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ATRASENTAN FOR THE TREATMENT OF IGA NEPHROPATHY: INTERIM RESULTS OF THE AFFINITY STUDY

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Objectives: Endothelin A (ET_A) receptor activation drives proteinuria, inflammation, and fibrosis in patients with glomerular diseases. Atrasentan, a potent and selective ET_A receptor antagonist, represents a potential therapy to reduce proteinuria and preserve kidney function in patients with IgA nephropathy (IgAN) and other glomerular diseases. AFFINITY is a phase 2, open-label study evaluating efficacy and safety of atrasentan in adult patients with proteinuric glomerular diseases.

Methods: Eligibility criteria for the IgAN cohort include adults with biopsy-proven IgAN; eGFR ≥ 30 mL/min/1.73m², UPCR ≥ 0.5 to < 1.0 g/g (first morning void) and on maximally-tolerated/stable RASi. Patients are treated orally with 0.75 mg atrasentan daily for 52 weeks. The primary endpoint is change in 24-hour UPCR from baseline to Week 12.

Results: Twenty patients have enrolled in the IgAN cohort. Median age was 45 years, with 50% women, 45% White and 45% Asian. Median baseline 24-hour total urine protein was 1.2 g/day (geometric mean; GM), 70% of patients had total urine protein of > 1 g/day, and median eGFR was 46 mL/min/1.73m².

Mean (range) treatment duration was 45 (13-53) weeks as of data cut-off (19 October 2022). Atrasentan was generally well-tolerated with no serious and no treatment-related severe adverse events (AEs). Treatment-emergent AEs observed in 16 patients were mild or moderate; most have resolved. One patient discontinued due to a related AE of headache. No significant fluid retention was observed. GM reduction from baseline in 24-hour UPCR was 48.3% at week 12 (95% CI 38.9,56.3; n=20) and 54.7% at week 24 (95% CI 46.1,61.9; n=19; **Figure**).

Conclusions: Treatment with atrasentan in addition to standard of care was generally well-tolerated and resulted in durable and clinically meaningful reduction in proteinuria at weeks 12 and 24,