HBM1022: AN AFUCOSYLATED ANTI-CCR8 ANTIBODY, DEPLETES SPECIFICALLY TUMOR INFILTRATING TREGS AND INHIBITS TUMOR GROWTH WITH EXCELLENT SAFETY PROFILE IN PRECLINICAL STUDIES

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Background Tumor-infiltrating lymphocyte-Treg cells (TIL-Tregs) contribute to establishment of an immunosuppressive tumor microenvironment (TME). Several immunotherapies, such as anti-CD25 antibodies, are designed to target this type of cells. However, the possibility of undesirable targeting Treg cells in peripheral blood hampers their clinical benefits. CCR8 is a chemokine receptor selectively upregulated on TIL-Tregs from cancers such as clear cell renal cell carcinoma (ccRCC), breast, and bladder cancers, but rarely on Tregs in peripheral blood. This tumor specific expression of CCR8 provides us with an opportunity to develop an immunotherapy targeting TIL-Tregs selectively.

Methods
HBM1022 is a novel Fc-optimized CCR8 antibody with a high affinity to both human and cynomolgus monkey CCR8. It acts through dual mechanisms of action (MOA). HBM1022 recognizes patient-derived TIL-Tregs, and potently depletes CCR8+Treg cells via enhanced antibody-dependent cellular cytotoxicity (eADCC) activity. Furthermore, it inhibits CCL1-CCR8 signaling pathway and blocks CCL1 induced cell migration. HBM1022 exhibits a potent antitumor activity as monotherapy and in combination with anti-PD (L)1 antibodies. HBM1022 has favorable pharmacokinetic properties and an excellent safety profile in cynomolgus monkey, which suggests a potential good safety profile in human.

Results

Conclusions HBM1022 is a novel Fc-optimized CCR8 antibody with a high affinity to both human and cynomolgus monkey CCR8. It acts through dual mechanisms of action (MOA). HBM1022 recognizes patient-derived TIL-Tregs, and potently depletes CCR8+Treg cells via enhanced antibody-dependent cellular cytotoxicity (eADCC) activity. Furthermore, it inhibits CCL1-CCR8 signaling pathway and blocks CCL1 induced cell migration. HBM1022 exhibits a potent antitumor activity as monotherapy and in combination with anti-PD (L)1 antibodies. HBM1022 has favorable pharmacokinetic properties and an excellent safety profile in cynomolgus monkey, which suggests a potential good safety profile in human.