FAVORABLE PRECLINICAL EFFICACY AND SAFETY PROFILE OF AVB-001 A NOVEL IL-2 CELL-BASED IMMUNOTHERAPY THAT ERADICATES OVARIAN CANCER IN MOUSE TUMOR MODELS AND SUPPORTS FIRST IN HUMAN CLINICAL DEVELOPMENT

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Background Aldesleukin, recombinant human IL-2 has been approved by the FDA for the treatment of melanoma and renal cancer. However, effective cytokine therapy is limited by its short half-life in circulation and the severe adverse effects associated with high systemic exposure when administered iv. To overcome these limitations, Avenge Bio has developed a localized cytokine delivery LOCOcyte™ platform comprised of polymer encapsulated epithelial cells that produce potent immune effector molecules for loco-regional delivery with temporal regulation. AVB-001 is engineered to produce native IL-2, for the treatment of ovarian cancer.

Methods Safety, PK and PD testing of AVB-001 using a combination of rodent and NHP animal models.

Results Tumor-adjacent local administration of AVB-001 demonstrated that mIL-2 local concentration (intraperitoneal space) was 100x higher than the systemic concentration (blood) demonstrating the ability of the LOCOcyte™ platform to deliver native cytokines in vivo and create a high locoregional concentration of cytokines with limited peripheral exposure. Additional studies in mice demonstrated dose-dependent levels of IL-2 in the IP cavity in mice. Treatment of solid tumors using a single administration of AVB-001 demonstrated complete responses as monotherapy and provided sustained eradication of peritoneal tumors in ID8 ovarian cancer mouse model. Our data in mice confirmed that AVB-001 leads to a local increase in activation and proliferation of cytotoxic T-cells within the IP space in comparison to sham mice. In addition, in MC38 colorectal cancer rechallenge model it was observed that a single local administration of AVB-001 leads to complete tumor eradication as a single agent and was accompanied by systemic antitumor immune responses. A single administration of AVB-001 in NHP led to therapeutic levels of IL-2 in the IP cavity and produced local and systemic T-cell biomarker profiles that predict efficacy. In safety assessments of AVB-001, no signs of cytokine storm and vascular leak syndrome and no evidence of adverse pathologic effects on local or systemic tissue were observed with administration of AVB-001 expressing up to 16.7 µg hIL-2/kg in mice and 12.8 µg hIL-2/kg in NHP giving a sufficient safety window for the planning of our first clinical study.

Conclusions It was demonstrated that the AVB-001 is dose adjustable, safe and efficacious in preclinical animal models. Avenge Bio aims to pursue a Phase 1 First in Human study of AVB-001 in ovarian cancer patients. The LOCOcyte™ platform enables delivery of a diverse set of cytokines alone or in combination which is presently being explored.