Background PD-L1 and VEGF play important roles in immune escape and tumor angiogenesis and thus enhance cancer growth and metastasis. PM8002 is a bispecific antibody targeting PD-L1 and VEGF-A. Here we present the results from a Phase I first-in-human dose-escalation and ongoing expansion study of PM8002 in advanced solid tumors.

Methods This study includes a standard 3+3 dose escalation stage (Part A: single dosing of 1, 3, 10, 20, 30, and 45 mg/kg for 3-week DLT evaluation, then administration Q2W if the subject did not experience DLT) followed by dose expansion (Part B). Primary endpoints include safety and tolerability for Part A, and ORR per RECIST 1.1 for Part B. Secondary endpoint includes pharmacokinetics (PK).

Results As of June 15, 2022, a total of 59 subjects had received at least one dose of PM8002, including 18 subjects in Part A (3 subjects per 1, 3, 10, 20, 30 and 45 mg/kg dose-levels), and 41 subjects in Part B (1mg/kg Q2W [n=1], 10mg/kg Q2W [n=18], 20mg/kg Q3W [n=17]). In part A, no DLTs were observed and MTD was not reached. Of the 59 subjects, the median duration of PM8002 exposure was 8.1 weeks (range, 3.0—29.0 weeks). Any-grade TRAEs occurred in 40 subjects (67.8%), with 9 subjects (15.3%) reported with ≥ Grade 3 TRAEs. 9 subjects (15.3%) discontinued PM8002 administration due to TRAEs. The most common TRAEs were proteinuria (18.6%), thrombocytopenia (11.9%), aspartate aminotransferase increase (10.2%). Any-grade irAEs occurred in 24 subjects (40.7%), with 4 subjects (6.8%) reported with ≥ Grade 3 irAEs. PK analysis showed a linear dose-exposure relationship with PM8002 dosing from 1 to 45 mg/kg. T½ varied from 4.2—8.9 days. Peripheral PD-L1 receptor occupancy exceeded 95% in the 10 mg/kg and higher dose groups. In part B, 30 subjects completed at least one efficacy evaluation. The ORR per RECIST 1.1 by investigator was 20%, with 6 PRs in subjects with ovarian cancer (n=1, 20mg/kg Q2W), colorectal cancer (n=1, 10mg/kg Q2W), renal cell carcinoma (n=3, 30mg/kg Q3W) and NSCLC (n=1, 20mg/kg Q2W). Fifteen subjects achieved best responses of stable disease, with a total DCR of 70%. 20 mg/kg Q2W and 30 mg/kg Q3W were recommended as the RP2D for further clinical study.

Conclusions PM8002 showed an acceptable safety profile and encouraging antitumor activity in refractory solid tumors. Phase II clinical trials with PM8002 as a monotherapy or in combination with chemotherapy are ongoing for multiple indications.