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BEYOND Study Design:
A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Zigakibart* in Adults with IgA Nephropathy

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***Zigakibart (BION-1301) is an investigational drug that has not been approved by regulatory authorities.**

The 17th International Symposium on IgA Nephropathy

COI disclosure

presenter: Dana V. Rizk, University of Alabama at Birmingham

I have the following relationships to disclose any COI for this research presentation within the period of 36 months:

Employment/Leadership position/Advisory role:	Novartis, Otsuka, Chinook, Vera
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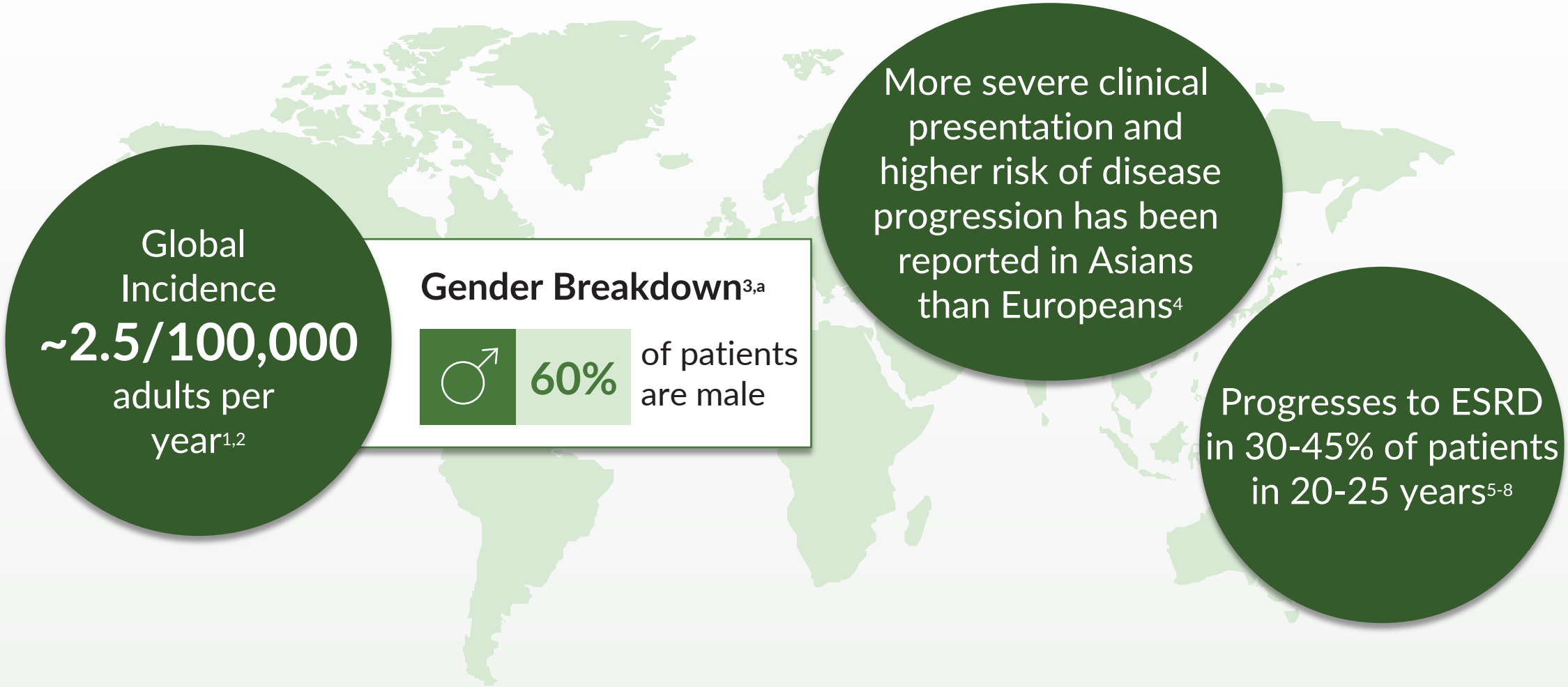
IgAN is a Progressive Kidney Disease and the Most Common Form of Primary Glomerulonephritis[1]



a. Among 667 patients with IgAN/IgA vasculitis (76% IgAN) from the CureGN cohort, which includes study sites across the USA, Canada, Italy, and Poland.

1. McGrogan A, et al. NDT. 2011. 2. Kwon CS, et al. J Health Econ Outcomes Res, 2021. 3. Selewski DT, et al. Kidney Int Rep, 2018. 4. Zhang H, et al. Sem in Immunopath, 2021. 5. Reich, H. N., et al. JASN, 2007. 6. Moriyama T, et al. PLoS ONE, 2014. 7. Rauen, T., et al. KI, 2020. 8. Hastings, M. C., et al. KI Reports, 2018

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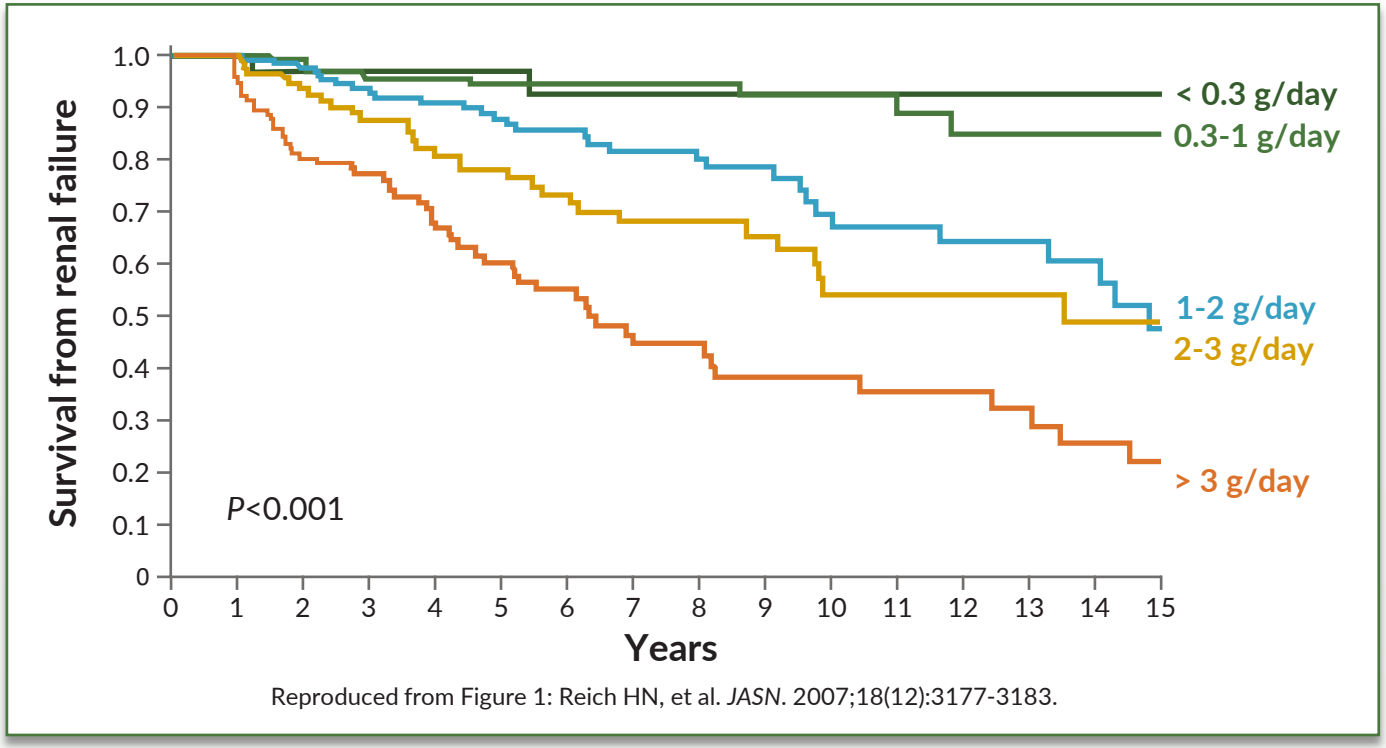
Proteinuria is Strongly Associated with Kidney Disease Progression and Renal Failure in IgAN[1-4]

- **Proteinuria > 1 g/day is associated with a 9.4-fold increased risk of ESKD compared to patients with proteinuria < 1 g/day[3]**



Reproduced from Figure 1: Reich HN, et al. *JASN*. 2007;18(12):3177-3183.

Each gram above 1 g/day (reference group) was associated with worse renal survival (defined as time from onset to ESKD)

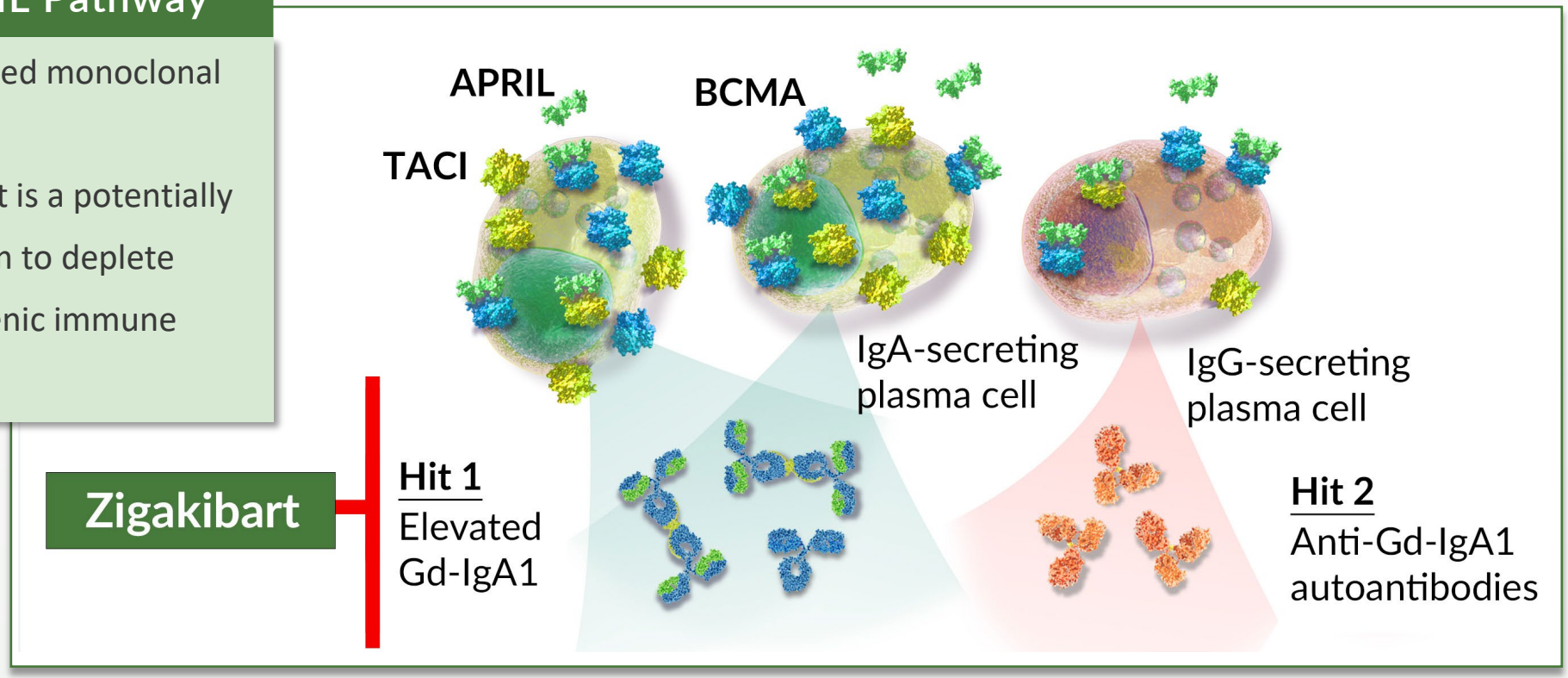
1. Rovin BH, et al. Kidney Int, 2021. 2. Reich HN, et al. JASN, 2007. 3. Le W, et al. Nephrol Dial Transplant, 2012. 4. Coppo R, et al. Kidney Int, 2014.

APRIL (A PRoliferation Inducing Ligand) is a Key Molecule Involved in Hit 1 of IgAN Pathogenesis[1,2]

Zigakibart* and the APRIL Pathway

- Zigakibart is a novel, humanized monoclonal antibody that blocks APRIL[3,4]
- Blocking APRIL with zigakibart is a potentially disease-modifying mechanism to deplete Gd-IgA1 and prevent pathogenic immune complex formation[4]

APRIL promotes plasma cell survival and IgA production leading to increased production of Gd-IgA1



APRIL, A PRoliferation Inducing Ligand; Gd-IgA1, galactose-deficient immunoglobulin A; IgA, immunoglobulin A; IgAN, IgA nephropathy; IgG, immunoglobulin G; mAb, monoclonal antibody.

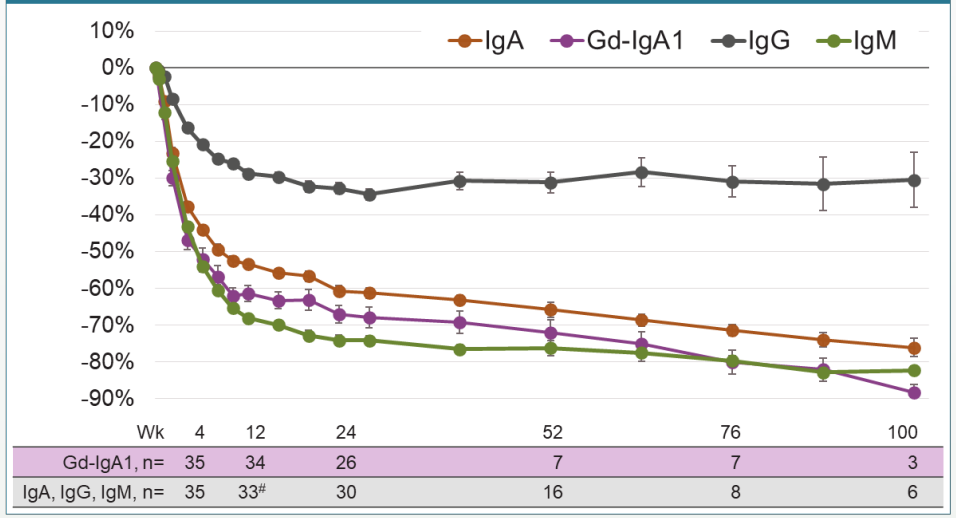
1. Lai KN, et al. *Nat Rev Dis Primers*, 2016; 2. Suzuki H, et al. *Semin Immunopathol*, 2021; 3. Lo et al, ERA-EDTA, 2020; 4. Barratt et al, ASN Kidney Week, 2022.

*Zigakibart (BION-1301) is an investigational agent and has not been approved for any use in patients.

Zigakibart treatment results in sustained, clinically meaningful proteinuria reduction in patients with IgAN

Interim results from a Phase 1/2 trial of zigakibart in patients with IgAN (NCT03945318) demonstrate rapid and durable reductions in Gd-IgA1, along with sustained, clinically meaningful reductions in proteinuria and an acceptable safety profile (Barratt, et al. 2023, ERA).

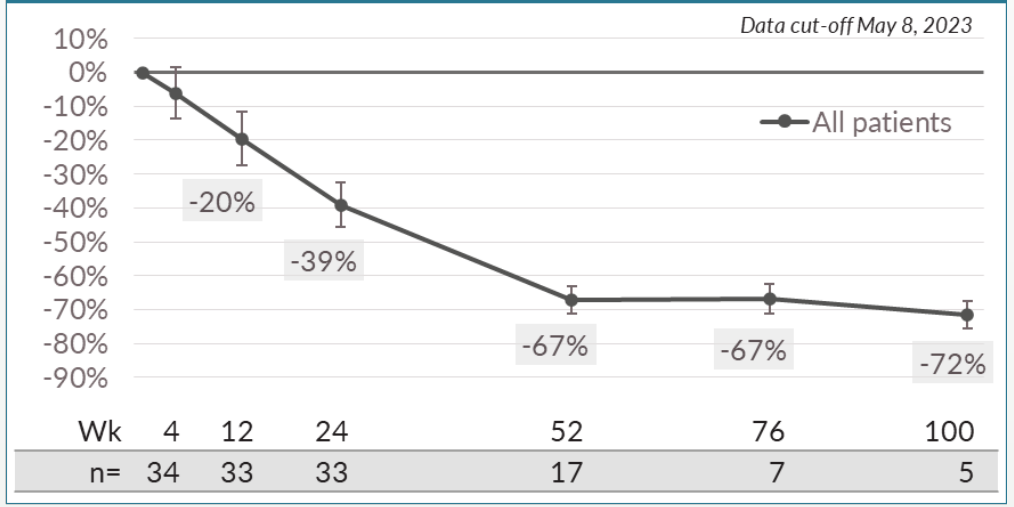
Immunoglobulins, Combined Cohorts
% Change from baseline (Mean ± SE)



Wk	4	12	24	52	76	100
Gd-IgA1, n=	35	34	26	7	7	3
IgA, IgG, IgM, n=	35	33#	30	16	8	6

#IgA n=33 at week 12

UPCR, Combined Cohorts
% Reduction (Geometric Mean ± SE)



Wk	4	12	24	52	76	100
n=	34	33	33	17	7	5

Median (range) baseline protein excretion: 1.1 (0.3, 7.0) g/day

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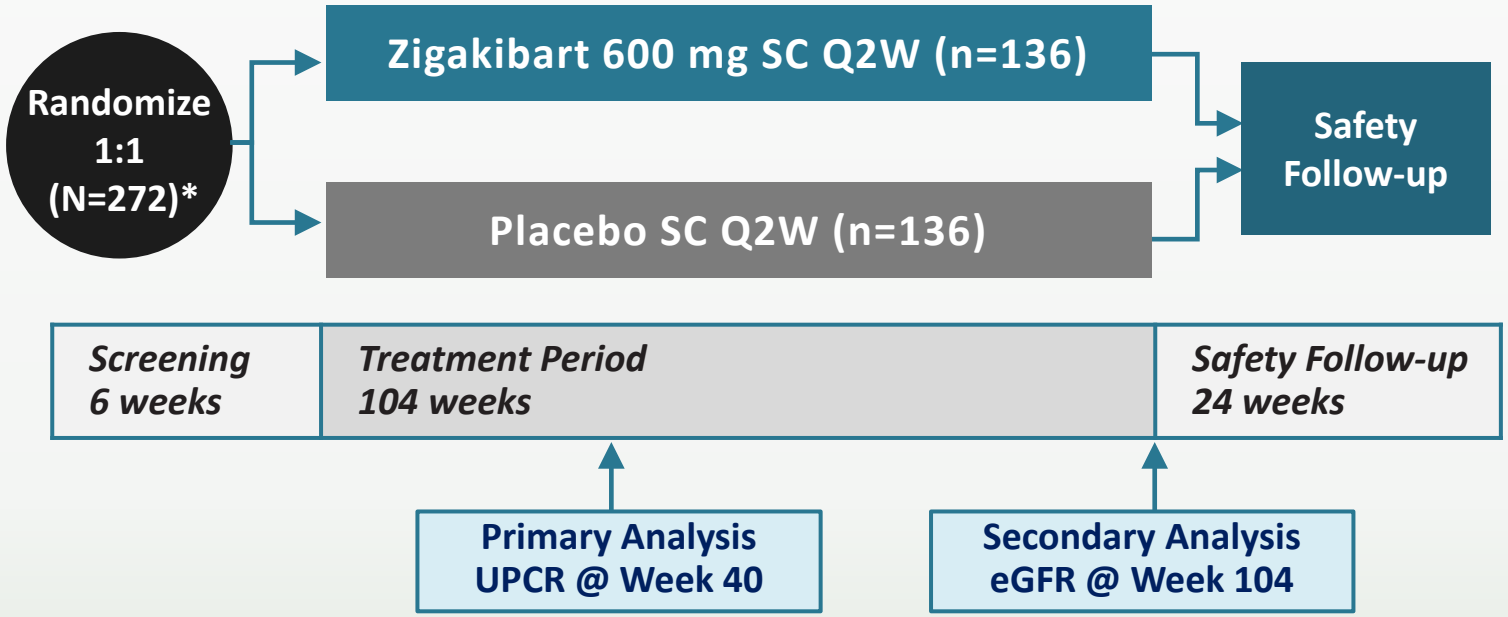
BEYOND Study Design

Study Objective

BEYOND™ (NCT05852938) is a Phase 3, randomized, double-blind, placebo-controlled study to evaluate the effect of zigakibart in adults with primary IgAN at risk of progressive kidney function loss.

Approximately 272 patients will be enrolled across North America, South America, Europe and Asia-Pacific



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BEYOND Key Inclusion Criteria

BEYOND™

Diagnosis	Adults with biopsy-proven IgAN within the past 10 years (not due to secondary causes)
eGFR	eGFR ≥ 30 ml/min/1.73m^2 (CKD-EPI)
Proteinuria	Total urine protein ≥ 1.0 g/day and UPCR ≥ 0.7 g/g at screening
RAS inhibitor	Receiving stable, maximally tolerated ACEi/ARB ≥ 12 weeks prior to screening or intolerant
Concomitant meds	May be on a stable dose of SGLT2i, mineralocorticoid receptor antagonist, and/or endothelin receptor antagonist ≥ 12 weeks prior to screening

BEYOND Study Endpoints

BEYOND™

Primary	Change in proteinuria (UPCR from a 24-hour urine collection) from baseline to week 40
Key secondary	Change in eGFR from baseline to week 104
Additional secondary	Composite clinical outcome, including at least one of the following: • 30% or 40% reduction in eGFR • eGFR < 15 mL/min/1.73m^2 • Dialysis, kidney transplantation or all-cause mortality
Safety	Type, incidence, severity and relatedness of adverse events (AEs) and serious AEs
Exploratory	Impact of zigakibart on disease biomarkers and health-related quality of life as well as analysis of zigakibart pharmacokinetics and immunogenicity

Summary

Zigakibart provides a potentially disease-modifying approach for the treatment of IgAN that directly targets the disease pathogenesis by blocking excess production of Gd-IgA1

The phase 3 BEYOND registrational study will evaluate the effect of zigakibart vs. placebo on proteinuria, eGFR and composite clinical endpoints as well as key safety measures in adult patients with IgAN at risk of progressive kidney function loss

For more information, scan QR or visit
https://clinicaltrials.gov/ct2/show/NCT05834738