

2022 Interim Results Conference Call Presentation

HBM HOLDINGS-B, 02142.HK

31 August 2022



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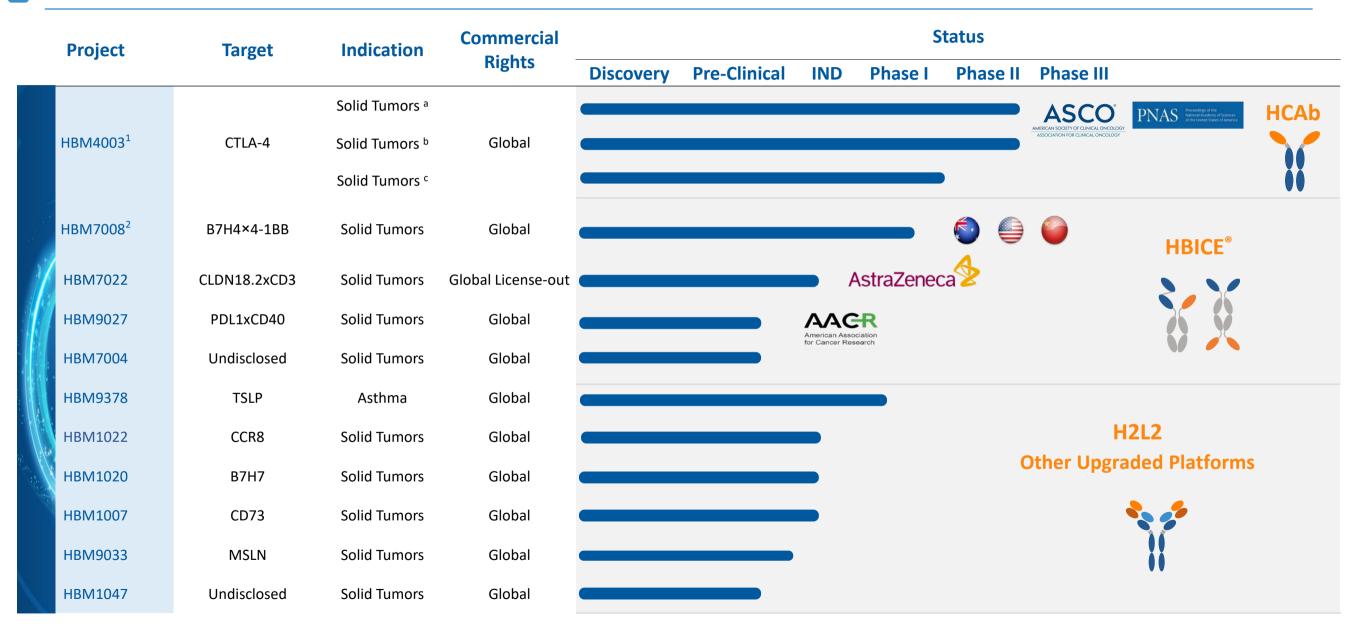
- **O1** Company Overview and Highlights
- **O2** Develop Global Innovative and Differentiated Product Pipeline
- **03** Upgrade Technology Platforms to Explore Novel Frontier
- 04 Product Updates on Regional Market Assets
- 05 Financial Results
- 06 Outlook

Continue Build-Up of Global Innovation Capabilities at Harbour BioMed

Continuously Upgrade Technology Platforms **Innovatively Broaden the Business Rapidly Develop Innovative Models of Global Collaborations Global Programs** for Multiple Modality Applications Global Programs: 16 Product global license-out • H2L2, HCAb, HBICE[®], SBC, HCAb Plus[®], HBIKE 2022 Platform license-out 4 clinical-stage assets • mAb, BsAb, ADC, CAR-T, CAR-NK, mRNA...... Co-discovery/Co-development 3 new IND in 2022 2H Joint venture License-in assets: 2 2 phase III Global Programs: 7 2020 (IPO) Product global license-out • H2L2, HCAb, HBICE®, SBC Platform license-out 1 phase I • mAb, BsAb Co-discovery/Co-development License-in assets: 2 Joint venture 2 phase II MDAnderson Cancer Center WISTAR abbyie Global Programs: 1 • Platform license-out • H2L2, HCAb 1 pre-clinical • mAb Erasmus MC License-in assets: 2 2 pre-clinical



Highly Innovative and Differentiated Global Portfolio Pipeline





^{1.} HBM4003 is a next-gen anti-CTLA-4 antibody with enhanced ADCC for Treg depletion

^{2.} HBM7008 completed Phase I FPFD in Australia in May, US IND clearance and China IND approval in June 2022

a. Melanoma, HCC, RCC and Other Advanced Solid Tumors

b. Melanoma, HCC, NEC/NET and Other Advanced Solid Tumors

c. NSCLC and Other Advanced Solid Tumors

Significant Advancements for Portfolio Product Developments in 2022 1H

3 Clinical Studies Milestones

Data Readout

- HBM4003 mono trial Phase I
- HBM4003 combo trial Phase I

Data Analysis

HBM9036 Phase III
 1st Interim Analysis



4 IND Approvals

- HBM7008 IRB in Australia
- HBM7008 IND in USA
- HBM7008 IND in China
- HBM9378







8 Ongoing Clinical Trials

- HBM4003 combo trial for Melanoma
- HBM4003 combo trial for NEC/NET
- HBM4003 combo trial for HCC
- HBM4003 mono trial
- HBM7008
- HBM9161 MG, TED
- HBM9036 DED

6 Global Publications

- HBM4003 at ASCO
- HBM4003 at PNAS
- HBM9161 MG at Neurology and Therapy
- HBM9036 at International Ophthalmology
- HBM9027 at AACR
- 87G7 at Science Immunology







Science Immunology





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Focus on Next-Gen IO Therapeutics Develop Global Innovative and Differentiated Product Pipeline

Leveraging HBM Antibody Platforms to Synergize Three Distinct Mechanisms ofAction in Immuno-oncology

1. Stimulate Immune Cells

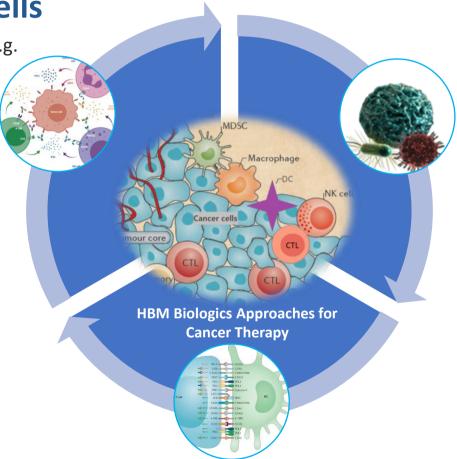
by Immune Cell Engager Bispecific, e.g.

HBICE technology

HBM7022 (CLDN18.2xCD3) HBM7008 (B7H4x4-1BB)

HBM9027 (PD-L1xCD40) HBM7004

ПОІУІ



2. Direct Killing

Deplete Treg cells or Tumor cells by eADCC and next-gen ADC technology

HBM4003 (CTLA4 -eADCC) HBM1022 (CCR8 -eADCC) HBM9033 (MSLN -ADC) HBM1039

• •

3. Overcome Immune Suppression

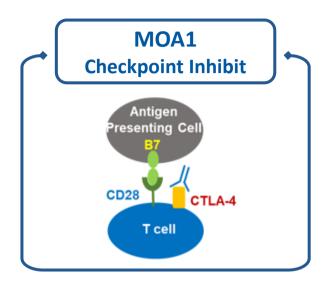
Modulate alternative immune evasion pathways beyond PD1/L1 using H2L2/HCAb/SBC technology

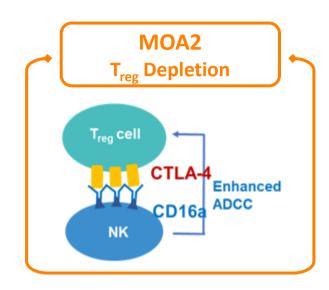
HBM1020 (B7H7) HBM7008 (B7H4x4-1BB) HBM1047 ...



HBM4003

Next-Gen Anti-CTLA-4 Antibody with Potential to be the Mainstream of IO Therapeutics









Deplete intra-tumoral Treg cells via enhanced ADCC strategy



Great safety profile resulted from the reduced drug exposure in the serum



Huge potential for combination therapies



Monotherapy

Phase Ib/II ASCO poster released

Combination Therapy

- Completed phase Ib/IIa Melanoma patient enrollment, phase Ia ASCO abstract released
- Completed first dosing of first patient of phase I trial for HCC







HBM4003

Next-Gen Anti-CTLA-4 Antibody with Potential to be the Mainstream of IO Therapeutics



Mono Therapy Phase I



Combination Therapy Phase I/IIa



Promising efficacy

- 2 patients with **PD-1 refractory HCC** (Australian, China) have been confirmed as **PR**
 - 1 HCC patient, tumor shrank by 64.4% at week 24
 - 1 HCC patient, tumor shrank by **38.3%** at week 12
- Another CRPC patient from Australia had PSA response of more than 50% reduction



Well tolerated

- No fatal TRAE
- Majority of TRAE were G1/2
- ≥G3 TRAE was 9.3% at 0.45mg/kg



Promising efficacy

- 2 of 6 patients in 0.3mg/kg dosing group confirmed as PR
 - 1 PD-1 resistant Mucosal Melanoma patient, tumor shrank by 37.2% at week 18
 - 1 PD-1 resistant Urothelial Carcinoma patient, tumor shrank by 57.4% at week 12
- Encouraging efficacy of melanoma expansion trial was observed in difficult to treat subtype and in both PD-1 naive and PD-1 pretreated populations



Well tolerated

- No G4/5 TRAE
- No new signals or unexpected toxicities in combo therapy



HBM4003

Next-Gen Anti-CTLA-4 Antibody with Potential to be the Mainstream of IO Therapeutics



2022 Scientific Publication

- Binds human CTLA-4 with high affinity reaching 10⁻¹¹ M, as one fully human heavy-chain antibody
- Effectively depletes tumor-resident Treg with enhanced antibody-dependent cellular cytotoxicity (ADCC)
- Potent tumor penetration with small size, thereby more widely exerting its effect on T cell activation
- Less systemic drug exposure in vivo potentially provides an improved therapeutic window in clinical applications



RESEARCH ARTICLE

APPLIED BIOLOGICAL SCIENCES



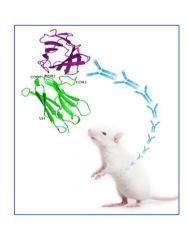


An anti-CTLA-4 heavy chain-only antibody with enhanced T_{reg} depletion shows excellent preclinical efficacy and safety profile

Xin Gan^a, Qianqian Shan^a, He Li^a, Rick Janssens^{a,b}, Yuqiang Shen^a, Yun He^a, Fei Chen^a, Rien van Haperen^{a,b}, Dubravka Drabek^{a,b}, Jin Li^a, Yang Zhang^a, Jiuqiao Zhao^a, Beibei Qin^a, Ming-Jin Jheng^a, Victor Chen^a, Jingsong Wang^a, Yiping Rong^a, and Frank Grosveld^{a,b,1}

Edited by Richard Flavell, Yale University, New Haven, CT; received January 17, 2022; accepted June 13, 2022







Advocated by Global Leading Experts in IO Therapeutics

HBM4003 aims to transform the global IO landscape with breakthrough innovation













Dr. Frank Grosveld

Fellow of Royal Society and Member of Royal Netherlands Academy of Arts and Sciences

Professor and former
Head of Department of
Cell Biology &
Department of Clinical
Genetics at Erasmus
University Medical Center



Venture Partner at Third Rock Ventures

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Specialty: Global Melanoma and Skin Cancer

Dr. Shivaani Kummar

Director, Phase 1 Clinical Research Program, Division of Oncology Stanford School of Medicine

Professor of Medicine & Radiology at Stanford University Medical Centre

Specialty: Sarcoma



HBM7008 (B7H4x4-1BB)

First-in-Class Bispecific Antibody from HBICE® Platform

Global Multi-Center Clinical Trials



Australia: Completed FPFD for Phase I Trial



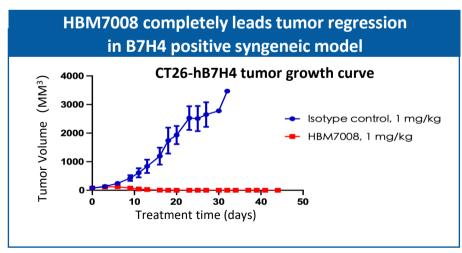
USA: Obtained IND Clearance

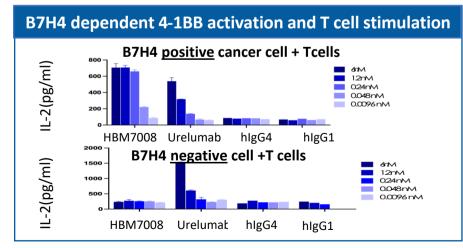


China: Obtained IND Approval

Competitive Advantages and Highlights

- Novel immune escape pathway **First-in-class** target (B7H4x4-1BB)
- ☐ Fully human **bispecific antibody** from the HBICE® platform
- Excellent safety profile, potential to avoid 4-1BB liver toxicity risk with the benefit of its innovative biology mechanisms and bispecific design









HBM9378 (TSLP)

Next-Gen Monoclonal Antibody Therapeutics



Highlights

- ☐ A fully human antibody targeting TSLP, for the treatment of moderate-to-severe asthma
- ☐ IND Approval in 2022 1H
- ☐ FPFD of phase I trial in 2022 2H



Significant Clinical Unmet Needs for Moderate-to-severe Asthma

- 45.7 million adult asthma patients (≥20 years) globally, 1.2 million severe asthma in China¹-¹
- Conventional therapies including ICS, LABA and OCS are not effective for moderate to severe asthma
- 17.8 billion market by 2028, where above 40% of patients will be treated with biologics

HBM9378 Highlights and Competitive Advantages

- Targeted TSLP signal, upstream of asthma T2 inflammation, while current biologics target downstream signals
- Tezepelumab Ph 2 & 3 clinical results showed significant decrease of asthma exacerbation without IgE, eosinophil count or FeNO limitation
- Less immunogenicity risk. The long half-life optimization, outstanding biophysical properties



Source:

- 1. The Global Asthma Network. The Global Asthma Report 2018
- 2. The China Pulmonary Healthy Study Group. Prevalence, risk factors, and management of asthma in China: a national cross-sectional study. Articles 2018.1

HBM7022 (CLDN18.2xCD3)

The First Global Out-licensed Bispecific Antibody Generated by HK-Listed Bio-tech



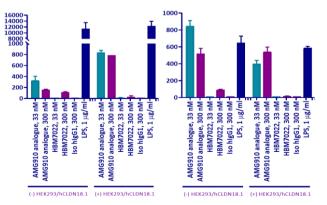
Highlights

☐ 2+1 format with better activity and potential larger therapeutic window

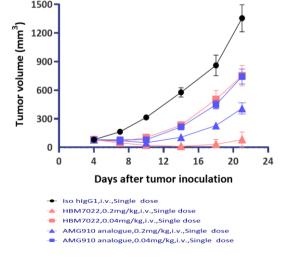


- ☐ Low CD3 and high CLDN18.2 affinity reduce systemic exposure and increase distribution to tumor
- ☐ Silent Fc extends half-life, avoids Fc crosslinking and ADCC

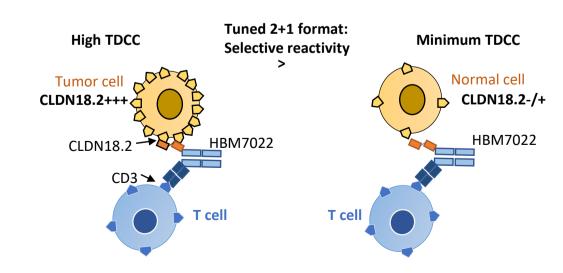
HBM7022 Pre-clinical Data







MOA of HBM7022



HBM9027 (PD-L1xCD40)

Innovative Bispecific Antibody Activating APC/T Cells

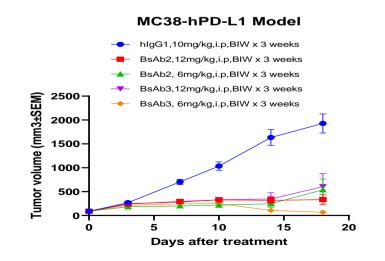


Highlights

- ☐ Synergistically activating both myeloid/DC cells and T cells is critical for some solid tumor therapy considering the most abundant myeloid cell population in TME
- \Box Well maintained αPD-L1 arm and αCD40 arm function activity with robust developability using fully human symmetrical HBICE® format
- ☐ Encouraging in vivo efficacy superior to Tecentriq and safety profile is much better than Selicrelumab

Anti-PD-L1 hVHH Anti-CD40 Fab APCs APCs CD40 Tumor

Strong TGI in hPD-1/hCD40 DKI Mice

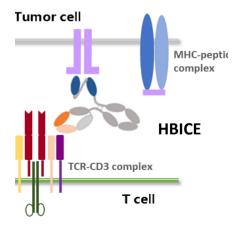


Continue to Advance CD3 Based HBICE® Using Novel TAA and Safer Anti-CD3 Arm Unique 2+1 Asymmetric Bispecific Antibody (TAAxCD3)

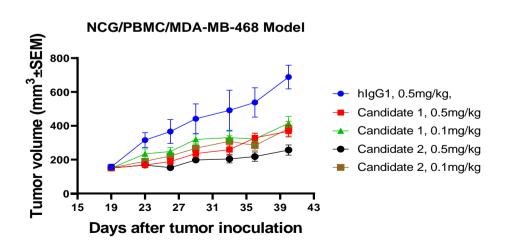


- ☐ HBICE® technology grants asymmetric structure but less light chain mispairings
- ☐ TAA is mainly expressed in low PD-L1 tumors, particularly in gynecological cancers and squamous cell lung cancer
- ☐ Potentially combine with PD1 therapy in acquired resistance or co-expression patients

MOA



NSG Mouse Human PBMC CDX Model





HBM1020 (B7H7)

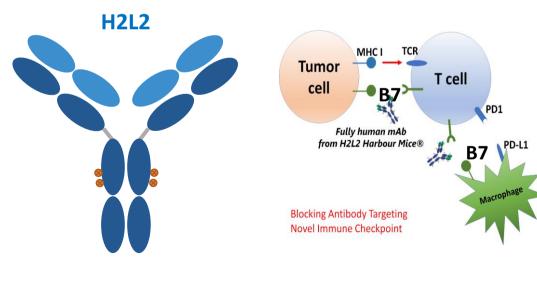
Novel B7 Family Plays an Alternative Immune Escape Mechanism Beyond PD-L1



Highlights

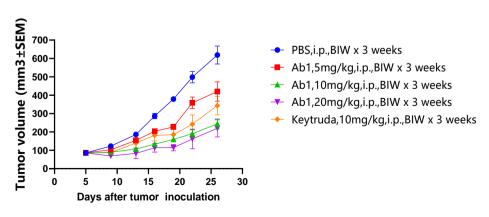
- ☐ B7H7 is a first-in-class target potentially serving as an alternative immune escape pathway
- ☐ Potent receptor blocking, T cell activation activity and excellent in vivo efficacy in humanized tumor models
- ☐ Huge potential to treat PD-L1 negative or anti-PD1/PD-L1 refractory cancer patients

IND 2022



Strong TGI in Breast Cancer Model

Breast Cancer Human PBMC Model





HBM1022 (CCR8)

Next-Gen Treg Depletion Therapeutics Targeting A Novel GPCR Target



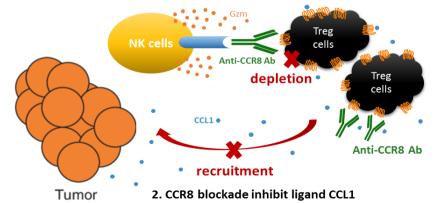
Highlights

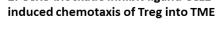
- Potent tumor resident Treg depletion activity
- ☐ Potent inhibition of CCL1-induced signaling pathway / in vivo anti-tumor efficacy
- ☐ Comparable human/cyno binding affinity
- ☐ Significant potential for breast cancer, colon cancer, and multiple solid tumors and hematological malignancies

Target CCR8 HBM1022 ECD ECL1 ECL2 ECL3 Extracellular 150 KDa

Mechanism of Action

1. High CCR8 expressing Tregs allow for antibody mediated depletion via ADCC







HBM9033 (MSLN)

Next-Gen Mesothelin ADC for Solid Tumors



Highlights

- ☐ Unique fully human antibody warhead with improved binding, internalization, blocking activity and less interference by sMSLN
- ☐ The 4th generation of serum stable and tumor-specific cleavable linker with novel payload
- ☐ Superior in vivo potency and promising safety profile compared to other ADC technologies

H2L2-ADC to MSLN





US IND in 2023



Patients of MSLN+ cancers

Cancer types	Percentage	
Ovary carcinoma	89.9%	
PDAC	70.5%	
Uterus,endometrioid adenocarcinoma	63.4%	
Colorectum adenocarcinoma	48.4%	
Lung, adenocarcinoma	47.4%	
Liver cancer	41%	
Stomach adenocarcinoma	31%	
SCLC	27.8%	
Thymic carcinoma	35.3%	
Mesothelioma	75%	
Clear cell RCC	4.4%	
Urothelial carcinoma	12.9%	
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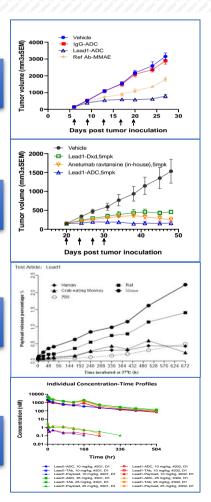
MSLN luminal/membrane expression percentage in 1562 pts tumors

Better efficacy than MMAE based ADC in mouse CDX model 1

Better efficacy than DXd based ADC in mouse CDX model 2

Excellent plasma stability

Confirmed in-vivo stability of ADC shows minimal payload release in monkey

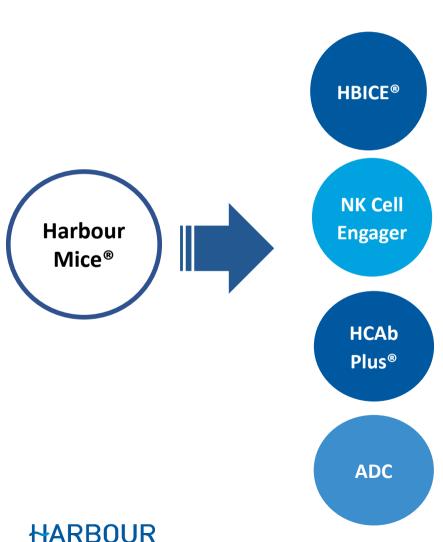


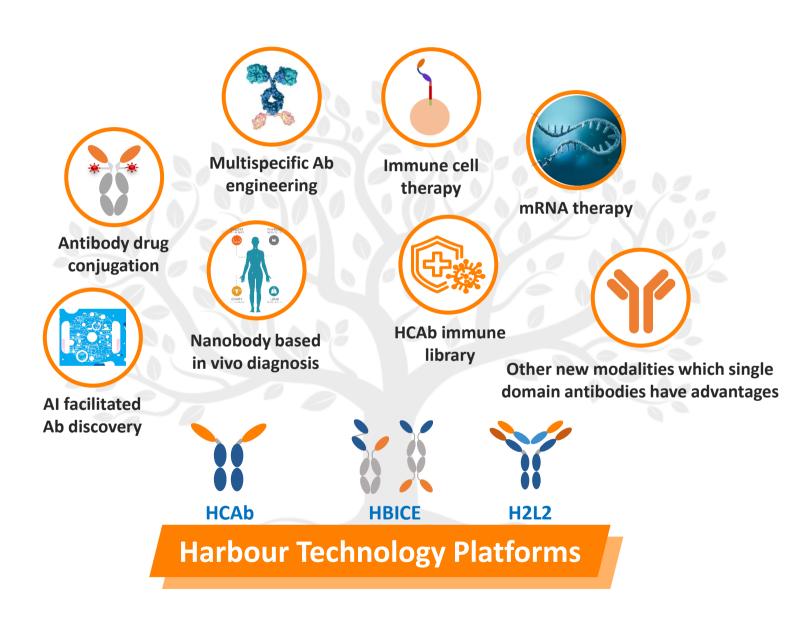


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Broad Applications of Technology Platforms Empower Global

Biotherapeutics Innovation







Further Exploration on Next-Gen Novel Therapeutics in ADC and NK

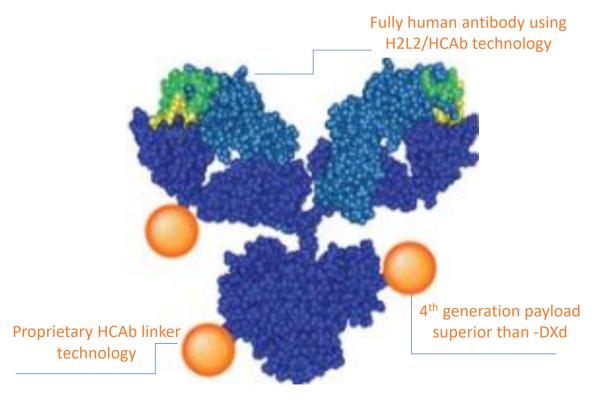


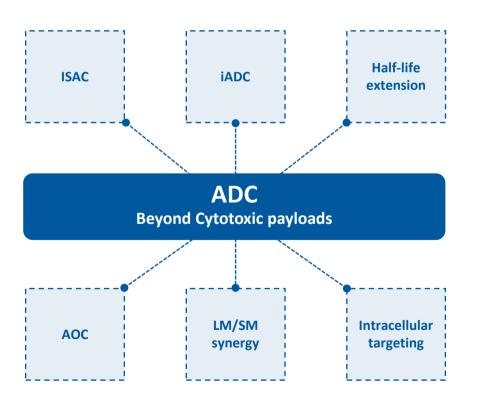
Develop Innovative ADC Therapeutics



Unique HCAb-based ADC Platform

- ☐ Promising potency for both cold and hot tumors
- ☐ Sensitize the tumor to immunotherapy with novel targets and payloads
- ☐ Combine SM and LM advantages to expand HBM portfolio















Further Exploration on Next-Gen NK Cell Engager Biologics

HBiKE

HCAb based Bispecific NK Cell Engager

NK Cell Engager Arms

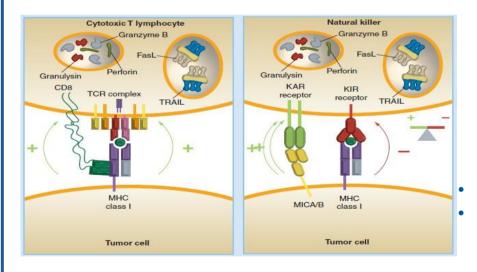


- NKstim1 (available HCAb leads)
- NKstim2 (available HCAb)
- **□** CD16a
- ☐ Others (screening)

In 2022, NK Cell Tech Successfully Completed fundraising of over RMB 100 million

CAR-NK Collaboration

HBM entered into a strategic collaboration with NK Cell Tech in 2021





Dr. Zhigang TianMember of Academia Europaea
Member of Chinese Academy of
Engineering





Global Collaboration and Innovation

Drive Product Developments Leveraging Technology Platforms



Global Collaborations to Maximize the Value of Technologies and Assets



Platform Licensing *



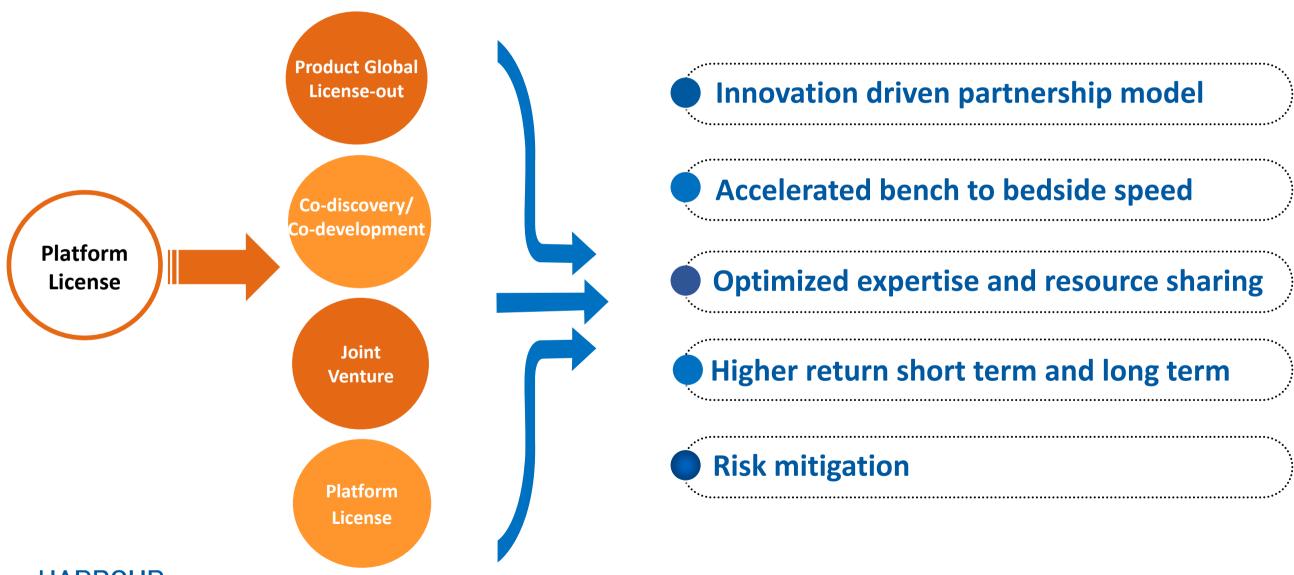




^{*}Previous and Current Licensees



Expanding Multiple Partnership Models to Drive Product Developments



Significant Advancements Were Achieved for Global Collaborations in 2022 1H

Product Global License-out

- ☐ HBM7022 out-license to AstraZeneca with total payments at least US\$350 million
- ☐ Commenced collaborations with LCB, Duality Biologics on ADC



- ☐ Collaborated with **Dana-Farber** to develop novel bispecific antibodies and CAR-T
- ☐ Collaborated with **Boston Children's Hospital** to develop novel antibody therapy
- ☐ Collaborated with **BioMap** to develop novel antibodies with AI technology

Joint Venture

☐ Incubated NK cell therapeutics, "NK Cell Tech" successfully completed fundraising















Platform License-out

☐ Certain molecules generated from HBM technology platforms were advanced into clinical stage by Innovent Biologics





HBM7022 (CLDN18.2xCD3)

The First Global Out-licensed Bispecific Antibody Generated by HK-listed Bio-tech





- ☐ In April 2022, HBM7022, one pre-clinical asset, was out-licensed to AstraZeneca
- □ In May 2022, HBM received **US\$25 million** upfront payment (total transaction value of **US\$350 million** + royalty fee)
- □ In July 2022, AstraZeneca and HBM teams have successfully completed HBM7022 transfer for subsequent developments

McKinsey & Company

Vision 2028: How China could impact the global biopharma industry

Enabling technologies. In 2021, several Chinafocused companies developed drugs using bispecific antibody or ADC platforms. Harbour BioMed was one of them; it used its proprietary platform to develop a bispecific antibody targeting CLDN18.2xCD3 and licensed it to AstraZeneca.



Harbour BioMed Reaches License Deal With AstraZeneca On Bispecific Antibody HBM7022

RTTNews

(RTTNews) - Harbour BioMed said that it has reached license agreement with AstraZeneca (AZN, AZN.L) for CLDN18.2xCD3 bispecific antibody (HBM7022).





By PBR Staff Writer

B iopharmaceutical firm Harbour BioMed (HBM) and AstraZeneca have entered into a global out-license agreement for CLDN18.2xCD3 bispecific antibody HBM7022.





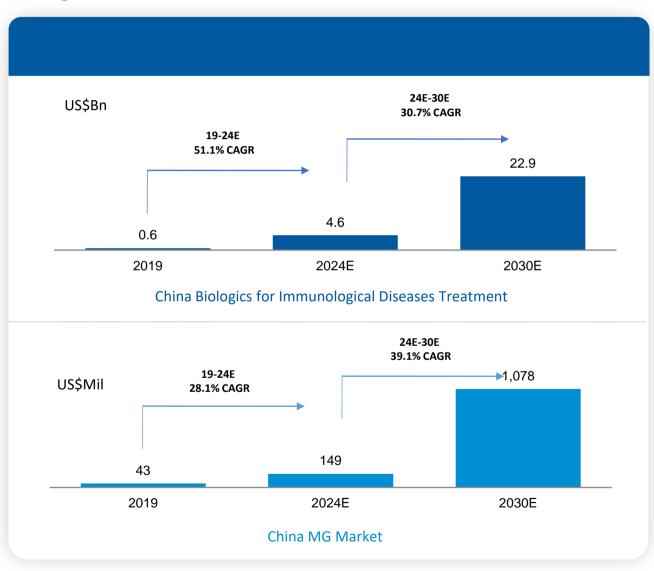


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Batoclimab (HBM9161)

A Breakthrough Therapeutics for IgG Mediated Autoimmune Diseases

Huge Market Potential



HBM9161 Competitive Advantages



Strong Efficacy

- Effectively eliminate pathogenic IgG
- Clinical POC established across indications



Great Safety

- Fully human IgG with low immunogenicity risk
- Less likely to lead to inflammation with reduced effector function Welltolerated, majority of AEs are mild and/or moderate



Convenient Treatment

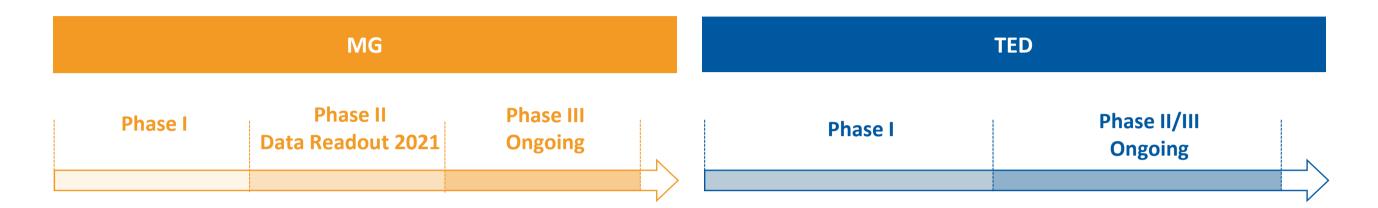
- Fixed-dose subcutaneous injection
- Possible for patient self-administration
- Improved patient compliance



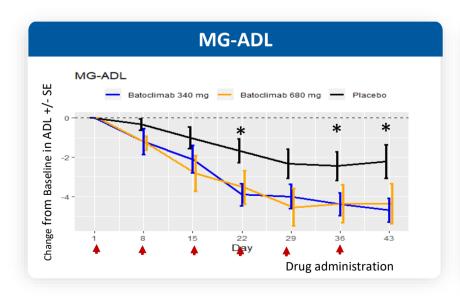
Source: Frost & Sullivan

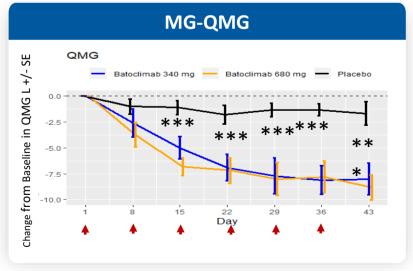
Batoclimab (HBM9161)

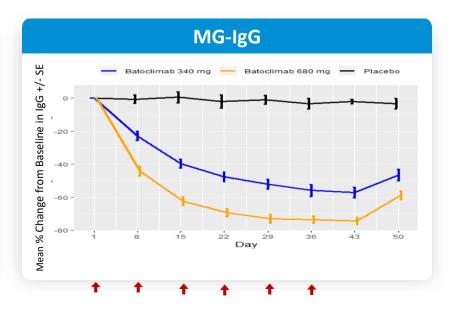
A Breakthrough Therapeutics for IgG Mediated Autoimmune Diseases



MG Positive Ph II Study Results, Presented at the 25th World Congress Neurology (WCN)







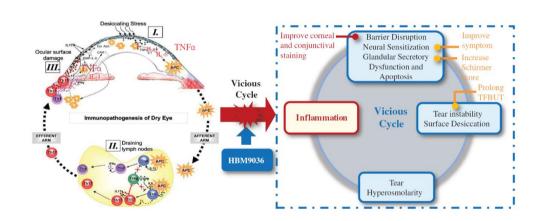


Tanfanercept (HBM9036)

A Differentiated Therapeutics to Treat the Growing Prevalence of Dry Eye Disease

First Global Innovative Biological Drug in China to Treat Moderate-to-severe DED

Mechanism of Action



Excellent Safety Profile

Highly Comfortable

Similar drop comfortable score with placebo

Rapid Onset

4 weeks vs. 3-6 months

Substantial improvement in clinical signs from the initiation of treatment (Tanfanercept vs. Competitors)

2022

- Completed the first interim analysis of phase III trial in 2022 1H
- Completed over half of patient enrollment
- Positive results of HBM9036 phase II clinical data was published on "International Ophthalmology" in 2022 1H



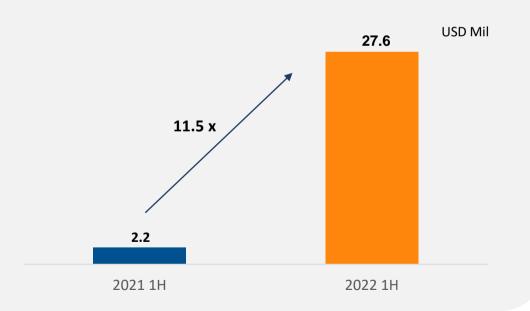


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Revenue Significantly Increased in 2022 1H

Revenue

Total revenue significantly increased from US\$2.2 million for the six months ended 30 June 2021 to US\$27.6 million for the six months ended 30 June 2022, primarily due to the increase in our revenue from recognizing molecule license fee. Our molecule license fee increased from US\$1.8 million for the six months ended 30 June 2021 to US\$27.1 million for the six months ended 30 June 2022, due to the recognition of the upfront payment of approximately US\$25 million received from AstraZeneca for our collaboration agreement.

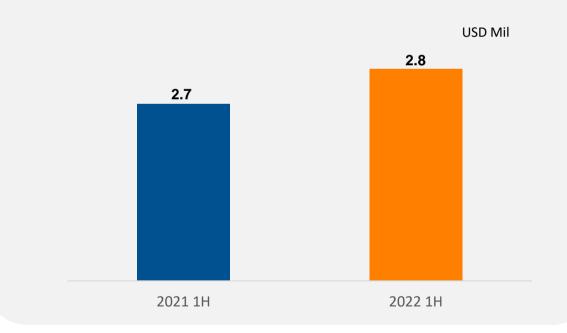


Other Income and Gains

Other income and gains were US\$2.8 million for the six months ended 30 June 2022, whereas US\$2.7 million for the six months ended 30 June 2021.

The item primarily consists of:

- Interest income
- Fair value change of other financial assets





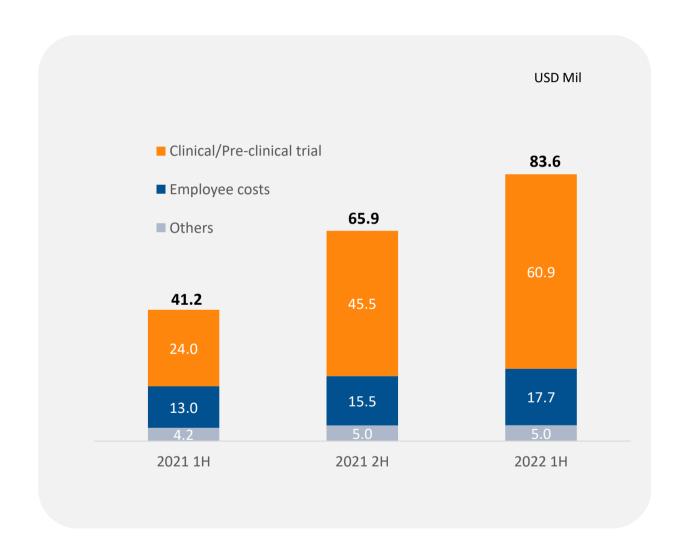
R&D Expenses Increased Mainly Due to Clinical Investments in Phase III Assets

Research and development costs

R&D expenses increased significantly from US\$41.2 million for the six months ended 30 June 2021 to US\$83.6 million for the six months ended 30 June 2022.

This increase was primarily attributable to:

- (i) increased investments in our key clinical programs
- (ii) increased investments in our molecule assets in discovery and pre-clinical stages
- (iii) an increase in employee cost from US\$13.0 million to US\$17.7 million due to the increase in our R&D staffs

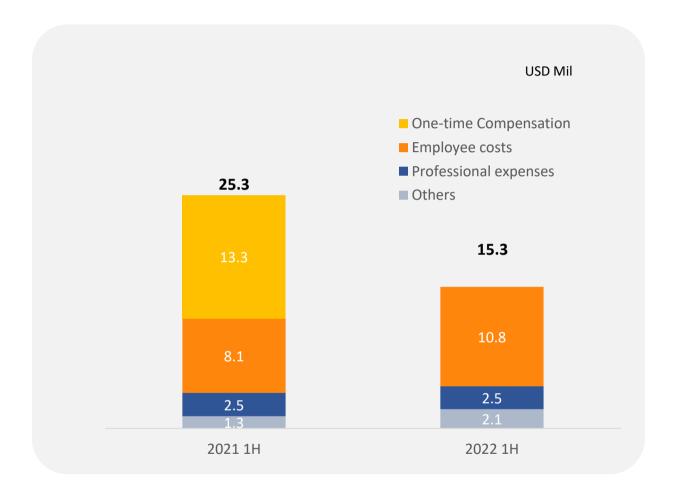




Administrative Expenses Decreased Due to One-time Expense in 2021 1H

Administrative expenses

Administrative expenses was US\$25.3 million in 2021 1H, decreased by US\$10.0 million to US\$15.3 million in 2022 1H, primarily attributable to one-time compensation expenses in 2021 1H.



Loss for the period

Loss for the period increased 19% from US\$61.6 million for the six months ended June 2021 to US\$73.1 million for the six months ended 30 June 2022.



E

Effective Cash Flow Management to Maintain Healthy Cash Position

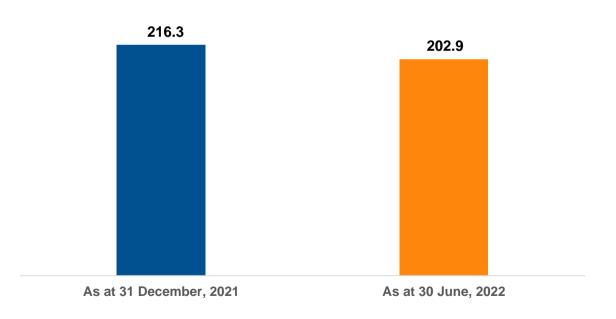
Summary of Consolidated Statements of Financial Position

USD Mil	30 June	31 December
	2022	2021
Non-current assets	47.3	41.5
Current assets	221.0	240.9
Include: Cash and bank balances	<u>202.9</u>	<u>216.3</u>
Current liabilities	55.9	41.1
Net current assets	165.1	199.8
Non-current liabilities	55.6	18.4
Net assets	156.8	222.9

Cash and bank balances

Cash and bank balances decreased from US\$216.3 million to US\$202.9 million.









- **01** Company Overview and Highlights
- **O2** Develop Global Innovative and Differentiated Product Pipeline
- **03** Upgrade Technology Platforms to Explore Novel Frontier
- 04 Product Updates on Regional Market Assets
- **05** Financial Results
- 06 Outlook

Outlook

Advancing Next-Gen Biotherapeutics by Leveraging Industry Leading Technology Platforms

- 8 ongoing clinical trials in phase I/II/III with differentiated targets
- 3 new assets targeting on IND submissions in 2022 2H

Global Innovative Products Powered by HBM's Technology Platforms
Start to Show Significant Values

Cutting-edge Technology
Platforms Grow and Broaden
HBM Ecosystem

- Broad applications of HBM Technology Platforms
- Novel business models of partnership
- Solid financial supports



- Global collaborations accelerate product developments
- Global collaborations generate cash flow

Sustainable Global Collaborations
Maximize the Assets Values

Healthy Cash Position Supports
Company Growth

- Revenue significantly increased 11.5x in 2022 1H
- Cash balance US\$202.9 million as of 30 Jun 2022





Q&A





THANK YOU

