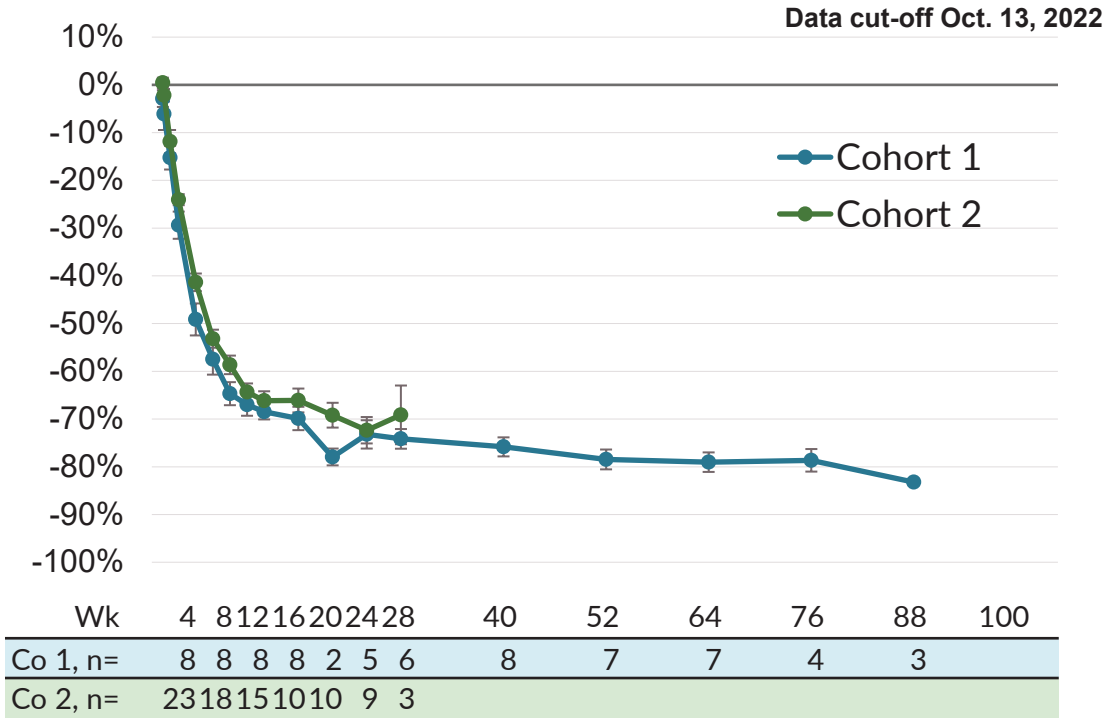
Reductions in IgM, and to a Lesser Extent IgG, Were Also Observed

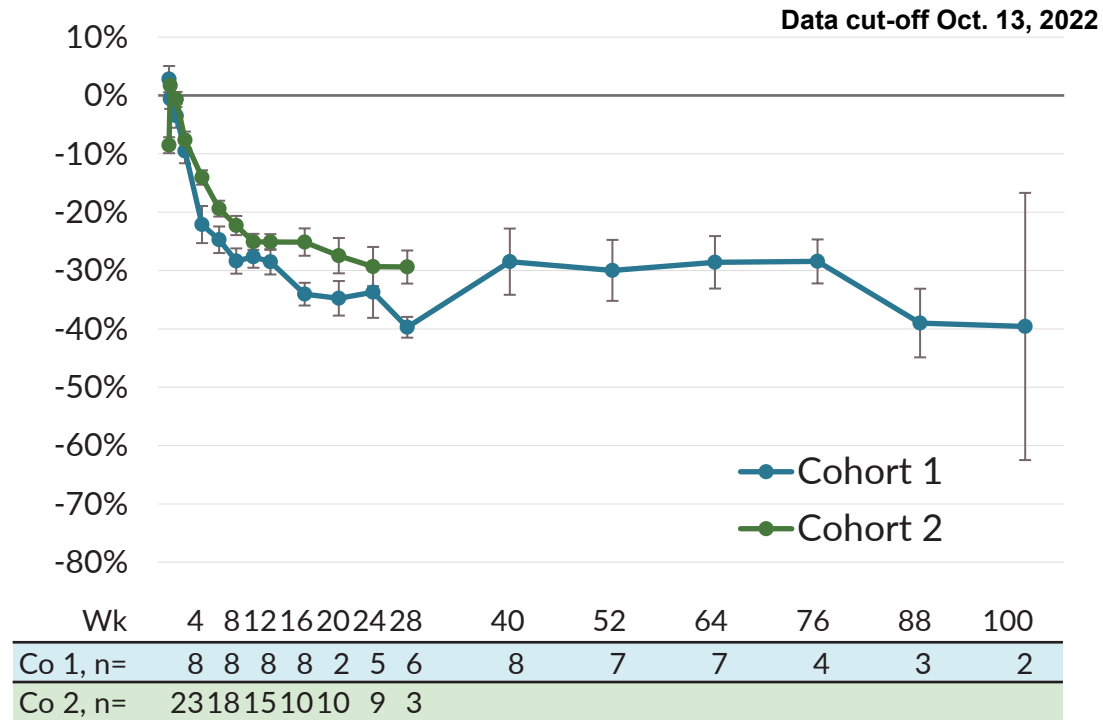


IgM % Change from Baseline (Mean ± SE)



Wk	4	8	12	16	20	24	28	40	52	64	76	88	100
Co 1, n=	8	8	8	8	2	5	6	8	7	7	4	3	
Co 2, n=	23	18	15	10	10	9	3						

IgG % Change from Baseline (Mean ± SE)



Wk	4	8	12	16	20	24	28	40	52	64	76	88	100
Co 1, n=	8	8	8	8	2	5	6	8	7	7	4	3	2
Co 2, n=	23	18	15	10	10	9	3						

Mean IgM are not available at week 100

Barratt, J, et al., ASN Kidney Week 2022, FR-PO659

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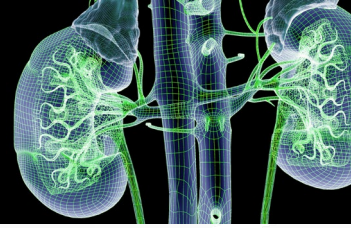
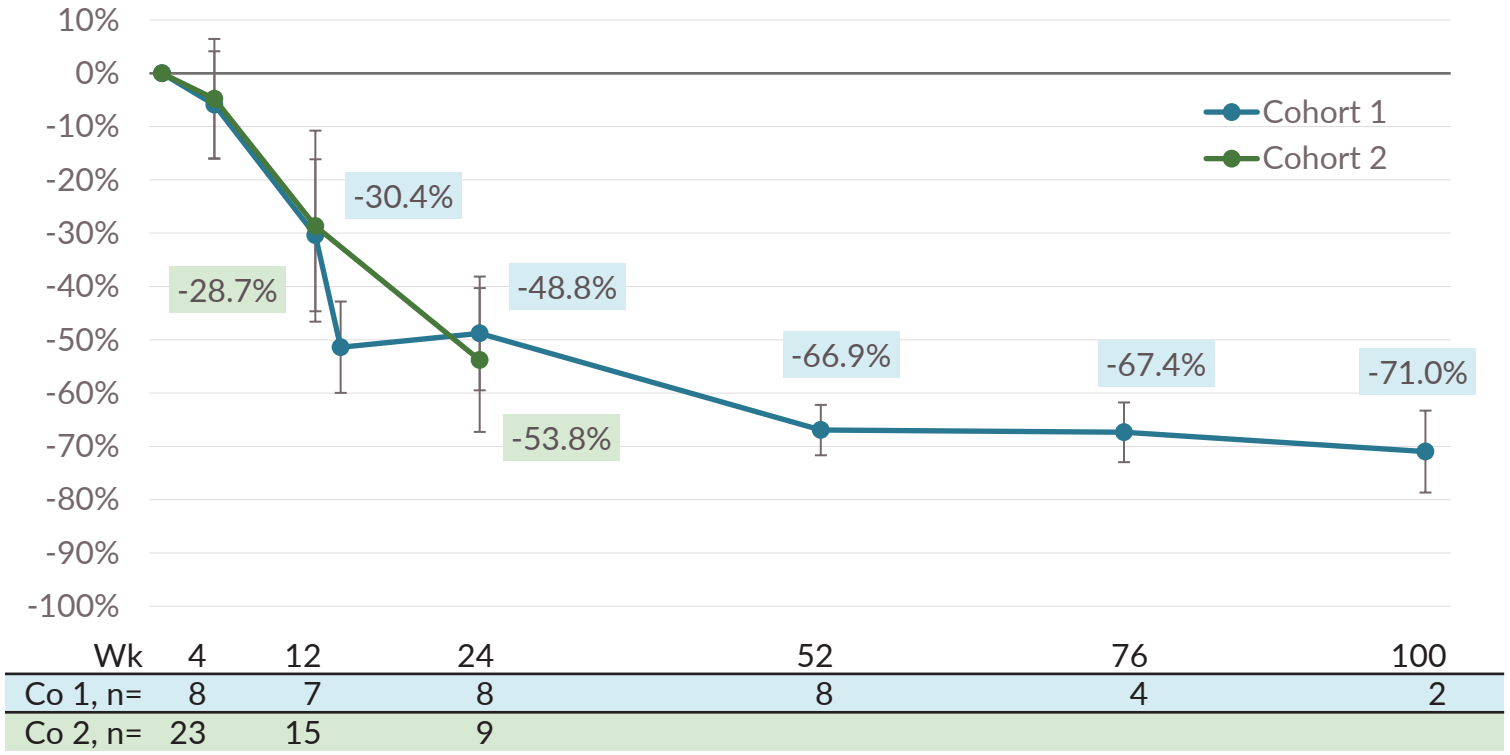
BION-1301 Treatment Results in Sustained, Clinically Meaningful Proteinuria Reductions



UPCR % Reduction (Geometric Mean ± SE)

Data cut-off Oct. 13, 2022



Wk	4	12	24	52	76	100
Co 1, n=	8	7	8	8	4	2
Co 2, n=	23	15	9			

Median (range) baseline protein excretion: Cohort 1, 1.2 (0.7, 6.5) g/day ; Cohort 2, 1.0 (0.6, 2.7) g/day

COHORT 1 (IV → SC)

- Clinically meaningful reductions in UPCR were seen in patients with IgAN across a wide range of baseline proteinuria levels
- UPCR continued to decline through one year and was maintained through two years, providing evidence of sustained efficacy
- At Week 52, 7/8 evaluable patients demonstrated >50% reductions in UPCR

COHORT 2 (de novo SC)

- Mean reduction in UPCR of >50% at 24 weeks in Cohort 2 with de novo SC administration is consistent with Cohort 1

Barratt, J, et al., ASN Kidney Week 2022, FR-PO659

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BION-1301 MOVING FORWARD

Plan to advance cohort 2 dose/schedule in pivotal trial, given strong clinical data

STATUS

Cohort 1 in IgAN	**450 mg IV → 600 mg SC q2w** Enrollment of 10 Patients Completed
Cohort 2 in IgAN	**600 mg SC q2w** Enrollment of 30 Patients Completed

NEXT STEPS

- **Align with global health authorities *(ongoing)***
- **Conduct site and country feasibility *(ongoing)***
- **Initiate pivotal trial in mid-2023**

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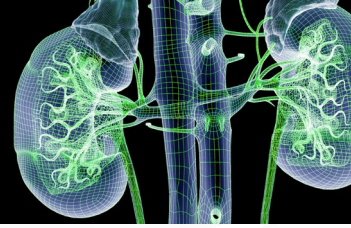
Leveraging Population PK/PD Modeling and Simulations to Support Phase 3



PopPK/PD Model Framework and Modules

Simulations Phase 3 Dose and Schedule

Preliminary IV PopPK Model HV IV

Test Patient Status on IV PopPK model IgAN

IV + SC PoPK HV SC

Final IV + CC PopPK model IgAN

ER Models → IgG

IgA → UPCR

Target optimal IgA reduction for max UPCR effect

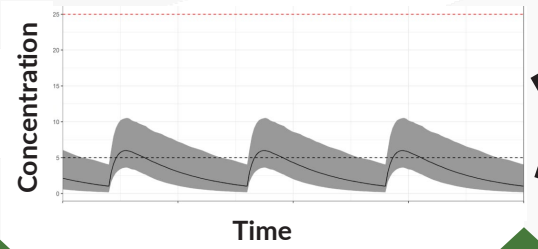
Virtual Patient Populations

Simulations of 1000 Subjects

Exposure Variability

Response Variability

DOSE



PK

PD

Efficacy (IgA)

Safety (IgG)

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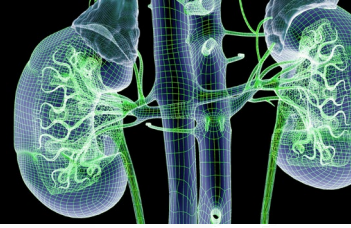
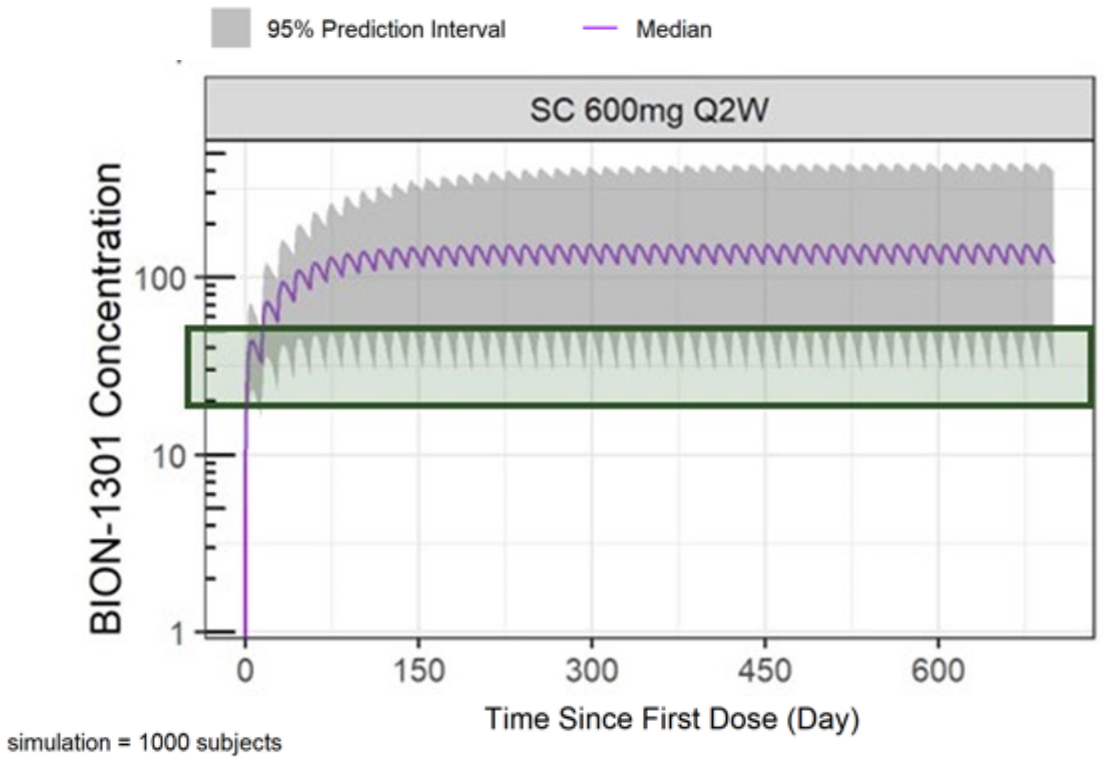
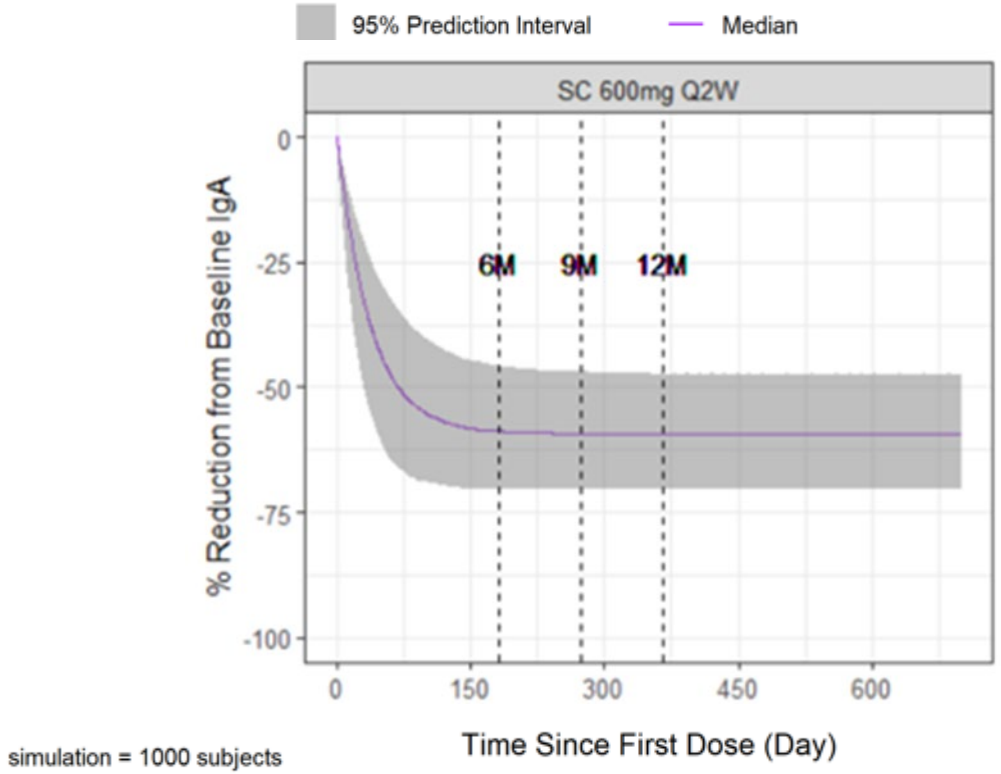
BION-1301 600 mg SC Q2W: Simulations



Pop PK Pharmacokinetics



Pop PD Serum IgA



600 mg SC Q2W provides broad coverage IgA>EC_{95} accounting for simulated PK variability

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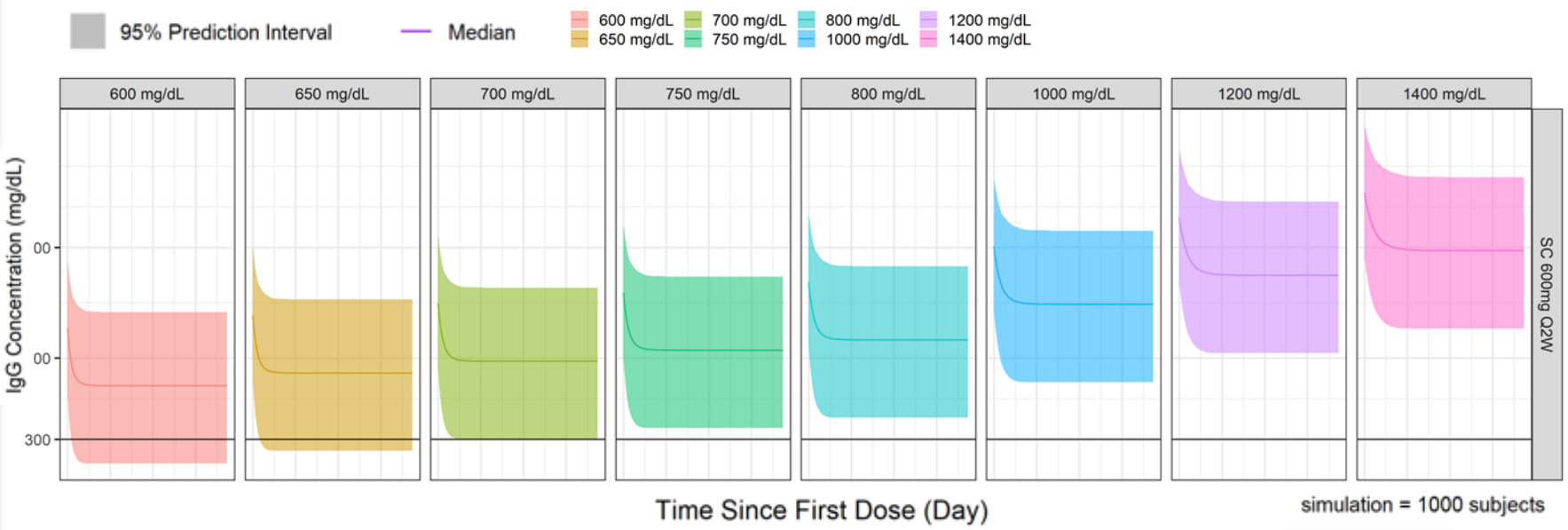
BION-1301 600 mg SC Q2W: Simulations

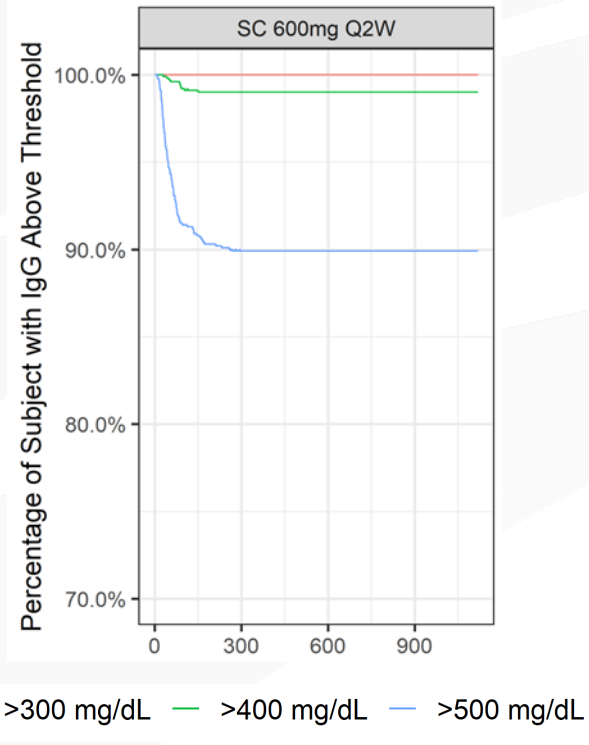
Pop PD — Simulated IgG Reductions Across a Range of Population Mean [IgG]



- Average baseline IgG in IgAN patients in ADU-CI-19 ~ 10 g/L
- IgG <3 g/L, arbitrary safety threshold to minimize immunosuppression

Simulations support Phase 3 dose selection to optimize IgA reduction accompanied by only modest IgG reductions and support I/E criteria as an added safety measure

Pop PD — IgG Thresholds



Exclude Baseline IgG < 6g/L

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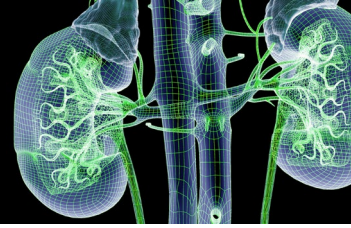
A Phase 3, Randomized, Double-blind, Placebo-controlled Study of BION-1301 in Adults with IgAN



Phase 3 Targeting IgAN Patients at Risk for Disease Progression

Key Inclusion Criteria

- Biopsy-proven IgAN
- Patients on maximally-tolerated, optimized and stable dose of RASi (≥12w), or RASi intolerant
- Background optimized and stable dose (≥12w), of SGLT2i or ERA (if approved) allowed
- Proteinuria >1 g/day; eGFR >30 ml/min/1.73m^2

Key Exclusion Criteria

- Secondary IgAN, IgA vasculitis, other CKD, RPGN
- Recent immunosuppressant use, immune-deficient state, current severe infection, IgG < 6g/L

Exploratory cohort eGFR 20 to < 30 mL/min/1.73m^2 (n~20)

Stratification Factors Proteinuria (≥ 2 g/day vs. < 2 g/day), eGFR (≤ 45 v > 45 mL/min , Region (Asia v ROW)

Randomize 1:1

BION 1301 SC Q2W

Placebo SC Q2W

Safety Follow-Up

Primary Endpoint

UPCR
@ 9 mos (40wks), n= 204

Key Secondary Endpoint

eGFR (change from baseline)
@ 2 yrs (104 wks), n=272

Additional Secondary Endpoints

Composite 30% or 40% reduction in eGFR, eGFR < 15 mL, dialysis, kidney transplantation or all-cause mortality

Percent of subjects achieving a ≥ 25% reduction of UPCR to < 1.0 g/day at week 40

Safety Endpoints

Type, incidence and severity of AEs and AESIs

Exploratory Endpoints

Characterize PK, exposure response, immunogenicity, QOL, MOA

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Summary: BION-1301 From Proof of Concept to Phase 3

Disease Modifying Potential of APRIL Neutralization in IgAN

- APRIL is a cytokine that drives IgA class switching, survival of IgA-secreting plasma cells and the excess secretion of GdIgA1
  - Potential for APRIL blockade to directly target the events initiating IgAN and prevent immune complex formation

Proof-of-concept for BION-1301 in IgAN to:

- ✓ deplete pathogenic Gd-IgA1 in patients with IgAN
- ✓ reduce proteinuria in patients with IgAN who remain at risk for progression with residual proteinuria despite optimized standard-of-care treatment

Efficient advancement of BION-1301 from POC to Phase 3 enabled by:

- ✓ biomarker rich Phase 1 HV SAD/MAD study enabling PopPK/PD modelling and simulations to support Phase 3 dose selection
- ✓ open label Phase 1/2 POC study in IgAN allowing interim data cuts with disease specific biomarkers assessments and demonstration of clinically meaningful reduction in proteinuria

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