Huaota Biopharma

A member of Huahai Pharmaceutical Group

March 2022

Profile

Huaota Biopharma is a clinical stage biotechnology company with a focus on discovery, development and commercialization of biologic cancer and autoimmune therapeutics.

Founded in 2013 with a vision of OTA, Open-To-All innovations and technologies, our mission is to create low-cost and high-quality medicines for improving patients' lives worldwide.

The parent company Huahai Pharmaceutical is one of the leading API and generic drug manufacturers in China, with a well-established sales network, supplying high quality products in more than 65 countries.

Executive Summary

- The company has the headquarter in Shanghai with operation space of 150,000 sf and state-of-the-art R&D facilities.
- The management team has global expertise in discovery and development of biologics in multiple therapeutical areas, and currently manages a team of 200+ scientists and engineers in several functions: Discovery, CMC/Quality, Clinical Development / Regulatory Affairs and Partnership.
- A strong pipeline of NMEs has been generated with IP positions in global markets, several of which are cleared INDs/CTAs in US, Australia, New Zealand, China and in clinical development, specifically second-generation Immune Oncology and anti-autoimmune therapies. **We are seeking partners to co-develop these programs in markets in and outside of China.**
- A manufacturing powerhouse of 200,000 L DS and 500 million doses of DP capacity is planned and being built in HangZhou. **We welcome opportunities to make and/or sell partners' products in China or regional markets through licensing and CDMO models.**

Management Team

CEO, Dr. Xiangyang Zhu, former executive with Boehringer Ingelheim in biologics discovery and CMC, inventor and team leader of the blockbuster drug Skyrizi. PhD in Microbiology and Immunology from The University of Illinois at Chicago. A former physician and entrepreneur.

CBO, Dr. Jason Lu, former executive of Business Development and Licensing, and marketing with MSD, PhD in Molecular Genetics and Biochemistry from Rutgers University, a former pediatric hematologist and a drug discovery scientist at Schering-Plough.

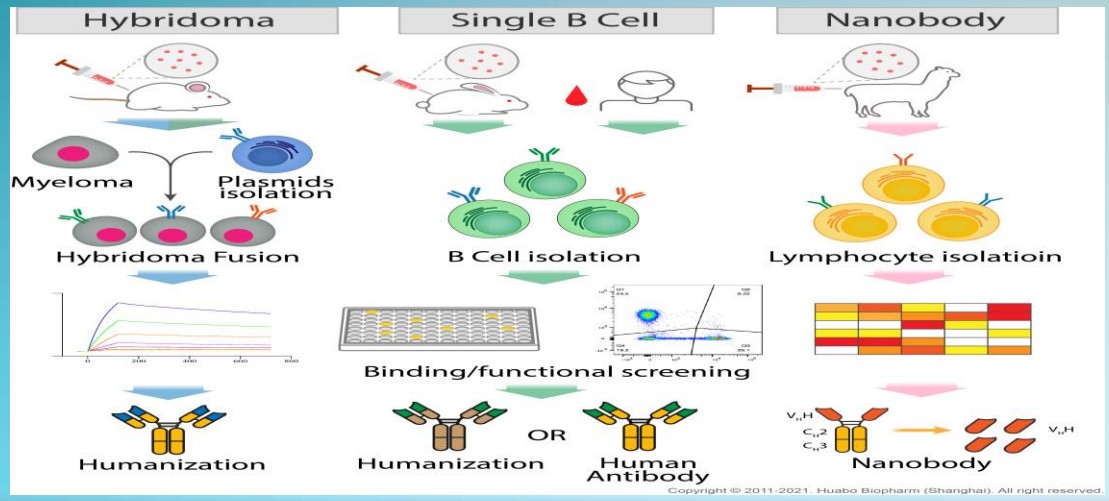
VP, Discovery & Pre-clinical Development, Dr. Yifan Zhan, former Senior Scientist and Immunologist in Walter and Eliza Hall Institute of Medical Research, Australia, with 100+ publications on Immunology. PhD in Immunology from The University of Melbourne.

VP, Quality, Dr. Qian Chen, former CMC and quality executive in analytics and compliance with Boehringer Ingelheim and Johnson and Johnson, PhD from The Pennsylvania State University.

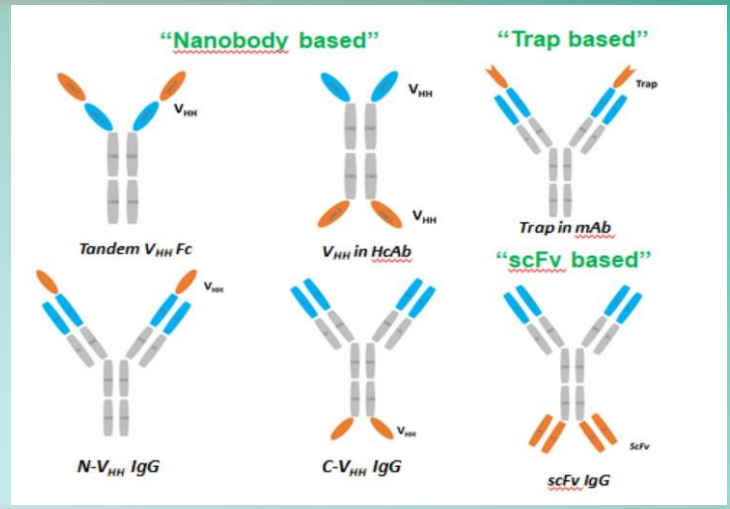
VP, Clinical Development, Dr. Yongmin Yang, former executive leading Ph I-IV clinical development and bioanalytical and pharmacokinetics studies with Covance and WuXi AppTec. PhD in Microbiology and Immunology from the Chinese Academy of Preventive Medicine now CDC.

Technology Platforms - multi-modality

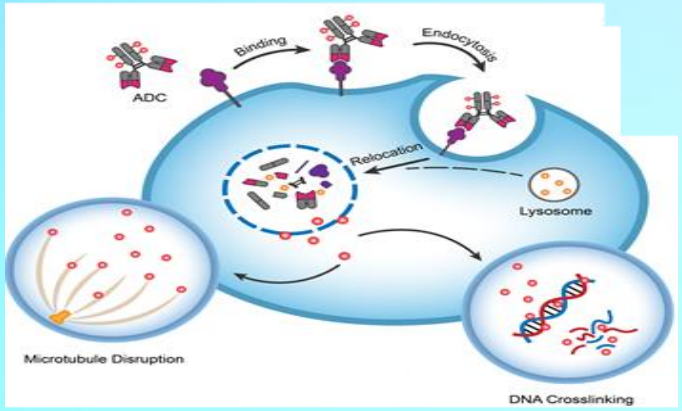
Antibody Drug Discovery



Synerbody: ab based multi-binder



Antibody Drug Conjugate



Pilot-Commercial DS & DP Production

Discovery - Novel MOAs & Combinations

Platform & Biosimilar → **Prolific & Innovative** → **High-Value & Diverse**

Before 2016

Platforms

Teams

Quality

HB002.1 (anti-VEGF)

2 biosimilars:

HOT-3010 (Humira)

HOT-1010 (Avastin)

2016-2020

Novel molecules

High potency

Differentiated

IL-17

CD137

PD-L1

TIGIT

LAG3

2021-2025

More TAs , MOAs

Multiple Modalities

Combinations

PD-L1/VEGF

PD-L1/TGF β

IL-36R

PD-L1/TIGIT

IL17/IL36R

CD73-ADC

CD73/CD39

CD73 x 2

CD96/PD-L1/TIGIT

IL-4R

Clinical Development - 3 Operation Models for Value

✓ 40 + staff + CROs

✓ 19 studies, 4 CSRs, 15 ongoing
✓ >600 subjects
✓ 3 countries, China, US, NewZealand

NME Model

Positive POC results for Global Partnerships

i.g. HB0017 (IL-17)
first NME demonstrates excellent clinical efficacy and safety profile, and best-in-class commercial potential with its favorable PK profile.

Partnering Model

Combination studies for Enriching Pipeline

i.g. HOT1030 (CD137)
Capability of tech/data transfer and launching clinical development and commercialization plan in licensed territories

Biosimilar Model

Quick MA and Revenue

i.g. HOT-1010 (Avastin)
HOT-3010 (Humira)

Established biosimilar clinical development and commercialization procedure for future portfolio expansion

Flexible Partnership – Expand the Global Market Reach & Pipeline

Strategy:

- Out-license: co-development partnership on Huaota NMEs worldwide.
- Co-discovery partnership: utilizing Huaota technology platforms.
- Out-license: licenses of Huaota biosimilars in regional markets.
- In-license: partners' biologic products for Chinese or regional markets.
- CDMO: Biologics DS & DP process scale-up, optimization and supply.
- Financing: VC or strategic investment in upcoming funding rounds.

Current Partnerships:

OUTLOOK THERAPEUTICS

君实生物 TopAlliance

QUACELL BIOTECHNOLOGY

Eminence 艾米能斯

Eutilex Co., Ltd.

Accelerating Clinical Development on NMEs

2020 - 2021

4 initiated Clinical Trials

1 has positive signals

1. HB0017, IL-17, Ib positive interim POC results
2. HB0025. PD-L1/VEGF, Ia good safety profile
3. HB0030, TIGIT, Ia FPI 2021Q4
4. HB0034, IL-36R, Ia FPI 2021Q4

2022

4 more into Ph I

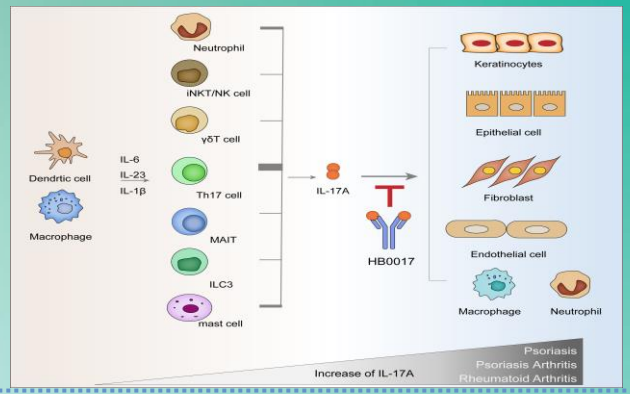
5. HB0036, PD-L1/TIGIT, Ia FPI 2022Q1
6. HB0028, PD-L1/TGFβ, 1a FPI 2022Q2
7. HB0043, IL36R/IL-17, Ia FPI 2022Q4
8. HB0045, CD73X2, 1a FPI 2022Q4

HB0017 – IL-17 blocker

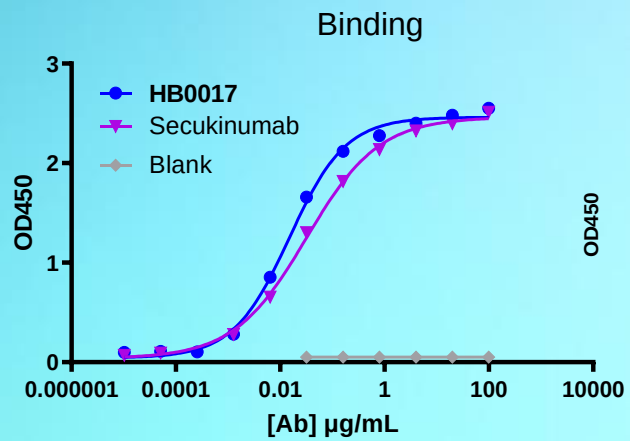
Features and Status

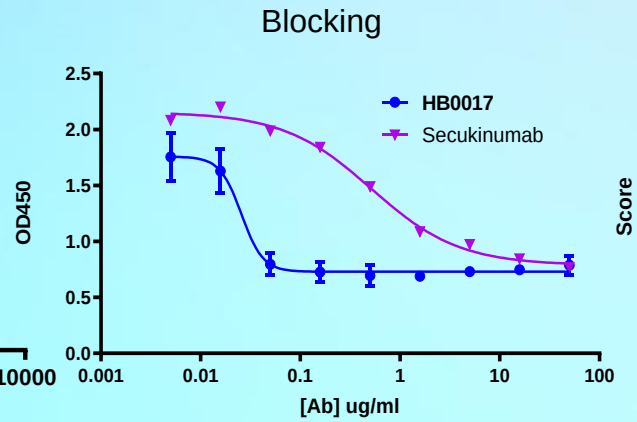
Key Features	➢ Significant efficacy to reduce psoriasis and arthritis in preclinical models. Strong blocking of IL-17A bioactivity ➢ Excellent safety profile: MTD of single dose ≥ 500mg/kg in cynomolgus monkeys; no obvious AE from Phase I study ➢ BLA planned in China and US
Status	Phase Ia competed in New Zealand; phase Ib ongoing in China

MoA

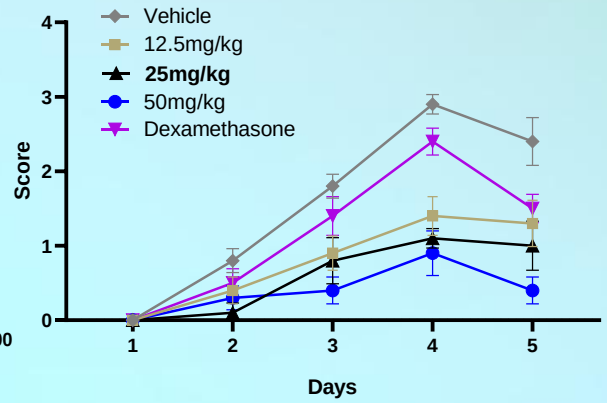


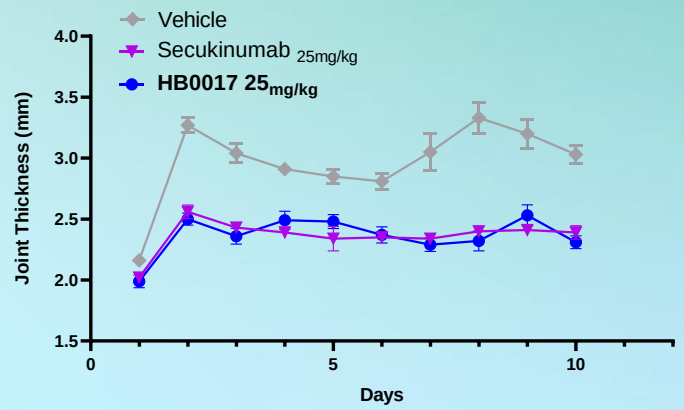
HB0017 strongly blocks IL-17A bioactivity in vitro





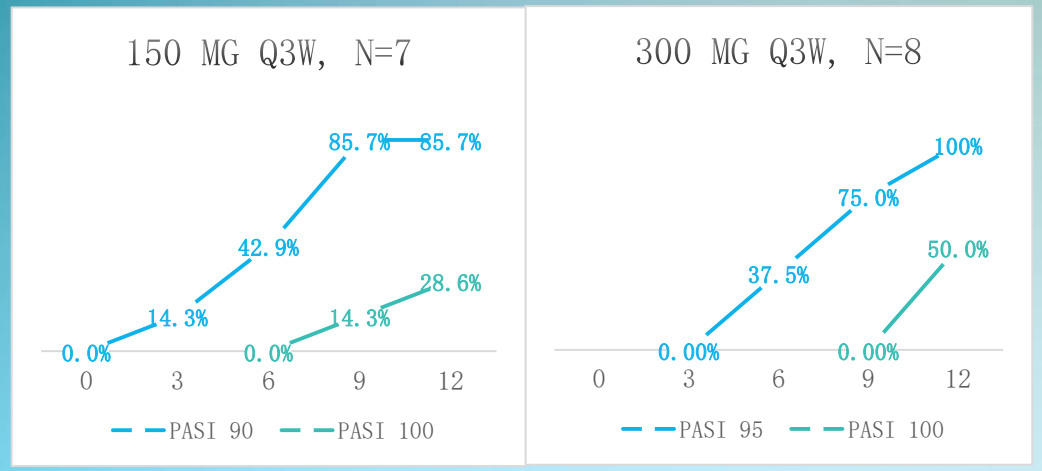
HB0017 significantly blocks psoriasis and arthritis in preclinical models

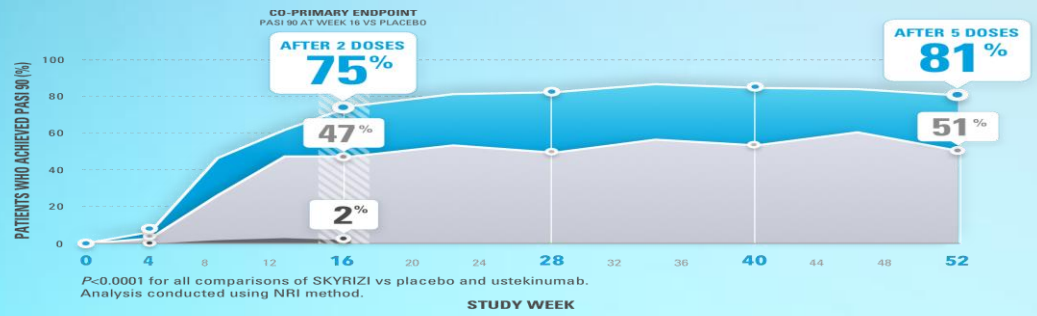


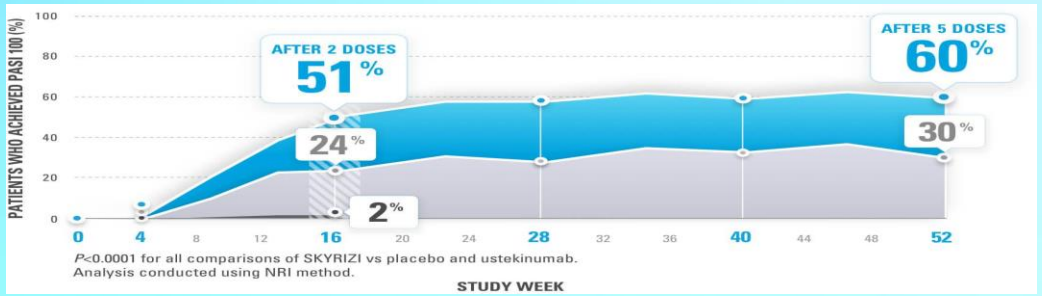


1st POC of Company NMEs: Efficacy Signal in Plaque Psoriasis

300 mg Q3W cohort has faster & stronger responses than SKIRIZI and ustekinumab treatments.

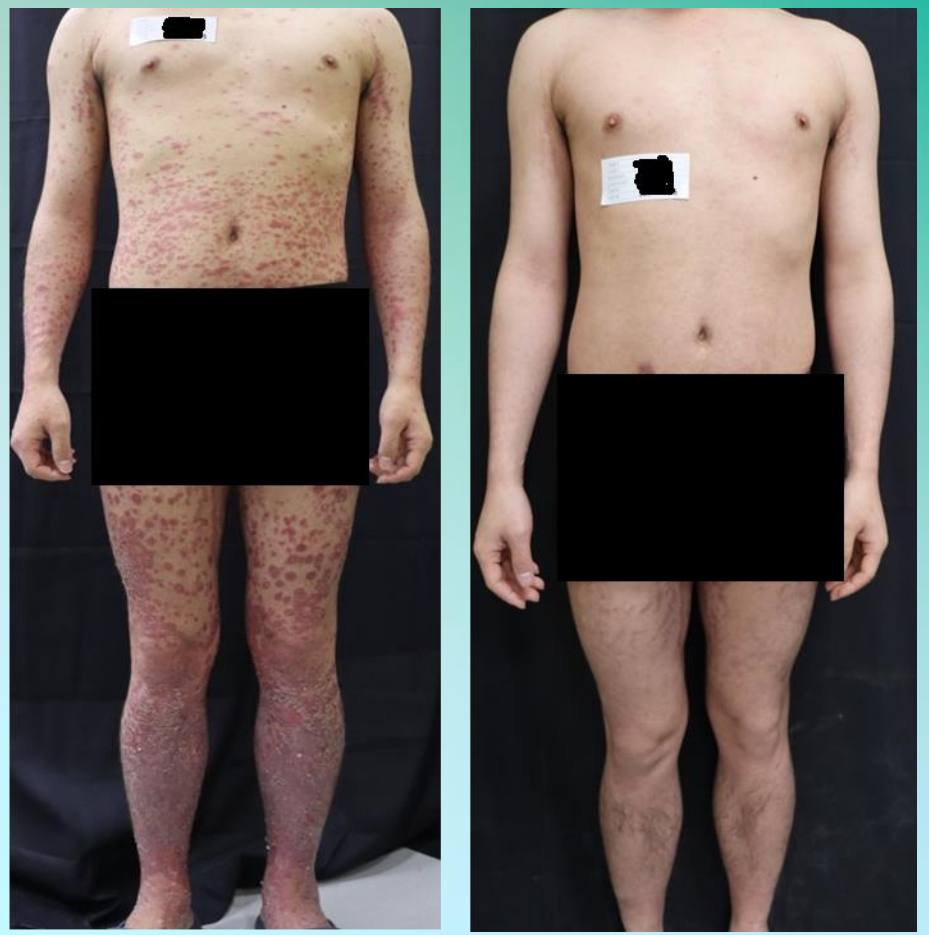






www.skirizihcp.com

A106 in 150 mg cohort at 12 weeks

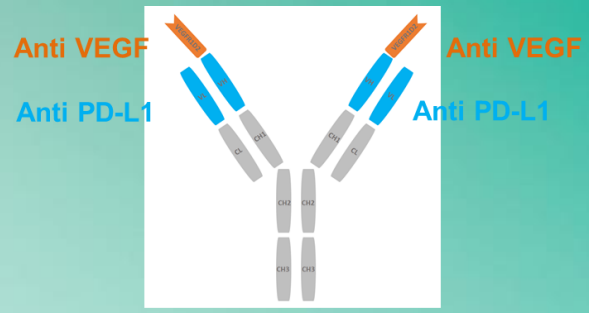


HB0025 – VEGF/PD-L1 BsAb

Features and Status

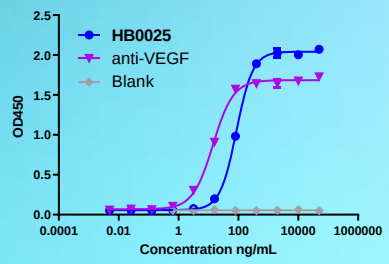
Key Features	➢ Synergistic anti-tumour effects in animal models (1+1>2) ➢ Potential benefits for treatment-refractory patients, as shown by Roche's Tecentriq and Avastin combination for liver cancer ➢ CMC advantages of high expression (one-step purification >98%)
Status	Phase Ia in US and China

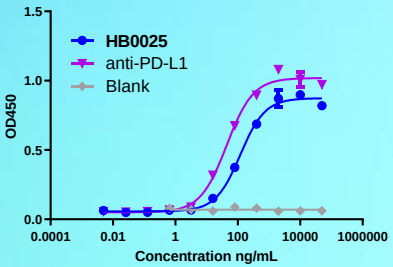
Molecular Structure



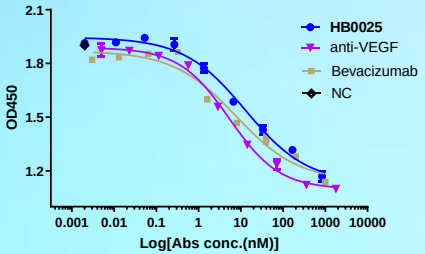
HB0025: Trap in Mab

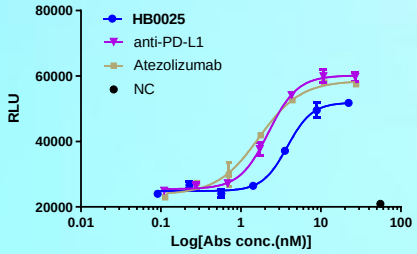
Binding activity



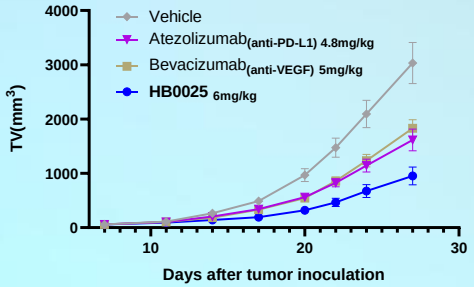


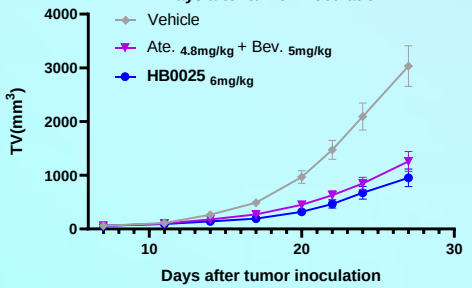
Blocking activity



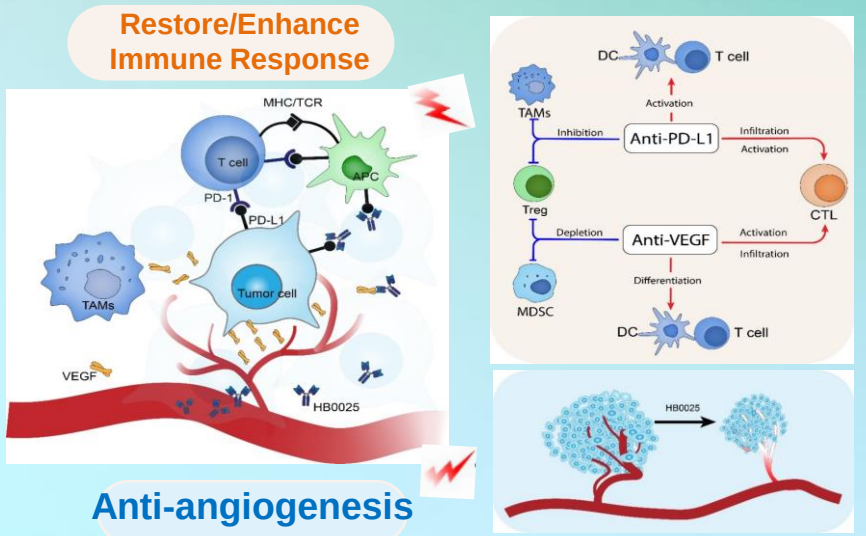


Anti-tumour efficacy





MoA

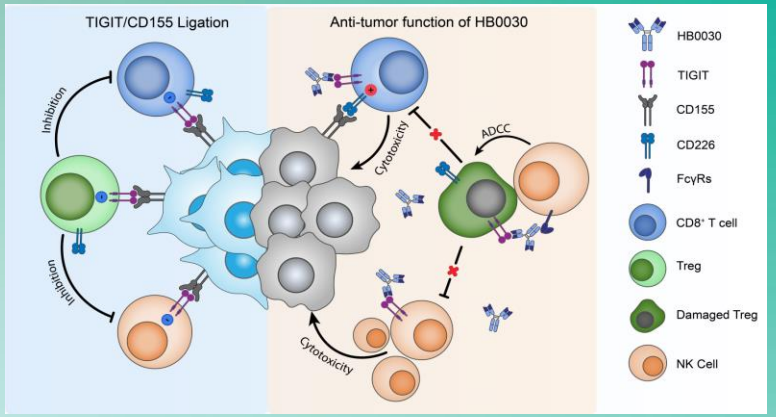


HB0030 – TIGIT mAb

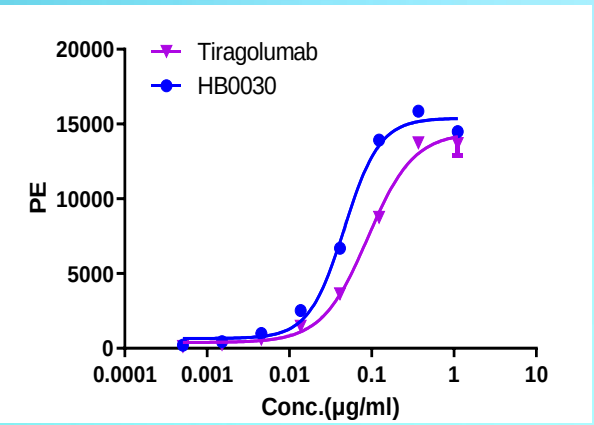
Features and Status

Key Features	➢ HB0030 has high affinity 0.04nM for TIGIT ➢ HB0030 has strong anti-tumor activity and shows synergistic anti-tumor activity with anti-PD1 in preclinical models
Status	Phase Ia ongoing in China,

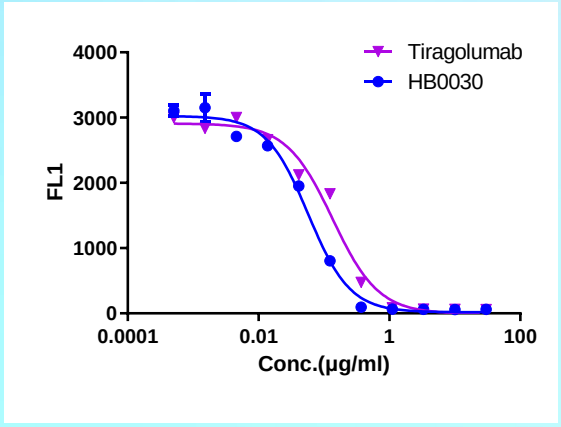
MoA



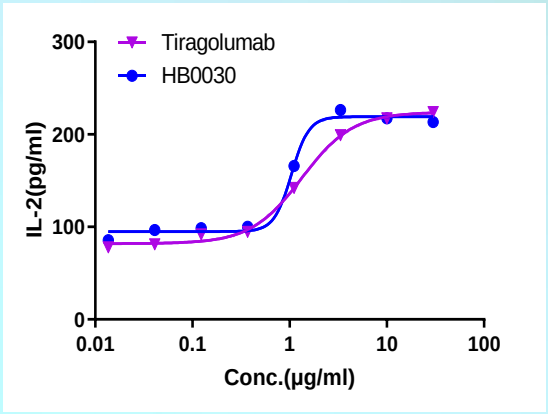
HB0030 binds to membrane TIGIT



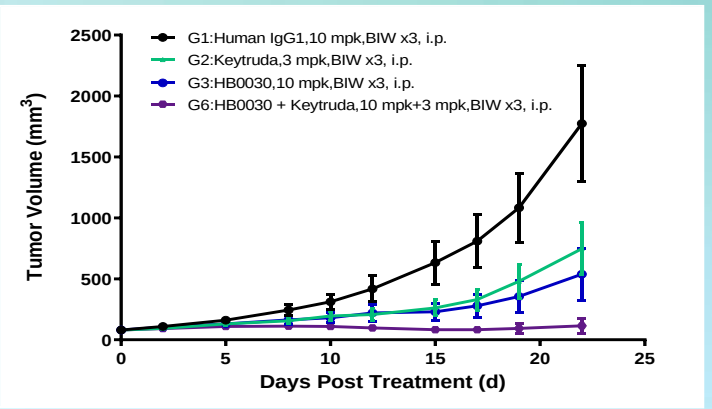
HB0030 competes with CD155



HB0030 restores T cell function



Anti-Tumor Efficacy

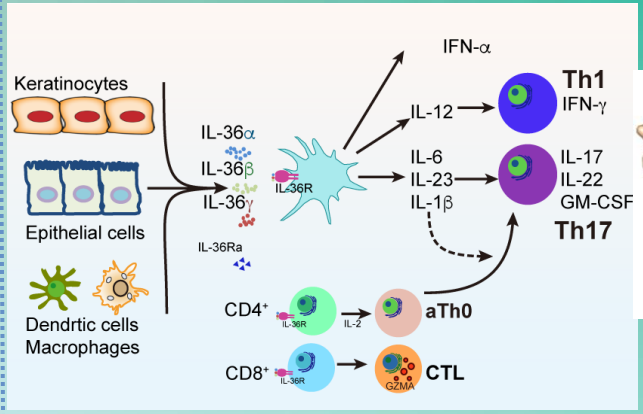


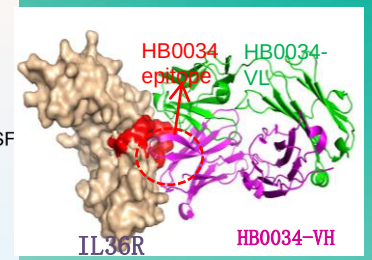
HB0034 – IL-36R mAb

Features and Status

Key Features	➢ IL-36R involves multiple inflammatory pathways, HB0034 blocks all three IL-36 ligands. ➢ First in China ➢ Indications: Pustular Psoriasis, IBD, SLE, Fibrosis
Status	Phase Ia ongoing in New Zealand

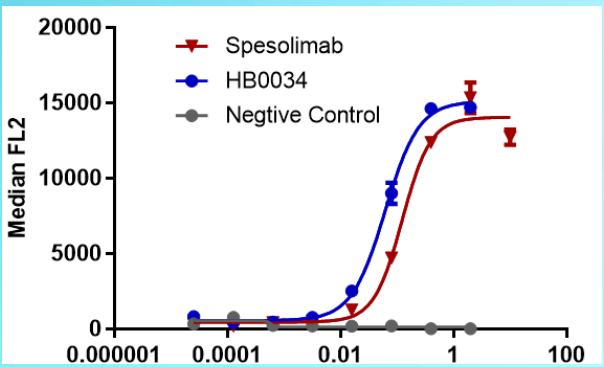
MoA





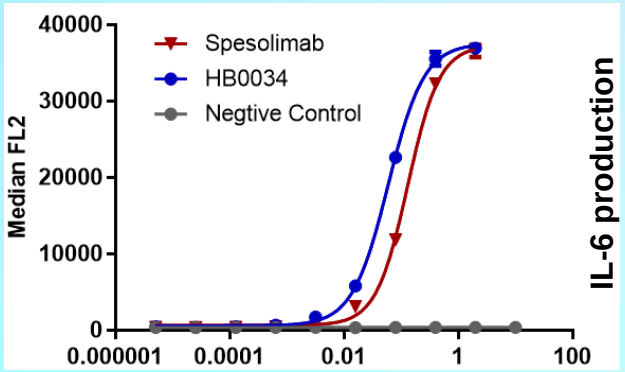
HB0034 binds to IL-36R

Human



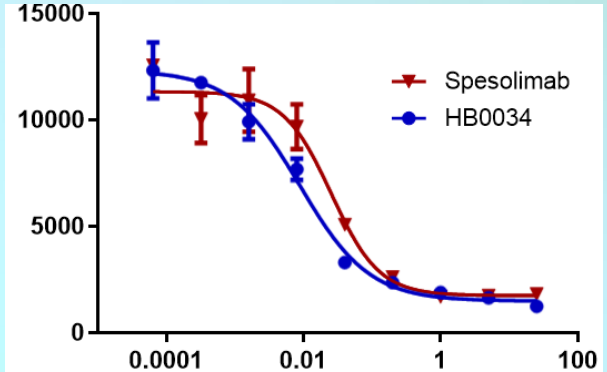
Concentration (μg/mL)

Monkey



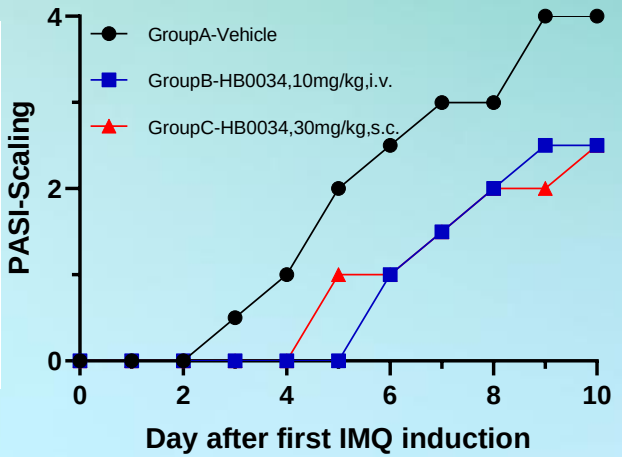
Concentration (μg/mL)

HB0034 blocks IL-6 production



Concentration (μg/mL)

In-vivo (Ps model)

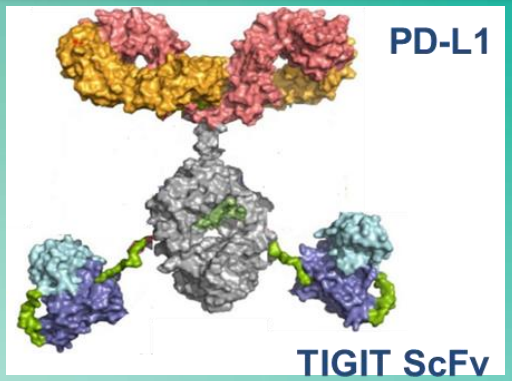


HB0036 – TIGIT/PD-L1 BsAb

Features and Status

Key Features	➢ Significant anti-tumor activity in preclinical models ➢ Potential benefits indicated by the encouraging efficacy of Roche's Tecentriq and Tiragolumab combination for NSCLC ➢ Strong affinity for both target ligands
Status	US IND opened January 17, 2022; PIND in China

Molecular Structure

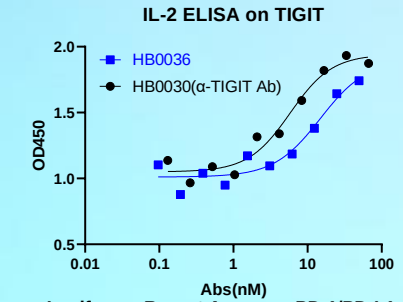


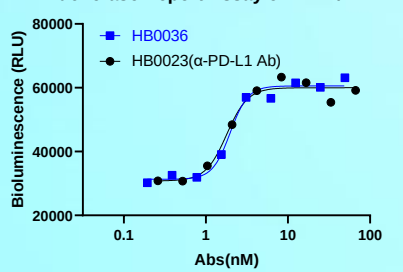
Affinity

Ligand: PD-L1		
Analyte	HB0036	HB0023 (PD-L1 mAb)
KD（M）	2.27E-9	2.77E-9

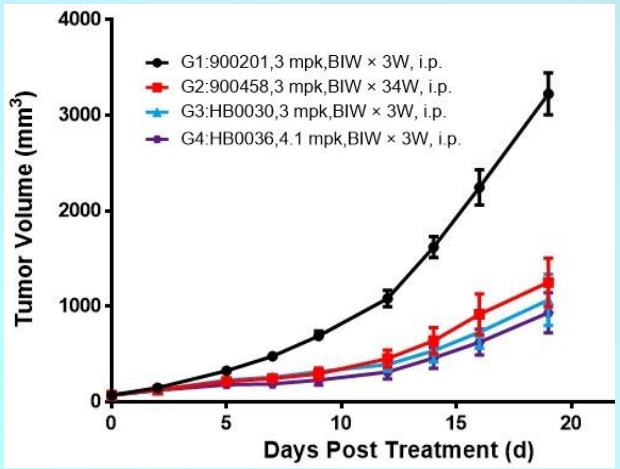
Ligand: TIGIT		
Analyte	HB0036	HB0030 (TIGIT mAb)
KD（M）	8.63E-11	3.45E-11

In-vitro



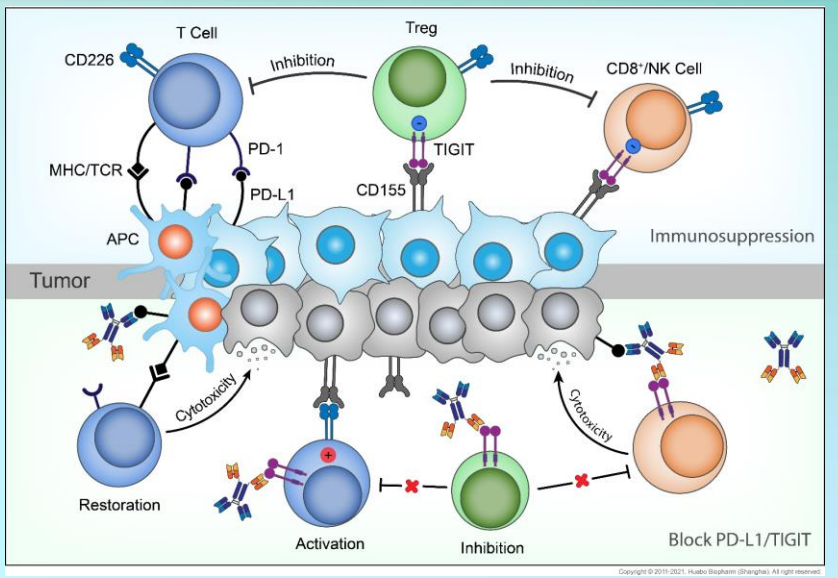


In-vivo



900201:IgG1 control 900458:PD-L1
HB0030:TIGIT

MoA

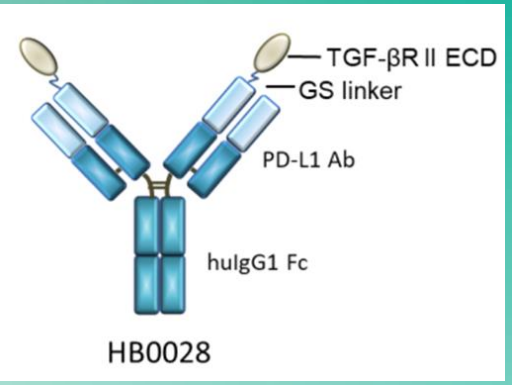


HB0028 – TGF-β/PD-L1 BsAb

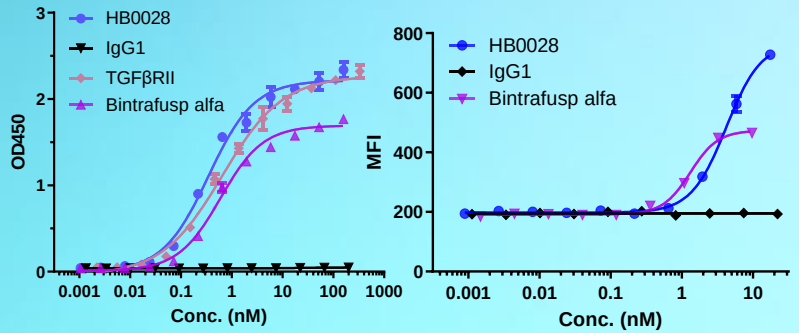
Features and Status

Key Features	➢ Effectively inhibiting TGF-β/SMAD signal pathway, Effectively restoring T cell activation. ➢ Unique design with high stability, High protein yield, Robust CMC. ➢ Strong tumor suppressive effects.
Status	China IND cleared February 18, 2022

Molecular Structure

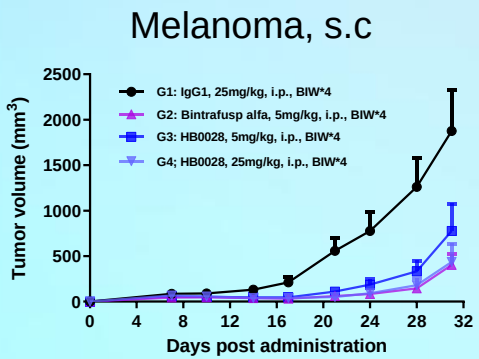


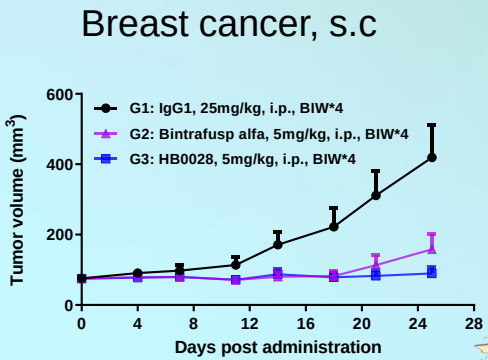
TGF-β binding



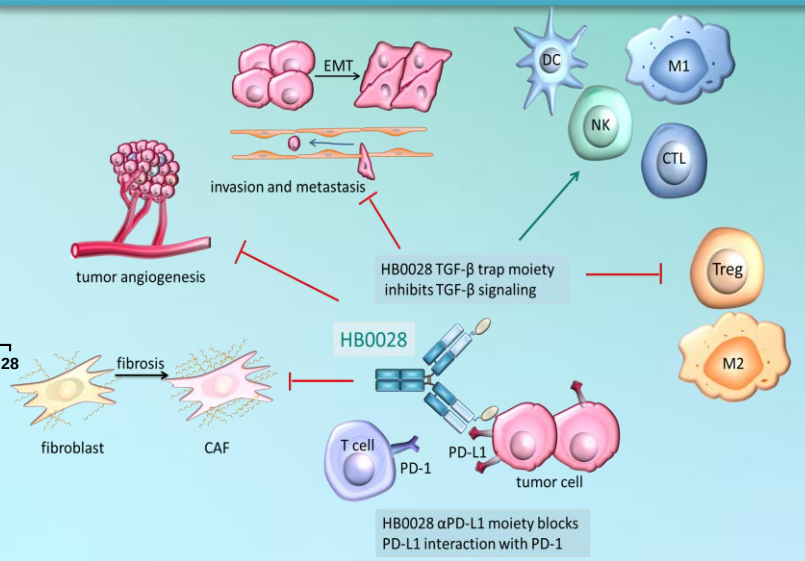
Co-binding PD-L1 and TGF-β

Strong anti-tumor effects





MoA



Partnering to Expand Pipeline and Market Reach

2013
In-license 2 biosimilar Mabs for initiating biologics business

2017
In-license anti-CD137 for investment and pipeline

2019
Out-license HOT-1010 for strategic partnership and income

Expanding Biosimilar Portfolio

2025

2 products on market

Two backbone products for cancer and autoimmune Therapeutic Areas:

1. HOT-1010, Avastin biosimilar, now in Ph III study
2. HOT-3010, Humira biosimilar, now in Ph III study

2030

5 products on market

An expansion strategy for high value and high product efficiency:

1. HOT-2000, target undisclosed
2. HOT-4000, target undisclosed
3. HOT-5000, target undisclosed

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