Phase I study of HFB200301, a First-in-Class TNFR2 agonist monoclonal antibody in patients with solid tumors selected via Drug Intelligent Science (DIS™)

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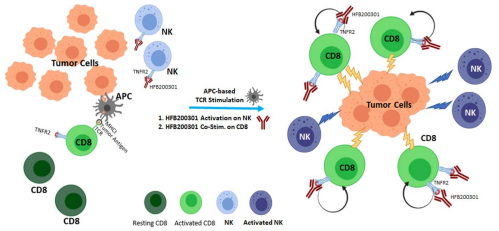
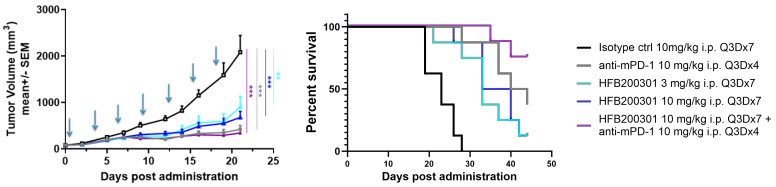
Therapeutic Hypothesis



HFB200301 stimulates TNFR2 on tumor infiltrating T and NK cells to activate NK cells and enhance CD8+ T cell mediated anti-tumor response.[1]

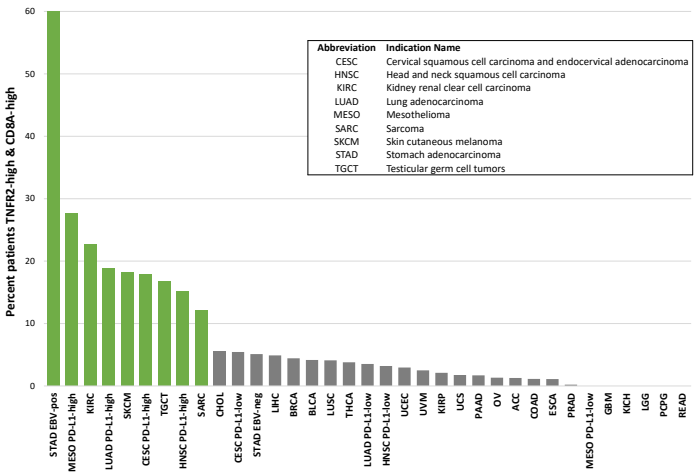


HFB200301 treatment (3 and 10 mg/kg, q3dx7) of MC38 bearing TNFR2 KI mice results in dose dependent antitumor activity (stasis) and improved survival compared to anti-PD-1 alone.[2]

HFB200301

- Humanized IgG1 mAb with sub-nM affinity for human TNFR2 with cyno cross-reactivity.
- Enhanced activation and proliferation of conventional CD4+ and CD8+ effector T cells and robust activation of NK cells in vitro and in the tumor microenvironment.
- Single agent anti-tumor activity comparable to anti-PD-1 in syngeneic tumor models and prolonged survival in combination with anti-PD-1 compared to anti-PD-1 alone.
- Acceptable safety profile in GLP toxicological studies; favorable developability and pharmacokinetic (PK) profiles.

DIS™ Selected Indications



Abbreviation	Indication Name
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma
HNSC	Head and neck squamous cell carcinoma
KIRC	Kidney renal clear cell carcinoma
LUAD	Lung adenocarcinoma
MESO	Mesothelioma
SARC	Sarcoma
SKCM	Skin cutaneous melanoma
STAD	Stomach adenocarcinoma
TGCT	Testicular germ cell tumors

Rationale for indication selection based on DIS™

- Single-cell immune-profiling platform used to identify unique tumor-infiltrating T cell signatures
- Focused on cytotoxic T lymphocytes as major component for HFB200301 activity using TNFR2-high and CD8A-high expression signature on The Cancer Genome Atlas dataset.
- Preclinical biomarker signatures identified based on single cell analyses of ex vivo models[3] will be validated from single-cell data from the Phase I study.

Study Design

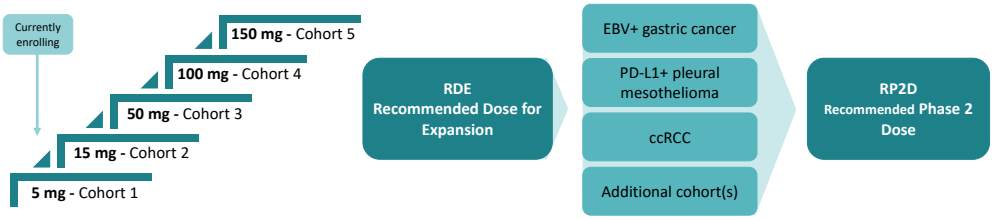
First-in-human, multicenter, open-label, dose escalation and dose expansion study

Dose Escalation

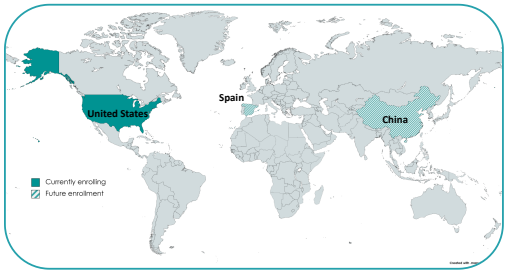
- Using modified Toxicity Probability Interval 2 (mTPI-2) design[4] with target dose-limiting toxicity (DLT) rate of 30%.
- Dosing initiated at 5 mg with provisional dose levels of 15, 50, 100, and 150 mg.
- At least 3 patients (up to 6) must be enrolled for dose escalation to occur. Back-filling cohorts is permitted.
- HFB200301 is administered as a 60-minute IV infusion every 4 weeks.
- DLT period is the first 28 days after cycle 1 day 1 treatment.

Dose Expansion

- Expansions of up to 3 cohorts with up to 20 patients each.
  - EBV+ gastric cancer, PD-L1+ pleural mesothelioma, and clear cell renal cell carcinoma (ccRCC)
- Pending emerging data, additional cohorts may be initiated for patients with soft tissue sarcoma (STS), testicular germ cell tumors (TGCT), cutaneous melanoma, and PD-L1+ cancers including cervical cancer, lung adenocarcinoma, and head and neck squamous cell carcinoma (HNSCC).



Enrollment



Enrollment opened	February 2022
Planned # US sites	7
Planned # Spain sites	3
Planned # China sites	5
Planned # patients – Escalation	30-60
Planned # patients – Expansion	60-180

Key Eligibility Criteria

- Male/female adult patients with histologically documented and advanced or metastatic solid tumors. Permitted tumor types:

EBV+ gastric cancer	***PD-L1+ cancers***
ccRCC	**Cervical cancer**
Cutaneous melanoma	**Pleural mesothelioma**
STS	**Lung adenocarcinoma**
TGCT	**HNSCC**

- Patient must have exhausted standard lines of systemic therapy.*
- Patient must be willing to undergo pre-treatment and on-treatment biopsies.
- Patient must have measurable disease based on RECIST 1.1 (or mRECIST for mesothelioma).
- Patient cannot have hemoglobin <9.0 g/dL or equivalent.
- Patient cannot be using sensitive substrates of major cytochrome P450 enzymes.

*Other protocol defined inclusion criteria may apply.

Key Objectives

Primary

- Dose escalation:
  - Characterize safety and tolerability of single agent HFB200301
  - Determine RDE(s)
- Dose expansion:
  - Determine RP2D

Secondary

- Assess the PK profile and pharmacodynamic effects of HFB200301 in the blood and tumor
- Evaluate immunogenicity
- Determine biologically active dose(s) and anti-tumor efficacy of HFB200301

Exploratory

- Assess relationship between PK, baseline and on treatment biomarkers, and/or anti-tumor efficacy
- Immune modulation

References

1. Wei et al. AACR 2021; Poster #1883
2. Wei et al. AACR 2020; Poster #2282
3. Lee et al. AACR 2022; Poster #4732
4. Guo et al. *Contemp Clin Trials*. 2017;58:23-33

Acknowledgments

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Contact Information

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