EARLY, DEEP, AND DURABLE RESPONSES, AND LOW RATES OF CYTOKINE RELEASE SYNDROME WITH REGN5458, A BCMAXCD3 BISPECIFIC ANTIBODY, IN A PHASE 1/2 FIRST-IN-HUMAN STUDY IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Introduction: REGN5458 is a BCMAxCD3 bispecific antibody currently under investigation in relapsed/refractory multiple myeloma (RRMM) in an ongoing Phase 1/2 trial (NCT03761108). Updated Phase 1 data are reported here.

Material and methods: Patients with progressive RRMM who are double- or triple-refractory or intolerant to prior lines of systemic therapy, including a proteasome inhibitor, immunomodulatory agent, and anti-CD38 antibody, are treated with REGN5458. The Phase 1 primary objectives are to assess safety, tolerability, occurrence of dose-limiting toxicities, and to determine a recommended Phase 2 dose regimen. The objective response rate by modified International Myeloma Working Group criteria is a key secondary objective.

Results: Seventy-three patients were treated with REGN5458 in the dose escalation cohort with full doses ranging from 3 to 800 mg. The median age at enrollment was 64 years (range, 41–81). As per the Revised International Staging System, stages were 1, 2 or 3 in 15.0%, 57.5%, and 23.3% of patients respectively. Patients had a median of five prior lines of systemic therapy (range, 2–17), with 38.4% of patients being penta-refractory. The median duration of follow-up was 3.0 months (range, 0.7–22.1).

The most common treatment-emergent adverse events were fatigue (45.2%), cytokine release syndrome (CRS, 38.4%), and pyrexia (35.6%). There were no Grade ≥3 CRS or Grade ≥3 neurotoxicity events and no treatment discontinuation due to CRS. The most common Grade 3/4 treatment-emergent adverse events were hematologic (39.0%).

Responses were observed at all dose levels with an overall rate of 50.7%. Among all responders, 86.5% (n=32/37) achieved at least a very good partial response and 43.2% (n=16/37) achieved complete or stringent complete responses. The median duration of response was not reached.

Conclusions: REGN5458 shows early, deep and durable responses with a manageable safety profile in triple- to penta-refractory patients with RRMM.