

HBM Holdings 2022 Investor Day

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HBM's Global Innovation with Robust Discovery Engines

Dr. Jingsong Wang

Founder, Chairman of the Board and Chief Executive Officer Harbour BioMed

Continuously Advancing Innovative Portfolio and Platform Technology

	Global Pipeline	Technology Platforms
2022	 Global Programs: 16 3 clinical-stage assets (4003, 7008, 9378) 2 new assets entering IND in 2022 2H 	 H2L2, HCAb, HBICE[®], SBC, HCAb Plus[®], HBIKE Modality: mAb, BsAb, ADC, CAR-T, CAR-NK, mRNA
2020 (IPO)	 Global Programs: 7 (1 in phase I) License-in assets: 2 phase II 	 H2L2, HCAb, HBICE[®], SBC Modality: mAb, BsAb
2017	 Global Programs: 1 License-in assets: 2 	 H2L2, HCAb Modality: mAb



Highly Innovative and Differentiated Global Pipeline

	Project	Target	Indication	Commercial	Status						
	rioject	laiget		Rights	Discovery	Pre-Clinical	IND	Phase I	Phase II	Phase III	BLA
	Porustobart (HBM4003)	CTLA-4 ¹	Solid Tumors ^a	Global					М	onotherapy Ph	1b/2
			Solid Tumors ^b						Со	mbo with PD-1	Ph 1b/2
			Solid Tumors ^c						Combo with	n PD-1/PD-1+Ch	iemo Ph 1
	HBM7008	B7H4×4-1BB	Solid Tumors	Global				Ph 1 ²			
	HBM7022	CLDN18.2xCD3	Solid Tumors	Global Out-license	AstraZeneca						
	HBM7004	B7H4×CD3	Solid Tumors	Global							
	HBM9027	PD-L1xCD40	Solid Tumors	Global							
	HBM9378	TSLP	Asthma	Global			P	h 1 😥			
	HBM9033	MSLN ADC	Solid Tumors	Global							
	HBM1022	CCR8	Solid Tumors	Global	US IND filing expected in Q1 2023						
	HBM1020	B7H7	Solid Tumors	Global	US IND filing expected in 2022						
	HBM1007	CD73	Solid Tumors	Global	US IND filing expected in 2022						
	HBM1047	CD200R1	Solid Tumors	Global							
	HBM9014	LIFR	Solid Tumors	Global			𝔅 Yin	uoke			



 HBM4003 is a next-gen anti-CTLA-4 antibody with enhanced ADCC for Treg depletion
 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

Global Collaborations to Maximize the Value of Technologies and Assets









Harbour BioMed: Leading Next-Gen Biotherapeutic Innovation

Lead Next-Gen IO Therapeutics

- **Global Innovation**
- Worldwide Collaboration





Empower Global Biotherapeutics Innovation

Building the Builders

Idea to IND





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Porustobart: Next-Gen Anti-CTLA4 Antibody with Potential to Become the Cornerstone Therapy

Dr. Humphrey Gardner

Chief Medical Officer Harbour BioMed

Porustobart (HBM4003) Leading Development of Next Gen Anti-CTLA-4 Therapeutics with Novel MoA



Porustobart (HBM4003)

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



Porustobart (HBM4003) MoA Reflected via Clinical Benefit in Chinese Melanoma Patients

Robust efficacy observed for HBM4003 + Toripalimab in PD-1 naïve melanoma cohort

Best Overall Response by RECIST 1.1, N (%)

Pts with tumor assessments	15 (100%)
CR	0 (0%)
PR	8 (53.3%)
ORR (CR + PR)	8 (53.3%)
SD	3 (20.0%)
DCR (CR + PR +SD)	11 (73.3%)
Tumor reduction	9 (60%)





- Preliminary data of 4003.2 study (NCT04727164), PD-1 naïve melanoma pts treated with RP2D (HBM4003 0.3mg/kg + Toripalimab 240mg Q3W) in Part 1 and Part 2
- 17 pts treated with median follow up of 105 days (range: 11-138 days), in which 15 pts had at least one post treatment tumor assessment

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- 1. NCT02545075. <u>https://www.clinicaltrials.gov/</u>
- 2. Keynote-151 study. Si et al, 2019.

3.

4

Data cutoff 27 Jun 2021

- POLARIS-01 study. Tang et al., 2020. NCT03545971. ESMO 2021 Abstract 1086P.13
- 5. NCT04640545. ASCO 2022 Abstract 9538.

Porustobart (HBM4003)

Near Term Registration and Further Opportunities in Hitherto Intractable Indications



Porustobart (HBM4003) Great Opportunities in NEC and HCC

Clinical Progress and Upcoming Milestone

Neuroendocrine Carcinoma



- ✓ Patients enrollment completed in Q3 2022
- Double the clinical response rate from preliminary data compared with available treatments
- ✓ **Durable** clinical benefit observed in multiple patients
- ✓ Planned publication in academic conference 2023

Hepatocellular Carcinoma



- ✓ Patients enrollment completed in Q3 2022
- Demonstrated best in class potential from preliminary data
- Clinical benefit was observed in heavily pre-treated patients, frontline treatments include TKIs and anti-PD-1 antibody
- ✓ Planned publication in academic conference 2023



Porustobart Cornerstone for new therapeutic avenues









Robust Portfolio Generated from Discovery Engines

Dr. Yiping Rong

Chief Scientific Officer Harbour BioMed

Research Strategy Leveraging HBM's Technology Platforms



3. Overcome Immune Suppression

Modulate alternative Immune Evasion Pathways (IEP) beyond PD1/L1 using H2L2/HCAb/SBC technology



Harbour Therapeutics Portfolio Strategy in Periodic Table

-We Innovate Cancer Therapy in Three Oncology MoA Strongholds

Direct Killing							Overcome Immune Suppression
CTLA4-eADCC HBM4003	St	CD73 HBM1007					
CCR8-eADCC HBM1022		T Cell Engager		BiKE	BiME/BiDE	T and NK	B7H7 HBM1020
CD25-eADCC HBM1039	CD3 HBICE®	4-1BB HBICE®	CD28 HBICE®	NKp30 HBICE [®]	CD40 HBICE®	Other HBICE®	CD200R1 HBM1047
MSLN-ADC HBM9033	BCMAxCD3 HBM7020 ビー本派も物	B7H4x4-1BB HBM7008	PDL1xCD28 HBM7024	ROR1xNKp30 HBM7025	PDL1xCD40 HBM9027	CD122xCD132 HBM1040	SigLec-7/9 HBM1057
CEACAM-ADC HBM1053	B7H4xCD3 HBM7004	MSLNx4-1BB HBM7021			5T4xCD40 HBM7023	CRTAM HBM1054	CD36 HBM1055
	CLDN18.2xCD3 AZD5863/HBM7022 AstraZeneca						LIFR HBM9014



HBM9014 (LIFR)

The First Antibody Targeting LIFR, a Novel Growth Factor Receptor in Multiple Tumors

Collaboration with Innuoke

Highlights

- One of the most important growth factor pathway in PDAC, CRC and prostate cancers. LIF is also a key paracrine factor from stromal cells acting on cancer cells and modulating tumor microenvironment.
- Blockage of LIFR inhibits the action of LIF and overlapping cytokines. LIFR inhibition is a potentially more efficient approach than LIF inhibition.
- Blocks both LIF and CLCF1 pathways, which expressions are significantly elevated in TME and correlate to poor prognosis
- **□** Encouraging in vivo efficacy superior to MSC-1(anti-LIF mAb in phase II trial for PDAC) and enhanced chemo drug efficacy in preclinical models



Enhanced efficacy in combination with Cisplatin



HBM7008 (B7H4x4-1BB) **First-in-Class Bispecific Antibody from HBICE® Platform**

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12nM 024nM 0.048nM

0.0096nM

12nM

024nM

0.048nM

0.0096 nM

HBM7004 (B7H4xCD3) Unique "2+1" Asymmetric HBICE[®] Using Novel TAA and Safer Anti-CD3 Arm

Highlights

BIOMED

- □ 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 or in-house HBM7008 to overcome T cell engager challenges in solid tumor

Molecule Design and MOA



Strong Anti-tumor Activity in Mouse Tumor Model



HBM7004 (Signal 1) Combined with HBM7008(Signal 2) are Critical for T Cell Engager Efficacy in Cold Solid Tumors



lgG1 iso 0 5000 10000 15000 20000 25000 Live T cell number T cell proliferation-generation% G3 G2 G1 G1 G0 Live/Apoptosis/Necrotic T cell %



Immune Cell

Engager

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
- 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



Strong Anti-tumor Activity in hPD-1/hCD40 DKI Mice





HBM1020 (B7H7) Novel B7 Family Plays an Alternative Immune Escape Mechanism Beyond PD-L1

Highlights

BIOMED

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 Dec 2022

Strong Anti-tumor Activity in Breast Cancer Model



Breast Cancer Human PBMC Model

HBM1047 (CD200R1) Novel IO Checkpoint Targets Regulating Both T Cells and Myeloid Cells

Highlights

- □ 1st fully human antagonistic antibody against CD200R1 for cancer therapy
- CD200R1 is highly expressed in ICI non-responders T/Myeloid cells serving as an alternative immune escape pathway
- Dual modulator for both tumor infiltrated T cells and myeloid cells with strong blocking activity and anti-tumor activity
- □ 1st CD200R1 antibody showing potent anti-tumor efficacy in syngeneic model with excellent monkey PK and safety profile



Anti-tumor Efficacy in Syngeneic Tumor Model





HBM1022 (CCR8) Next-Gen Treg Depletion Therapeutics Targeting CCR8

Highlights

- Potent tumor resident Treg depletion activity 1)
- Potent inhibition of CCL1-induced signaling pathway / in vivo anti-tumor efficacy 2)
- 3) Comparable human/cyno binding affinity
- Significant potential for breast cancer, colon cancer, and multiple solid tumors and hematological malignancies 4)





Function Activity and Anti-tumor Efficacy

BABIC Continuously Drives Innovative Portfolio and Leads the Next-Gen Therapeutics







Platform Empowering Global Innovation with Strong Growth

Mr. Weihao Xu

Chief Financial Officer and Chief Business Officer Harbour BioMed

Significant Advancements Achieved for Global Collaborations in 2022

Product Global License-out

- HBM7022 out-license to AstraZeneca with total payments US\$350 million and royalties
- HBM9161 out-license to **CSPC** with total payments **RMB\$1,011 million and royalties**
- Commenced collaborations with LCB, Duality Biologics on ADC

Co-discovery/Co-development

- 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

INNOVENt 信达生物制药

AstraZeneca

CSPC

Dual^{*}tyBio

Dana-Farber

BioMap 百图生科



Develop Innovative BsAb - 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



HBM7022 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

MOA of HBM7022



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

Harbour Mice[®] ADC Ecosystem

H2L2-ADC to MSLN



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HARBO

- 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



Further Exploration on Next-Gen NK Cell therapeutics

HBM entered into a strategic collaboration with NK
 Cell Tech in 2021 with HCAb out-license





Innovative NK cell precision therapy

- Remodeling immune microenvironment, for both cold and hot tumors
- Sensitize the tumor to immunotherapy with special targets
- Unique full human CAR/ nano antibody/ engager technology



Dr. Zhigang Tian

- Member of Academia Europaea
- Member of Chinese Academy of Engineering

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





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Nona Biosciences: A Platform-based Enabler from Idea to IND

Dr. Yun He

Chief Technology Officer, Nona Biosciences

Dr. Jiyong Zhang

Head of Business Development, Nona Biosciences

Nona Biosciences Empowers Global Therapeutic Innovation



Nona Provides Fully Integrated Antibody Discovery Solutions





Harbour Mice[®]- New Generation of Fully Human Antibody Platforms

Highly Effective Engine for Generating Novel Therapeutics

Industry Leading Technology Platforms

- Worldwide patent protection
- Validated by **50+** industry and academic partners
- Applied in 200+ discovery programs
- 10+ projects having entered clinical stage





Harbour Mice[®] HCAb Transgenic Mice

A Unique Human Heavy Chain Only Antibody Platform for Generation of Next-Gen Therapeutics





Nona's Technology Platforms Have Been Endorsed by Partners





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Nona Biosciences Enters into HCAb Based Drug Discovery Collaboration Agreement with Dragonfly Therapeutics

Published: Nov 21, 2022



"We aim to leverage Nona's fully human antibody transgenic mice platform to obtain novel antibody molecules on specific targets and strive to develop innovative ADC drug which can meet global needs better and faster."

> Dr. Junyou Ge, CEO of Kelun Biotech

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Nona Consistently Advances Technologies to Help Our Partners



Delivery Technology

mRNA-encoding target gene as immunogen to tackle difficult targets

Protein Engineering



Combine human antibody platforms and protein engineering to generate multifunctional molecules Novel conjugation technology for bringing new modalities against solid tumors

Conjugation Technology

Artificial Intelligence



Artificial Intelligence for accelerating antibody discovery and optimization



Utilize mRNA Technology to Tackle Difficult Immunization Projects



NONA BIOSCIENCES

High Throughput Screening in "Single Day" by Beacon® Single B Cell Technology

Single B Cell (SBC) technology greatly shortens the workflow from months to days



NONA

> 30,000 B cells were screened in 2-3 days by SBC, and diverse sequences of fully human antibodies were retrieved.

SBC	Mice	Immunogen	Cells screened	cDNA cloned	Total Sequence	Unique Sequence VH/VL pairs
#1	H2L2	Cyno MSLN	11000	1 - 1	1 4 4	120
#2	H2L2	Human MSLN	10900	151		120
#3	H2L2	Cyno MSLN	11000	(94%)	(95%)	(79%)



Leverage Artificial Intelligence and Single B Cell Technology to Efficiently **Identify Diverse HCAb Sequences for Novel Target**



Utilize single B cell technology (SBC) to identify functional antibodies for a novel target



hyperSCREEN combines NGS and 2 **Machine Learning to search greater** sequence space

Identify diverse sequences with excellent biological activities or molecular properties

3



Phylogenetic tree of HCAbs from different sources



HCAbs (SBC) binding to Target



HCAbs (hyperSCREEN) binding to Target 800000hcab-9245 600000hcab-9246 hcab-9251 ¥ 400000hcab-9257 200000 hcab-9258

10

100

0.001 0.01

0.1

1

Ab conc. (nM)

lgG1 iso



hyperSCREEN / SBC



Integrated Discovery Solutions

- ✓ From Idea to IND
- ✓ High quality project delivery



Empowering Global Therapeutic Innovation





Healthy Financial Situation

Mr. Weihao Xu

Healthy Financial Situation

Revenue

Expanded Collaboration Driving Strong Revenue Growth

- Products out-licensing by Harbour Therapeutics
- Broad networks ofcollaboration weaved byNona Biosciences



Operation

Optimization on Operational Efficiency & R&D Expenses

- Diversified co-development to spread R&D costs
- Organizational optimization to reduce labor costs
- Improvement on efficiency to control project costs

Cash

Strong Cash Position

Extended cash runway for over two years

□ Flexible credit facility and draw tenor



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HARBOUR BIOMED

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Closing Remark

Dr. Jingsong Wang

Harbour BioMed: Leading Next-Gen Biotherapeutic Innovation

Lead Next-Gen IO Therapeutics

Global Innovation

Worldwide Collaboration



Empower Global Innovation

Building the Builders

Idea to IND





Harbour BioMed: Strong Growth with Expectable Catalysts

Longterm Value

Near-

term

Catalysts

(2022-2023)

- Robust and highly differentiated portfolio
- Strong and productive global collaboration
 network
- Optimized capital efficiency
- Advancing key assets into registration trial
- 2 new highly innovative assets into clinical every year
- Expanding collaborations with Nona as a global innovation enabler

Value Realization Value Creation Value Proposition

HBM Holdings' Strong Business and Value Growth







THANK YOU