HBM1020 IS A FULLY HUMAN NOVEL ANTI-B7H7 ANTIBODY WITH EXCELLENT PRECLINICAL EFFICACY AND SAFETY PROFILE

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Background Immunotherapeutic targeting immune checkpoints such as programmed death-1 receptor (PD-1)/PD1 ligand (PD-L1) and cytotoxic T-lymphocyte antigen-4 (CTLA4) offer effective treatment alternatives to traditional cancer therapies. However, a considerable proportion of patients remains unresponsive to treatment indicating that a more complex immune inhibitory tumor microenvironment is involved. B7H7 is a novel B7 family member and reported to be highly expressed on a variety of human cancers such as colon, kidney, bladder, lung cancers; and is associated with metastatic disease and poor survival. B7H7 can inhibit T cell and NK cell activation and its co-inhibitory function makes it a new checkpoint and candidate for cancer immunotherapy other than PD-L1 or other immune checkpoints.

Methods Fully human Anti-B7H7 antibodies were generated from H2L2 Harbour Mice® transgenic platform. The binding and blocking activities were tested by fluorescence-activated cell sorting (FACS) method. In vitro function of the antibodies was tested for their abilities to activate T cell and NK cell. In vivo efficacy was tested on multiple NOD-PrkdcscidIl2rgm26Cd22/NjuCrl (NCG) mouse models engrafted human PBMC tumor. The dose range-finding (DRF) tox study was evaluated on a non-human primates (NHP) 4-week repeat-dose toxicity study.

Results HBM1020, a fully human anti-B7H7 antibody, bound specifically to cell lines that over-express either human B7H7 or cynomolgus monkey B7H7, as well as human tumor cell lines that express endogenous B7H7, with high selectivity against other B7 family members. HBM1020 blocked the interaction between B7H7 and its receptors and potently promoted T cell activation and NK cell cytotoxicity in vitro. Furthermore, HBM1020 showed potent anti-tumor activity in multiple murine tumor models. In DRF 4-week repeat-dose NHP toxicity study (20, 60, 147 mg/kg), HBM1020 was well tolerated up to 147 mg/kg dosed weekly (total 5 doses) with no notable test article-related adverse finding but increased anti-KLH IgG and IgM after KLH immunization at ≥ 60 mg/kg.

Conclusions HBM1020 is a fully human novel anti-B7H7 antibody with potent activity on T cell activation, NK cell cytotoxicity, excellent in vivo anti-tumor efficacy, and excellent safety profile. HBM1020 may present a promising novel anti-tumor agent as monotherapy and/or combination therapy with currently established immune-oncology agents.

Ethics Approval The anti-tumor efficacy studies in mice were approved by the internal ethics board of the respective contract research organization (CRO). The dose-range finding toxicity studies in non-human primates were approved by Ethics Board of an appropriate contract research organizations (CROs).