**VISTA-101: A phase 1/2 clinical trial of KVA12123, an engineered IgG1 targeting VISTA alone and in combination with pembrolizumab in advanced solid tumors**

**Background**

VISTA (V-domain Ig suppressor of T cell activation) is a strong driver of immunosuppression in the tumor microenvironment (TME).

- A negative immune checkpoint that suppresses T cell function in a variety of solid tumors
- Highly expressed in cold tumors and correlates with poor outcomes in cancer patients
- Up-regulated after checkpoint inhibitor therapy and associated with treatment failure
- Blocking VISTA induces a polyfunctional immune response that addresses immunosuppression and drives anti-tumor responses

**VKA12123** is a VISTA blocking immunotherapy in development as a twice weekly infusion

- An engineered IgG1 mAb that binds to a unique epitope at acidic and neutral pHs
- Induces a strong anti-tumor response as a single agent and in combination with anti-PDL1 in multiple preclinical tumor models
- Well tolerated and does not induce the release of CRS associated cytokines in non-human primates or in human whole blood
- May be an effective immunotherapy for many types of cancer including NSCLC, colorectal (CRC), renal cell carcinoma (RCC), head and neck (SCCHN), and ovarian (OC) cancers

**VISTA-101 study objectives**

- **Primary**: safety and tolerability, recommended Phase 2 dose (RP2D) or maximum tolerated dose (MTD) of VKA12123
- **Secondary**: pharmacokinetics, immunogenicity, tumor response in subjects with advanced solid tumors per RECIST (ORR)
- **Exploratory**: biomarker and receptor occupancy

**VISTA-101 study design**

Cleared initial monotherapy cohorts and started combination cohort with pembrolizumab

**KVA12123 monotherapy safety**

KVA12123 was well tolerated in 3, 10 & 30 mg monotherapy cohorts

- No dose limiting toxicities (DLT) were observed
- All KVA12123 treatment emergent adverse events (TEAE) were grades 1-2

**Pharmacokinetics and VISTA receptor occupancy (RO)**

VKA12123 exhibited a greater than dose-proportional pharmacokinetic profile

**Biomarkers**

KVA12123 demonstrated dose proportional induction of pro-inflammatory biomarkers and on-target immune cell responses involved in anti-tumor activity

- Induces pro-inflammatory myeloid derived cytokines/chemokines involved in immune cell activation and recruitment in the tumor microenvironment
- Increases anti-tumor Non-classical monocytes and NK cells in peripheral blood
- Increases helper (CD4+) and cytotoxic (CD8+) T cells in the blood

**Conclusions**

- VISTA is a promising innate immune drug target that is nonredundant with T cell focused therapies
- Cleared first three VKA12123 monotherapy cohorts (3, 10, 30 mg) with 11 patients dosed
- Clinical safety profile established as VKA12123 was well tolerated and no DLTs were observed
- No evidence of CRS-associated cytokines (IL-6, TNFα & IL-10) were detected
- VKA12123 exhibited a greater than dose-proportional pharmacokinetic profile
- Achieved >90% VISTA RO across patients in the 30 mg dosing cohort approaching an optimal clinical dose
- Demonstrated efficacy-related cytokine secretion of CXCL10, MCP1, MIP1α & MIP1β
- On-target changes in anti-tumor immune cell subpopulations were observed after treatment
- VISTA-101 trial is advancing to higher monotherapy dose levels and in combination with pembrolizumab
- Additional monotherapy data and combination therapy clinical data anticipated in Q2 2024

**Tumor type and best overall response (BOR)**

- Discrete tumor types enrolled in VISTA-101 clinical trial
- Additional monotherapy safety and efficacy data anticipated in Q2 2024

**Immunophenotyping**

Changes of peripheral blood immune cell subpopulations after the first administration of VKA12123. Flow cytometry data acquisition and analysis were performed using the FACSCalibur™ Flow cytometer. Data was acquired and analyzed using BD FACSDiva™ software. Fold change per dose was calculated for each subpopulation (mean ± SD).