

of  $10^7$  PFU/mL. Of the six patients treated with single agent RP2, three (50%) have ongoing partial responses. Objective responses (including in uninjected tumors) were observed in patients with uveal melanoma (prior ipilimumab/nivolumab; extensive liver metastases), mucoepidermoid carcinoma (prior carboplatin/paclitaxel, bicalutamide, ceralasertib), and esophageal cancer (prior durvalumab, M6620, capecitabine, oxaliplatin, cisplatin, chemoradiation; liver and abdominal node metastases). Enrollment is underway in HSV seronegative patients and in combination with nivolumab. Updated data including biomarker and biodistribution data will be presented. **Conclusions** The Phase 1 clinical data supports the safety and efficacy of single agent RP2, including demonstration of uninjected tumor response in patients with difficult to treat advanced cancers. This data supports the hypothesis that anti-CTLA-4 delivered intra-tumorally through oncolytic virus replication, with accompanying antigen release and presentation, can provide potent anti-tumor effects.

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#### AN OPEN-LABEL, MULTICENTER, PHASE 1/2 CLINICAL TRIAL OF RP1, AN ENHANCED POTENCY ONCOLYTIC HSV, COMBINED WITH NIVOLUMAB: UPDATED RESULTS FROM THE SKIN CANCER COHORTS

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**Background** RP1 is an enhanced potency oncolytic HSV encoding a fusogenic protein (GALV-GP R-) and GM-CSF which has previously demonstrated tolerable safety and tumor regression alone and with nivolumab in patients with a number of tumor types. Updated data from the phase 1 expansion with nivolumab, melanoma phase 2 (enrollment complete) and non-melanoma skin cancer (NMSC; enrollment ongoing) cohorts will be presented (NCT03767348). Enrollment of a further 125 patient anti-PD1 refractory cutaneous melanoma cohort; and activation of a cohort of anti-PD1 refractory NSCLC is underway.

**Methods** Stage IIIb-IV melanoma patients for whom anti-PD-1 was indicated or who were refractory to prior anti-PD-1 alone or in combination with anti-CTLA-4, were enrolled. NMSC patients were anti-PD1 naïve. Patients received  $\leq 8$  doses of RP1 ( $\leq 10$  mL/visit Q2W; first dose  $10^6$  PFU/mL then  $10^7$  PFU/mL) with nivolumab (240 mg IV Q2W for 4 months then 480 mg IV Q4W up to 2 years) from the second RP1 dose.

**Results** As of 24th June 2020, 36 melanoma and 16 NMSC patients had been enrolled with follow up of <1–17 months. Of the melanoma patients, 16 previously anti-PD1 treated cutaneous (8 also prior anti-CTLA-4), 8 anti-PD1 naïve

cutaneous, 6 mucosal, and 6 uveal. Of the NMSC patients, 10 had squamous cell (CSCC), 3 had a basal cell, 1 had Merkel cell carcinomas, and 2 had angiosarcoma. Treatment emergent adverse events (TEAEs) remain consistent with phase 1, with RP1 side effects generally of Grade 1/2 constitutional-type symptoms, with no exacerbation of the side effects expected for nivolumab. At the data cut-off, 5 previously anti-PD1 treated (4 also anti-CTLA-4) cutaneous melanoma patients, 4 anti-PD1 naïve cutaneous melanoma patients, two mucosal melanoma patients (one anti-PD1 refractory) and one uveal melanoma patient (ipi/nivo refractory) have achieved response (WHO criteria for uveal). For NMSC, for the 13 patients with >8 weeks follow up, one of two angiosarcoma patients and seven of eight CSCC patients (5 CR) have achieved response (CSCC ORR 87.5%; CR rate 62.5%, including of uninjected visceral disease). Tumor biopsies in patients continue to routinely show immune activation, including robust recruitment of CD8+ T cells, reversal of T cell exclusion, and increased PD-L1 expression. Treatment remains ongoing, and current data will be presented.

**Conclusions** RP1 and nivolumab have continued to be well tolerated, with continued promising anti-tumor activity in patients with skin cancers, including those with anti-PD1 refractory and other difficult to treat melanomas, and in patients with CSCC.

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#### SAFETY AND PRELIMINARY EFFICACY OF INTRATUMORAL CAVROTOLIMOD (AST-008), A SPHERICAL NUCLEIC ACID TLR9 AGONIST, IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

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**Background** Spherical nucleic acids (SNAs) are nanostructures consisting of radially oriented, densely packed oligonucleotides arranged in a spherical 3D architecture. SNAs have different properties than linear oligonucleotides, including increased cellular uptake, which may enhance efficacy. Cavrotolimod (AST-008) is an SNA toll-like receptor 9 (TLR9) agonist designed to robustly activate innate and adaptive immune responses. Cavrotolimod is in development for the treatment of advanced solid tumors in combination with PD-1 blockade. Prior studies demonstrated that cavrotolimod, alone and in combination with PD-1 blockade, increased circulating levels of Th1-type cytokines and activated peripheral T cells and NK cells.