ONCE-MONTHLY EFIMOSFERMIN ALFA (BOS-580) IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS WITH F2/F3 FIBROSIS: RESULTS FROM A 24 WEEK, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 TRIAL

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Background: In a Phase 2a multiple dose/ regimen study, efimosfermin alfa (BOS-580), an FGF21 analogue, significantly improved liver steatosis, markers of liver injury, and fibrosis in patients with phenotypic metabolic dysfunction-associated steatohepatitis (MASH). A Phase 2, randomized, double-blind, placebo-controlled study was conducted in patients with biopsy-confirmed MASH, F2/F3 fibrosis, and Nonalcoholic Fatty Liver Disease Activity Score (NAS) ≥4. (NCT04880031)

Methods: Patients (N=84) were randomized to receive once-monthly efimosfermin 300mg or placebo for 24 weeks. The primary endpoint was safety and tolerability. Exploratory efficacy endpoints included the proportion of patients achieving fibrosis improvement ≥1 stage without worsening of MASH, MASH resolution without worsening of fibrosis, and a composite endpoint of fibrosis improvement ≥1 stage and MASH resolution which were analyzed in the biopsy analysis set (N=65).

Results: Patients (52.4% female; mean age 54 yrs; mean BMI 37.3 kg/m^2; mean HFF 20.4%; 43% F3 fibrosis; 57% type 2 diabetes) were administered efimosfermin 300mg (N=43), or placebo (N=41). In the biopsy analysis set, a significantly higher proportion of patients treated with efimosfermin 300mg (N=34) achieved improvement in fibrosis without worsening of MASH (45.2% v 20.6%, p=0.038), and resolution of MASH without worsening of fibrosis (67.7% v 29.4%, p=0.002) versus placebo (N=31). The proportion of patients who achieved the composite endpoint of ≥1 stage fibrosis improvement and MASH resolution was 38.7% for efimosfermin 300mg versus 17.6% for placebo (p=0.066). In both groups, the most frequent treatment-related adverse events (AEs) were mild to moderate gastrointestinal events of nausea, diarrhea and vomiting. Overall, discontinuations were balanced with two efimosfermin patients who discontinued due to low-grade AEs. There was 1 treatment-related grade 3 serious AE.

Conclusion: Once-monthly efimosfermin significantly improved both regulatory key endpoints including MASH resolution and fibrosis improvement at 24 weeks in patients with F2/F3 fibrosis due to MASH. In this study, efimosfermin was generally well-tolerated with a low rate of discontinuation due to AEs. These data support further development of once-monthly efimosfermin for the treatment of MASH-related fibrosis.