UPDATE FROM A FIRST-IN-HUMAN PHASE 1 STUDY OF MODAKAFUSP ALFA (TAK-573), A FIRST-IN-CLASS IMMUNOCYTOKINE, IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

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Introduction: Modakafusp alfa is designed to deliver attenuated interferon alpha-2b to CD38+ cells. In this phase 1 study, treatment with modakafusp alfa starting at 0.1 mg/kg induced responses in RRMM patients; thrombocytopenia and neutropenia were dose-limiting toxicities with dosing every 1, 2, or 3 weeks (NCT03215030). We provide updated results, focusing on an expansion cohort dosed every 4 weeks (Q4W).

Material and methods: Patients with ≥3 previous lines of anti-myeloma treatment (LoT) received modakafusp alfa at 10 dose levels from 0.001 to 6 mg/kg. Initial dosing was weekly for 8 doses, biweekly for 8 doses, then monthly. Subsequent cohorts received dosing every 2, 3, or 4 weeks. Expansion cohorts received biologically-active doses below/equal to the maximum tolerated dose (MTD).

Results: 88 patients received treatment across all doses/schedules. At 6 mg/kg Q4W, the MTD was exceeded due to a grade 3 infusion reaction and prolonged thrombocytopenia and neutropenia. Results henceforth are for the 29 patients who received modakafusp alfa 1.5 mg/kg Q4W, after a median follow-up time of 4.2 months. Median prior number of LoTs was 7; 26 patients were anti-CD38 monoclonal antibody (mAb)-refractory and 25 were triple-class refractory. The most common grade 3-4 treatment-emergent adverse events included neutropenia in 18 (62%), thrombocytopenia in 13 (45%), and leukopenia in 12 (41%) patients. Three patients had grade 3 infections, one had a grade 3 infusion reaction, and another experienced a grade 3 bleeding event. Overall response rate was 38% among all patients and also in anti-CD38 mAb-refractory patients. Median progression-free survival was 5.7 months. Evidence from correlative studies support activation of T-cells, natural killer-cells and interferon signaling by modakafusp alfa in CD38+ cells.

Conclusions: Modakafusp alfa showed encouraging activity in heavily pretreated RRMM patients, including those refractory to anti-CD38 mAbs. Q4W dosing is viable; the optimal dose and combinations are being investigated.