783TiP Phase I study of HFB301001, a novel OX40 agonist monoclonal antibody, in patients with solid tumors selected via Drug Intelligence Science (DIS)

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Background: OX40 agonist antibodies have shown promising preclinical activity but limited clinical success thus far, likely owing to a suboptimal pharmacological profile, inappropriate dosing regimen, and lack of a biomarker strategy for patient selection. HFB301001 is a novel human IgG1 agonist antibody that binds to a unique epitope on OX40 allowing for agonistic activity without competing with the endogenous OX40 ligand, inducing minimal OX40 downregulation upon co-stimulation of T cells. Also, HFB301001 can both enhance effector T cells and deplete regulatory T cells. It demonstrated more potent *in vivo* anti-tumor activity than a benchmark OX40 agonist, suggesting potentially superior patient benefit compared to first generation OX40 antibodies.

Trial design: HFB301001 is being evaluated in a first-in-human, open-label, multicenter, dose escalation and expansion study in adult patients with advanced solid tumors. It is hypothesized that high levels of OX40 expression associated with effector T cells or T regulatory cells in solid tumors may represent a tumor microenvironment more sensitive to OX40 agonism. Based on this, the following cancer indications have been prioritized using DIS (Drug Intelligence Science is a HiFiBiO Inc. trademark): soft tissue sarcoma (STS), uterine carcinosarcoma (UCS), renal cell carcinoma (RCC), head and neck squamous cell carcinoma (HNSCC), and hepatocellular carcinoma (HCC). The dose escalation portion of the study explores increasing doses in four cohorts of up to six patients, utilizing an mTPI-2 design to determine recommended dose(s) for expansion (RDE(s)). Once the RDE(s) is determined, expansion of up to 5 cohorts is planned to determine the recommended phase 2 dose (RP2D). The primary objective is to characterize safety and tolerability of HFB301001, and to determine RDE(s) and RP2D. Secondary objectives include pharmacokinetic parameters, preliminary evidence of anti-tumor efficacy, and pharmacodynamic evaluation in blood and tumor. Furthermore, a potential predictive biomarker signature derived based on the DIS™ single-cell immune profiling platform will be investigated.

Clinical trial identification: NCT05229601.

Legal entity responsible for the study: HiFiBiO Inc.

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Disclosure: A. Spira: Financial Interests, Personal, Consulting or Advisory Role: Incyte, Mirati Therapeutics, Gritstone Oncology, Jazz Pharmaceuticals, Janssen Research & Development, Mersana, Gritstone Bio, Daiichi Sankyo/AstraZeneca, Array Biopharma, Blueprint Medicines; Financial Interests, Personal, Consulting or Advisory Role / Honoraria: Amgen, Novartis, Takeda, AstraZeneca/MedImmune, Merck, Bristol Myers Squibb; Financial Interests, Personal, Honoraria: CytomX Therapeutics, Janssen Oncology, Bayer; Financial Interests, Institutional, Officer, CEO: NEXT Oncology Virginia; Financial Interests, Personal, Stocks/Shares: Eli Lilly; Financial Interests, Institutional, Invited Speaker: LAM Therapeutics, Roche, AstraZeneca, Boehringer Ingelheim, Astellas Pharma, MedImmune, Novartis, Newlink Genetics, Incyte, AbbVie, Ignyta, Trovagene, Takeda, Macrogenics, CytomX Therapeutics, Astex Pharmaceuticals, Bristol Myers Squibb, Loxo, Arch Therapeutics, Gritstone, Plexxikon, Amgen, Daiichi Sankyo, ADCT, Janssen Oncology, Mirati Therapeutics, Rubius, Synthekine, Mersana, Blueprint Medicines. 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