Background/Methods

IGA Nephropathy (IGAN)

• IGA is the leading cause of primary glomerulonephritis worldwide with approximately 30-40% of IGA patients progressing to ESKD over 20-25 years.
• Proteinuria is strongly associated with kidney disease progression in IGA.

Zigakibart and the APRIL Pathway

• In IGA, elevated levels of APRIL are associated with increased Gd-IgA1 and proteinuria and lower eGFR.
• Zigakibart is a novel, humanized monoclonal antibody that blocks APRIL (A Proliferation-inducing Ligand), a TNF superfamily cytokine that drives IgA class switching, plasma cell survival and the excess secretion of Gd-IgA1.

Study Design and Baseline Characteristics

ADU-CL-19 (Part 3) is an ongoing phase 1/2 trial investigating zigakibart in patients with IGA.

Key eligibility criteria: Biopsy-proven IgAN within past 10 years; total protein excretion >= 0.5 g/day OR UPCR > 3.5 g/g based on 24-hour urine collection at screening; eGFR >= 30 mL/min per 1.73 m²; Stable/optimal dose of RAS for ≥ 3 months prior to screening (or intolerant to RAS).

Results

Zigakibart treatment results in rapid and sustained reductions in IgA and pathogenic Gd-IgA1.

• Similar reductions in IgM were also observed; reductions in IgG were more modest.
• Data was consistent between cohorts.
• Reductions in immunoglobulins were maintained through study week 100 in cohort 1.

Conclusions

• Interim data continues to demonstrate disease-modifying potential of zigakibart in patients with IGA.
• Zigakibart has been generally well tolerated and directly targets IGA pathogenesis by depleting Gd-IgA1, leading to sustained, clinically meaningful reductions in proteinuria in patients with IGA.

The global phase 3 BEYOND registrational study (NCT01852938) 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 IGA at risk of progressive kidney function loss.

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