KVA 12.1 a novel fully human anti-VISTA antibody
to treat cancer patients with advanced solid tumors

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Background

- VISTA (V-domain Ig Suppressor of T cell Activation) is a unique CD28/87 family member with poorly defined receptors. However, VISTA itself, PSLG-1, VSIG3, VSIG8 and VRG1 have been suggested as putative receptors.
- VISTA is highly expressed on circulating and intratumoral myeloid cells especially MDSCs.
- VISTA is a negative regulator that directly suppresses T cell activation and proliferation.
- High VISTA expression correlates with poor survival in cancer patients.
- VISTA is a unique immune checkpoint inhibitor for tumor immunotherapy.

Objectives

- Select a lead clinical candidate against VISTA → KVA12.1
- Develop a clinical plan for patients with advanced solid tumors

Results

- Exceptional antibody diversity in both Heavy and Light Chains
  - 107 fully human Scv antibodies directed against Human VISTA were generated
    - 15 V\(\text{H}\), diversity groups
    - 15 V\(\text{L}\), diversity groups
    - Highest diversity in CDR3H

- KVA antibodies bind only to VISTA and not other B7 family proteins

Mechanism of action of our lead anti-VISTA antibody: KVA12.1

Safety: KVA12.1 is well-tolerated in NHP toxicity studies

Clinical Development Plan

Clinical Protocol Design

Phase 1/2 trial is proposed as follows:

Part A: Monotherapy

Part C: Expansion - Monotherapy

Part B: Combination Therapy

Part C: Expansion - Combination Therapy

Study Endpoints

- Clinical
  - Safety measurements and DLTs as single agent and in combination with anti-PD1
  - Overall Response Rate and durability of response using RECISTv1.1
  - Determined MTD and R2PD

- Pharmacologic and Biomarker
  - PK
  - Receptor occupancy
  - Cytokine and Chemokine profiles in plasma samples
  - Flow Cytometry for PD marker on immune cells

Conclusion

- 107 fully human Scv anti-VISTA antibodies were generated and analyzed
- KVA12.1 was selected as our clinical lead
- KVA12.1 has an extended PK and a unique epitope
- KVA12.1 induces strong anti-tumor response as a single agent or in combo-therapies with anti-PD1 in multiple tumor models
- KVA12.1 is safe and does not exhibit any sign of Cytokine Release Syndrome in NHP as well as human whole blood
- Clinical Trial will start end of 2022