CO-002 - POSITIVE RESULTS FROM REGENERATE: A PHASE 3 INTERNATIONAL, RANDOMIZED, PLACEBO-CONTROLLED STUDY EVALUATING OBETICHOLIC ACID TREATMENT FOR NASH

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Introduction: Obeticholic acid (OCA), an FXR agonist, improved both fibrosis and histologic features of nonalcoholic steatohepatitis (NASH) in the Ph2 FLINT study. This Month 18 pre-specified interim analysis of the ongoing Ph3 REGENERATE study evaluated the effect of OCA on liver histology in patients (pts) with biopsy-confirmed NASH.
Methods: Pts with NASH and fibrosis stages F2-3 (ITT), and an exploratory group of F1 pts with metabolic syndrome, were randomized to placebo (PBO), OCA 10mg, or OCA 25mg QD. Primary endpoints were fibrosis improvement (≥1 stage) with no worsening of NASH, or NASH resolutionwith no worsening of liver fibrosis. The safety population included all randomized and dosed pts (F1-3, N=1968). Clinical outcomes will be evaluated at the end-of-study.
Results:ITT population included 931 pts (PBO [n=311], OCA 10mg [n=312] or OCA 25mg [n=308]), comprised of 44% F2 and 56% F3. Baseline characteristics were well-balanced across groups. The primary fibrosis endpoint was met by 11.9% PBO, 17.6% OCA 10mg (p=0.0446), and 23.1% OCA 25mg (p=0.0002) pts (ITT). The primary NASH endpoint was not statistically significant (ITT); however, in a pre-specified analysis that included F1-F3 pts (N=1218), more OCA 25mg pts achieved NASH resolution. Pruritus was the most common AE (19% PBO, 28% OCA 10mg, 51% OCA 25mg) and was predominantly mild to moderate in severity. More OCA 25mg pts discontinued due to pruritus (<1% PBO, <1% OCA 10mg, 9% OCA 25mg; protocol mandated discontinuation of treatment with severe

pruritus). SAEs occurred in 11% PBO, 11% OCA 10mg and 14% OCA 25mg pts. Three deaths occurred; none were considered treatment-related (PBO n=2; OCA 25mg n=1).

Conclusion: Treatment with OCA 25mg improved liver fibrosis, key histologic features of steatohepatitis and liver biochemistry, demonstrating consistent efficacy with an overall AE profile similar to previous studies.