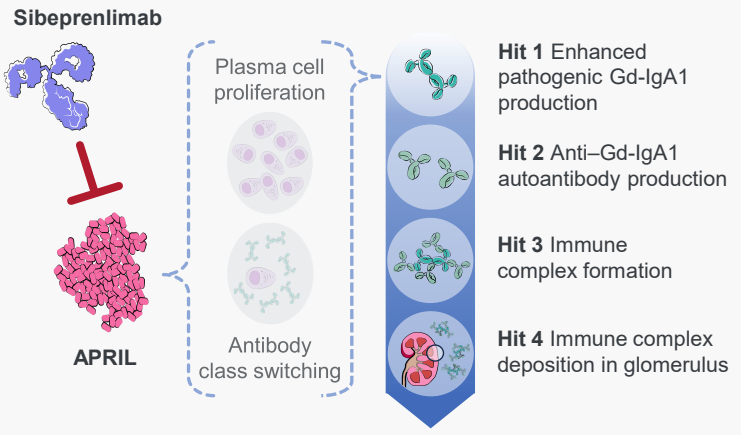
Interim Analyses of the Phase 3 VISIONARY Trial of Sibeprenlimab for Patients With IgA Nephropathy

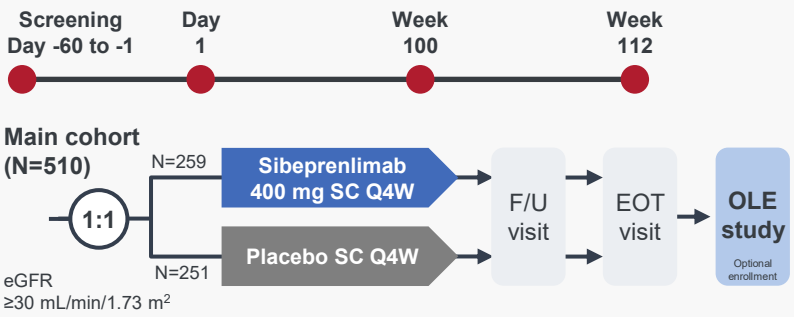
Sibeprenlimab is an IgG2 antibody that selectively binds to and blocks the biologic activity of **APRIL** (**A PR**oliferation-**I**nducing **L**igand), a key driver of IgAN pathogenesis[1-3]



The VISIONARY Phase 3 trial is an ongoing, multicenter, double-blind, placebo-controlled trial evaluating the **efficacy and safety of sibeprenlimab SC** in adult patients with biopsy-confirmed IgAN (NCT05248646)[4]

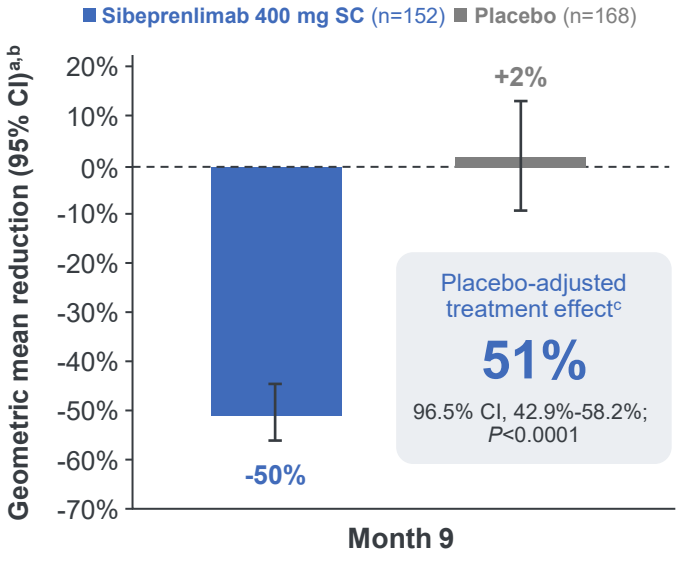
Primary endpoint

Ratio of uPCR-24h at 9 months compared with baseline



In the VISIONARY trial, sibeprenlimab reduced proteinuria up to 12 months

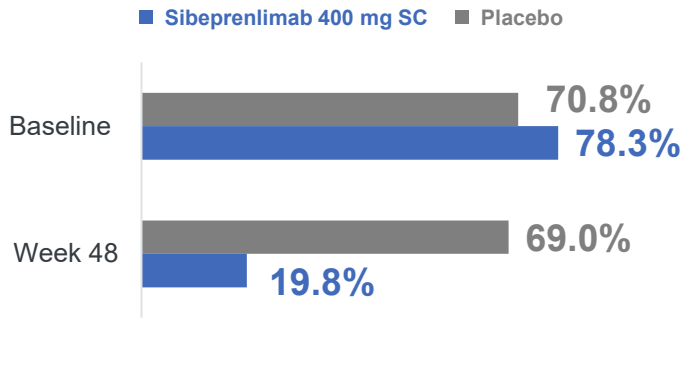
Change from baseline in uPCR-24h (g/g) at month 9 (primary endpoint)



Placebo-adjusted treatment effect in uPCR-24h at 12 months (exploratory) **54.3%** (95% CI, 46.4%-60.9%)[d]

Sibeprenlimab was associated with improvements in exploratory endpoints

Sibeprenlimab was associated with a higher rate of hematuric resolution compared with placebo



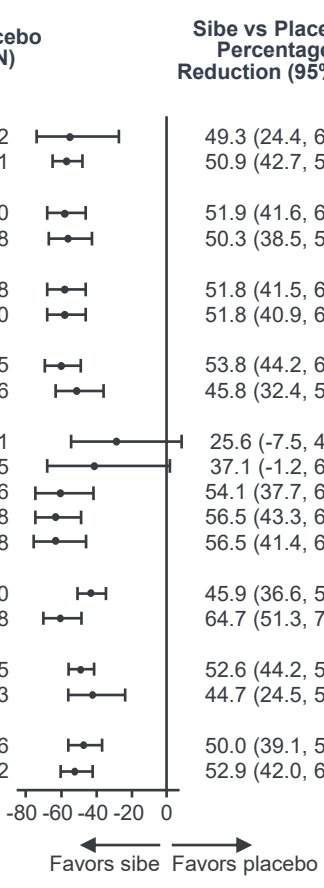
Sibeprenlimab was associated with a higher rate of proteinuric remission (<0.5 g/d) at week 52

34.3% Sibeprenlimab **vs** **12.7%** Placebo

Sibeprenlimab demonstrated consistent efficacy across predefined subgroups

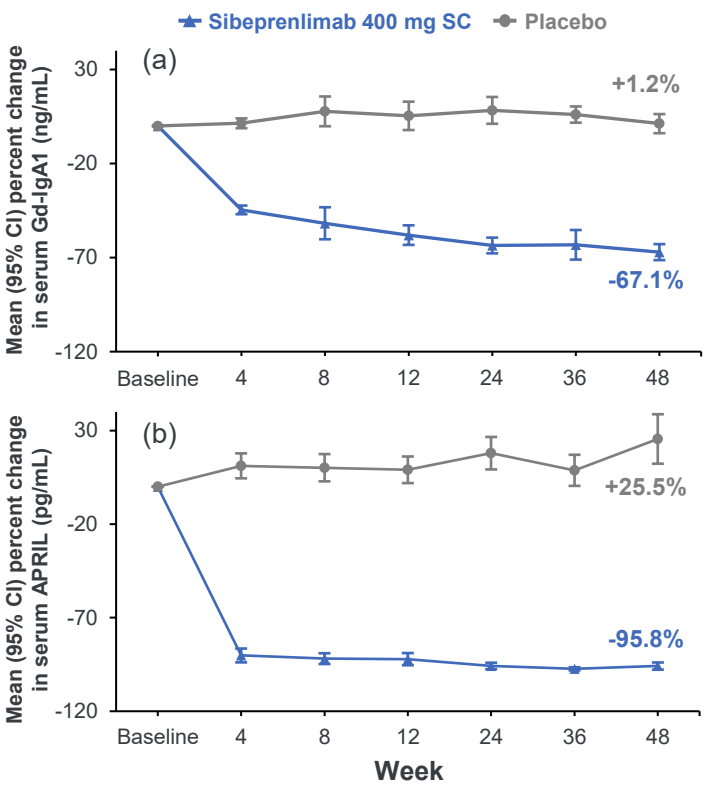
uPCR-24h subgroup analysis by baseline demographics and stratification factors

Subgroup	Sibe (N)	Placebo (N)	Sibe vs Placebo Percentage Reduction (95% CI)
Ethnicity			
Hispanic or Latino	16	22	49.3 (24.4, 65.9)
Not Hispanic or Latino	132	141	50.9 (42.7, 57.9)
Sex at birth			
Male	100	100	51.9 (41.6, 60.4)
Female	52	68	50.3 (38.5, 59.8)
Age group			
≤40 years	69	68	51.8 (41.5, 60.3)
>40 years	83	100	51.8 (40.9, 60.7)
Race			
Asian	94	95	53.8 (44.2, 61.8)
White	55	66	45.8 (32.4, 56.6)
Region			
North America	22	21	25.6 (-7.5, 48.6)
South America	11	15	37.1 (-1.2, 60.8)
Europe	30	36	54.1 (37.7, 66.2)
East Asia	43	48	56.5 (43.3, 66.7)
South/Southeast Asia	46	48	56.5 (41.4, 67.7)
Screening uPCR-24h			
uPCR ≤2.0 g/g	116	130	45.9 (36.6, 53.9)
uPCR >2.0 g/g	36	38	64.7 (51.3, 74.4)
Screening eGFR			
≥45 mL/min/1.73 m²	115	125	52.6 (44.2, 59.8)
30-44 mL/min/1.73 m²	37	43	44.7 (24.5, 59.4)
Screening SGLT2i use			
No	98	96	50.0 (39.1, 59.0)
Yes	54	72	52.9 (42.0, 61.8)



Sibeprenlimab reduced disease biomarkers (Gd-IgA1 and APRIL)

Percent change in serum (a) Gd-IgA1 and (b) APRIL levels from baseline over time[e]



At week 48, serum IgA levels decreased by 68.8%, IgG by 35.0%, and IgM by 74.5% with sibeprenlimab, while minimal changes were observed with placebo

TEAEs were similar in the sibeprenlimab (74.1%) and placebo (82.1%) groups, with most being mild-to-moderate in severity

- **Sibeprenlimab group achieved significant proteinuria reductions, which was consistent across patient subgroups**
- **Sibeprenlimab group had higher rates of hematuric resolution, proteinuric remission, and reductions in disease biomarkers compared with placebo group**
- **Safety findings were comparable across both treatment groups**
- **eGFR slope will be evaluated at 24 months in the ongoing VISIONARY trial**

[a] The interim analysis set comprises the first 62.5% of randomized patients who completed the 9-month uPCR-24h evaluation. [b] The percentage reduction of uPCR-24h at month 9 is compared with baseline using ANCOVA. [c] The percentage reduction for treatment effect was calculated as (1 - ratio of GM of uPCR-24h ratio for sibeprenlimab over placebo estimated from ANCOVA model) x 100%. The 95% CI corresponds to the treatment-specific reductions. The 96.5% CI corresponds to the between-treatment difference. [d] The percentage reduction for treatment effect is an exploratory endpoint and was calculated as (1 - ratio of GM of uPCR-24h ratio for sibeprenlimab SC 400 mg over placebo estimated from MMRM model) x 100%. [e] This analysis was performed on all randomized patients who received ≥1 dose of sibeprenlimab and had ≥1 postbaseline PD measurement.

ANCOVA, analysis of covariance; eGFR, estimated glomerular filtration rate; EOT, end of trial; F/U, follow-up; Gd-IgA1, galactose-deficient IgA1; GM, geometric mean; Ig, immunoglobulin; MMRM, mixed model for repeated measures; OLE, open-label extension; PD, pharmacodynamic; Q4W, every 4 weeks; SC, subcutaneous; SGLT2i, sodium-glucose cotransporter 2 inhibitor; TEAE, treatment-emergent adverse event; uPCR, urine protein-to-creatinine ratio; uPCR-24h, uPCR based on 24-hour urine collections.

1. Mathur M, et al. *Kidney Int Rep*. 2022;7(5):993-1003. **2.** Cheung CK, et al. *Clin J Am Soc Nephrol*. 2023;19(3):394-398. **3.** Muto M, et al. *Int J Mol Sci*. 2024;25(19):10340. **4.** Perkovic V, et al. *Kidney Int Rep*. Published online October 1, 2025. doi:10.1016/j.ekir.2025.09.031.

November 2025 US.VIS649.X.25.00011