Introduction

- VISTA (V-domain Ig Suppressor of T Cell Activation) is a unique CD88/B7 family member with poorly defined receptors. However, PSGL-1, VISTA, VSG8, UEG1 and VISTA itself have been suggested as putative receptors.
- VISTA is highly expressed on circulating and intratumoral myeloid cells.
- VISTA is a negative regulator that 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.

Background

- 107 fully human scFv anti-VISTA antibodies were generated and analyzed.
- The wild-type (WT) IgG1-Fc of KVA12104 was optimized to obtain our clinical lead, KVA12123.
- KVA12123 is highly specific, has extended PK, reduced ADCC and binds to a unique VISTA epitope.
- KVA12123 activates monocytes, and this activation is NK dependent.
- KVA12123 reverses MDSC suppression of T cells.
- KVA12123/mPD1 as a single agent or in combo induces strong anti-tumor activity.

Objectives

- KVA12123 IgG1-Fc region has been optimized (YTE) to improve PK and reduce ADCC, and compared to published anti-VISTA antibodies.
- KVA12123 anti-tumor response has been evaluated as a single-agent or in combo-therapies (e.g. anti-PD1) in multiple mouse tumor models.
- Safety and tolerability of our clinical lead KVA12123 have been evaluated.

KVA12123 antibody induces strong anti-tumor response as a single agent or in combo-therapies

Results

- KVA12123 Fc modification increases binding to FcRn and decreases tumor response.

KVA12123 Fc modification extends serum exposure

- KVA12123 does not induce Cytokine Release Syndrome (CRS) in human whole blood

Conclusions

- KVA12123 has been selected as our clinical lead.
- KVA12123 has an extended PK and binds to a unique epitope.
- KVA12123 induces a strong anti-tumor response as a single agent or in combo-therapies with anti-PD1 in multiple tumor models.
- KVA12123 is well tolerated and has been shown not to induce release of CRS cytokines in non-human primate studies or in human whole blood.
- Clinical trial to start December 2022.