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Pegozafermin, a FGF21 Analog, for the Treatment of Non-alcoholic Steatohepatitis (NASH) Patients with F2/F3 Fibrosis

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Abstract

Background and Aims: Pegozafermin (PGZ) is a long-acting glycopegylated analog of fibroblast growth factor 21 (FGF21). This Phase 2b study evaluated the efficacy and safety of PGZ given weekly (QW) or every two-weeks (Q2W) versus placebo on histologic parameters in NASH patients with biopsy proven F2/F3 fibrosis.

Method: Patients were randomized to PGZ 15 mg QW, 30mg QW and 44mg Q2W or placebo for 24 weeks. The primary endpoint was the proportion of patients achieving either: 1) improvement of fibrosis by ≥1 stage with no worsening of NASH or 2) resolution of NASH without worsening of fibrosis. Key secondary endpoints included additional liver histology measures, changes in liver fat content by magnetic resonance imaging proton density fat fraction, fibrosis and inflammatory markers, metabolic effects, safety and tolerability.

Results:. A significant proportion of patients treated with higher doses of PGZ achieved the dual primary endpoint(s) for at least one stage of fibrosis improvement without worsening of NASH and/or NASH resolution without worsening of fibrosis. PGZ treatment significantly improved NAS score by ≥ 2 points, LFC, non-invasive markers of hepatic inflammation and fibrosis with meaningful changes in lipids and HbA1c. PGZ was generally safe and well tolerated, the most common treatment emergent adverse events (TEAEs) being mild/moderate nausea and diarrhea. No deaths occurred; six early terminations for TEAEs including one drug-related serious AE occurred.

Conclusion: PGZ treatment significantly improved histology, hepatic and metabolic parameters in NASH patients with F2/F3 fibrosis. These robust Phase 2b results support advancing PGZ into phase 3 development.