Interim results of the ongoing phase 1/2 clinical trial of KVA12123, an engineered IgG1 targeting VISTA, alone and in combination with pembrolizumab in advanced solid tumors.


KVA12123 is a VISTA-blocking immunotherapy in development as a twice-weekly infusion and combination therapy. KVA12123 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. Blocking VISTA induces a polyfunctional immune response that addresses immunosuppression and drives anti-tumor responses. Noodle et al. Front Oncol (2021).

VISTA-101 trial:
- Phase 1/2 open-label clinical trial of KVA12123 alone and in combination with pembrolizumab in patients with advanced solid tumors (NCT05708950).
- **Primary:** safety and tolerability, recommended Phase 2 dose (RP2D) or maximum tolerated dose (MTD) of KVA12123.
- **Secondary:** pharmacokinetics, immunogenicity, tumor response in subjects with advanced solid tumors per RECIST (ORR).
- **Exploratory:** biomarker and receptor occupancy.

Clinical efficacy and safety profile: KVA12123 was well tolerated in evaluated monotherapy and combination therapy cohorts and no DLTs were observed.

Conclusions:
- February 23rd 2024 - Cleared first five KVA12123 monotherapy cohorts (3, 10, 30, 100, 300 mg) with 21 patients dosed, and two KVA12123+pembrolizumab cohorts (100 mg + 400 mg pembrol) with 9 patients dosed.
- Clinical safety profile: KVA12123 was well tolerated in evaluated monotherapy and combination therapy cohorts and no DLTs were observed.
- No evidence of CRS-associated cytokines (IL-6, TNFα & IL-10) were detected after KVA12123 administration.
- Achieved >90% VISTA RD across patients in >30 mg dosing cohorts with 300mg of KVA12123 approaching an optional clinical dose.
- Demonstrated efficacy-related cytokine secretion of CXCL10, IFNγ, CCL2, CCL3, CCL4, CXCL8 and on target changes in anti-tumor immune cell subpopulations.
- Monotherapy: 9 of 12 patients who received at least 1 follow-up scan achieved stable disease (SD) as BOR and mean duration of SD is 15 weeks with the longest duration of 28 weeks in ongoing CPI-failed NSCLC.
- Combination Therapy: 3 patients received one follow-up scan, 1 Mucoepidermoid carcinoma patient achieved a partial response with 52.7% reduction of target lesions and 1 RCC patient with SD and 23.7% reduction of target lesions.
- VISTA-101 trial is advancing to the last monotherapy dose level and the last two cohorts in combination with pembrolizumab.