accelerated titration design was utilized for the initial dose escalation followed by a modified 3+3 design and the option to back-fill cohorts. Dose-limiting toxicities (DLTs) were reported during the first cycle of each schedule. The primary study objectives include the safety profile and RP2D of PRS-343. Secondary objectives include ORR and DCR, PD biomarker response and PK profile. PD response was assessed in tumor biopsies (CD8+ T cell IHC) pre- and post- PRS-343 treatment.

Results 51 patients (median age 61.2 years, 61% female, 82% caucasian, 57% with more than three lines of prior therapy) with a variety of solid tumor indications [gastric/GEJ (n=19); BC (n=12); gynecological cancer (n=6); CRC (n=5); BTC (n=4); UC (n=2); melanoma, pancreatic and salivary duct (n=1 each)] have been treated with PRS-343. Based on pharmacokinetic analyses and observed kinetics of the CD8+ T cell expansion post-treatment, the low end of the active dose range is considered 2.5 mg/kg. 19 patients treated at active dose levels before the data cut-off on 09-06-2019 were evaluable for response [DCR 58% (11% confirmed PR) as per RECIST 1.1]. At the active doses, we observed significant and pronounced post-treatment expansion of CD8+ T cells particularly in the tumor nests, consistent with the MoA of PRS-343, while there was no increase in the doses below 2.5 mg/kg. The post-treatment expansion of CD8+ T cells was more pronounced in patients with a confirmed PR or prolonged SD. PRS-343 was very well tolerated, with no SAEs reported. The most frequent TRAEs were fatigue (9%), chills (6%) and diarrhea (5%) of mild to moderate severity. None qualified as a DLT.

Conclusions PRS-343 is the first molecule of its kind to demonstrate encouraging evidence of safety and clinical benefit with a correlative PD effect in a heavily pre-treated population. These initial data suggest that PRS-343, the first 4-1BB bispecific to enter clinical development, merits further investigation in clinical trials.

Trial Registration NCT03330561

083 PHASE 1 STUDY OF AN ANTI-CD27 AGONIST AS MONOTHERAPY AND IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background MK-5890 is a humanized agonist monoclonal antibody that binds to CD27 to provide a costimulatory signal that enhances T-cell–mediated responses. This first-in-human phase 1 study of MK-5890 evaluated the safety and efficacy of escalating doses of MK-5890 as monotherapy and in combination with pembrolizumab in patients with advanced solid tumors.

Methods Key eligibility criteria included histologically or cytologically confirmed advanced solid tumor, measurable disease by RECIST v1.1, and ECOG PS ≤1. MK-5890 was tested alone (dose range, 2-700 mg) or with pembrolizumab (fixed dose, 200 mg). Patients with disease progression following MK-5890 monotherapy were eligible to cross over to combination treatment. The primary objective was safety and tolerability. Objective response rate by investigator per RECIST v1.1 was also evaluated. The database cutoff for this analysis was May 30, 2019.

Results Of 44 patients enrolled, 25 received MK-5890 and 19 received MK-5890 plus pembrolizumab; their median age was 59.0 years, 61.4% were female, 47.7% had ECOG PS 1, and 13.6% previously received immune checkpoint inhibitor therapy. In the initial phase, dose-limiting toxicities (DLTs) were reported in 3 patients receiving MK-5890 and 1 patient receiving MK-5890 plus pembrolizumab; all DLTs were associated with infusion-related adverse events. Maximum tolerated dose was defined. Treatment-related adverse events (TRAEs) were reported in 40 patients (90.9%): 22 patients (88.0%) receiving MK-5890 and 18 patients (94.7%) receiving MK-5890 plus pembrolizumab. The most common TRAEs were fatigue (28.0%) and infusion-related reactions (28.0%) with MK-5890 and fatigue (36.8%) and pruritus (31.6%) with MK-5809 plus pembrolizumab. Grade 3-4 TRAEs were reported in 10 patients (22.7%): 6 patients (24.0%) receiving MK-5890 and 4 patients (21.1%) receiving MK-5890 plus pembrolizumab; no grade 5 events were observed. One patient (4.0%) achieved a partial response (PR) with MK-5890 and 1 patient (5.3%) achieved a PR with MK-5890 plus pembrolizumab. Fourteen patients entered the crossover phase to receive MK-5890 plus pembrolizumab. In the crossover phase, no DLTs were reported. TRAEs were reported in 12 patients (85.7%); the most common were pruritus (21.4%), rash (21.4%), and headache (14.3%). One patient (7.1%) reported grade 3-4 TRAEs of increased amylase and increased lipase; no grade 5 events were observed. Two patients (14.3%) achieved a complete response and 2 patients (14.3%) achieved a PR.

Conclusions Treatment with MK-5890, alone and in combination with pembrolizumab, demonstrated an acceptable safety profile. Early antitumor activity was observed in patients with advanced solid tumors in both monotherapy and combination therapy arms.

085 DURABLE RESPONSES IN ANTI-PD-1 REFRACTORY MELANOMA FOLLOWING INTRATUMORAL INJECTION OF A TOLL-LIKE RECEPTOR 9 (TLR9) AGONIST, CMP-001, IN COMBINATION WITH PEMBROLIZUMAB

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Background Intratumoral (IT) injection of CMP-001, a CpG-A TLR9 agonist packaged within a virus-like particle, is designed