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BMF-219: A Novel Therapeutic Agent to Reestablish Functional Beta Cells and Provide Long-Term Glycemic Control

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Abstract

Background: Inhibition of menin drives an increase in beta-cell proliferation and function. BMF-219, an oral menin inhibitor, is being developed to manage diabetes. Herein we summarize BMF-219 ex-vivo human islet and T2D clinical data.

Methods: BMF-219 was evaluated in ex-vivo human islet cultures to assess beta-cell function and proliferation. In T2D, a randomized, double-blind, placebo-controlled study is ongoing. We report patients treated with BMF-219 100mg QD for 4 weeks, followed until Week 26. Endpoints include glycemic efficacy and safety.

Results: With human islet microtissues cultured for 2-3 weeks under high glucose conditions, BMF-219 increased the fraction of proliferating beta cells resulting in an increase in insulin content and glucose-stimulated insulin secretion. Gene expression changes with CCNA2 and PbK were observed, supporting beta cell proliferation, consistent with published data.
Twenty T2D patients received BMF-219 100mg QD for 4 weeks (with or without food). A reduction in HbA1C of 0.5% or greater was seen in 50% patients at Week 4, which improved to 60% at Week 12. A sustained reduction ≥0.5% was seen in 40% patients at Week 26. At this timepoint, 20% of patients experienced ≥1% HbA1c reduction, with a maximum reduction of 2.5%. BMF-219 was well tolerated (no SAEs or dose discontinuations).

Conclusions: In ex-vivo cultured islets, BMF-219 improved human beta-cell function and proliferation. In T2D, BMF-219 for 4 weeks resulted in meaningful HbA1c reductions at treatment completion (Week 4) and during the 26-week follow-up. Combined results support BMF-219 mechanism of action of beta-cell preservation, reactivation, and proliferation.