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A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ATRASENTAN IN PATIENTS WITH IGA NEPHROPATY- THE ALIGN STUDY

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Objectives: IgA nephropathy (IgAN) is the leading cause of primary glomerulonephritis. Approximately 30-45% of IgAN patients progress to end-stage kidney disease (ESKD) over a period of 20-25 years and proteinuria is the strongest predictor of disease progression. Endothelin A (ET_A) receptor activation drives mesangial cell activation, kidney inflammation & fibrosis, and proteinuria, all hallmarks of IgAN. Therefore, atrasentan, a potent and selective ET_A antagonist, represents a potential approach to reduce proteinuria and preserve kidney function in IgAN. Atrasentan has demonstrated clinically significant and sustained proteinuria reduction with an acceptable safety profile in over 5,100 patients with DKD. Interim results from the IgAN cohort of the ongoing atrasentan AFFINITY study have shown a mean reduction in UPCR of 54.7% at week 24 in 19 patients with a generally well-tolerated safety profile.

Methods: The ongoing ALIGN study (NCT04573478) is a global, phase 3, randomized, double-blind, placebo-controlled study to determine the effect of atrasentan in patients with IgAN who are at high risk of kidney function loss. Approximately 320 patients will be enrolled across North America, South America, Europe, and Asia-Pacific with biopsy-proven IgAN with total protein excretion ≥1 g per 24 hr and eGFR ≥30 mL/min/1.73m^2. Patients will continue to receive a maximally-tolerated and stable dose of a RASi; a limited number of patients (up to 5%) that are unable to tolerate RASi therapy may be enrolled. An additional stratum of up to 64 patients receiving a stable dose of SGLT2i for at least 12 weeks will be enrolled. Patients will be randomized to receive 0.75mg atrasentan or placebo daily for 132 weeks.

Results: The primary outcome is change in proteinuria at Week 24. Secondary measures include change from baseline in eGFR, safety and tolerability, and quality of life.

Conclusions: This study is enrolling and ongoing as of abstract submission.