HFB301001, a novel OX40 agonist antibody with a unique pharmacological profile and innovative biomarker strategy

Andreas Raue1, Yun-Yueh Lu1, Duyang Li1, Minmin Lu1, Joyce Pi1, Jia Wu1, Mingfang Feng1, Qian Zhang1, Ross Fulton1, Matthieu Delince1, Juliana Crivello1, Zachary Duda1, Alexandra Staskus1, Charina Ortega1, Surendar Arumugam1, Yuan Wang1, Ruina Jin1, Hongkai Zhang1, Pascaline Mary1, Nicole Belmontinelli1, Francisco Adrián1, Lian Schweizer1

Institut National de la Santé et de la Recherche Médicale, Service Universitaire de Cancérologie, Hôpital Saint-Louis, Paris, France.

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HIGHLIGHTS

- A novel OX40 agonist antibody with unique pharmacological profile and biomarker strategy.
- HFB301001 binds to a unique epitope on OX40 and does not interfere with OX40L, unlike benchmarks.
- HFB301001 does not lead to receptor downregulation, unlike benchmarks.
- Blocking OX40L and OX40 simultaneously increases anti-tumor activity.

RESULTS

- HFB301001 binds to a unique epitope on OX40.
- HFB301001 leads to increased survival in MC38 tumor model compared to benchmark.

SUMMARY

- HFB301001 demonstrates enhanced agonistic activity in vitro and in vivo.
- HFB301001 shows promising clinical activity in a phase I study.
- The biomarker strategy allows for the discovery of predictive response biomarkers.

LIMITATIONS OF PREVIOUS OX40 ANTIBODIES

- 1) Pharmacological profile did not optimally leverage the target for activity.
- 2) Toxicity and immunogenicity issues.

METHODS

- Full human IgG with low immunogenicity.
- T cells.
- T cells stimulated.
- Advanced cell cultures.

- Pharmacological profile addresses limitations of first-generation OX40 antibodies:
  - High affinity binding epitope not overlapping with those of other OX40 antibodies.
  - Interference with endogenous signaling and potency of OX40 agonists.
- Produces optimal receptor agonism and therapeutic benefit at target engage.

- Provides tumor biomarker strategy enabling single cell technology to identify responding patients.

- Detects specific T cell subsets and cell-type interactions associated with efficacy of HFB301001.

- Provides hypotheses for biomarker strategy in clinical trials to enrich for responding patients.

- P-0.0181

- Benchmark 1

- Benchmark 2

- Benchmark 3

- Benchmark 4

- Cell activation

- T cell proliferation

- APC

- OX40

- OX40L

- Anti OX40

- T cell activation

- T cell proliferation

- APC

- OX40

- OX40L

- Anti OX40

- CD4+ T cells after antibody treatment

- Ox40 modulation CD4+ T cells after antibody treatment

- Concentration of Ligand (nM)

- Concentration of Antibody (nM)

- Reporter activity of OX40L

- Concentration of Ligand (nM)

- Reporter activity of antibodies in the presence of OX40L at 10nM

- Additional data

- HFB301001 demonstrated decreased agonistic activity using a reporter cell assay or peripheral human T cells.

- Benchmark 1

- Benchmark 2

- Benchmark 3

- Benchmark 4

- Anti-tumor activity in MC38 tumor model in hOX40 K/I mice

- Days post randomization

- Percent of survival

- Data from preclinical assays of OX40L (10nM) and OX40 antibodies (1000 nM) in the presence of OX40L at 10nM. Treatment time points are indicated by bars, and legend is below. OX40L + Benchmark 1: 50% decreased cell viability compared with OX40L alone (p < 0.05) and OX40L + Benchmark 3: 30% decreased cell viability compared with OX40L alone (p < 0.05). OX40L + HFB301001 at 1 mg/kg: 80% decreased cell viability compared with OX40L alone (p < 0.05). OX40L + HFB301001 at 10 mg/kg: 100% decreased cell viability compared with OX40L alone (p < 0.05).

- Percent 

- OX40 positive cells

- Benchmark 1

- Benchmark 4

- Benchmark 3

- Benchmark 2

- HFB301001

- Isotype control (IgG1)

- Anti-OX40 activity in MC38 tumor model in hOX40 K/I mice

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