

29 March 2023

HARBOUR
BIOMED

2022 Full Year Results

Conference Call and webcast for investors and analysts

HBM HOLDINGS-B, 02142.HK



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01 Full Year 2022: A Landmark Year

02 Innovation: Robust Portfolio & Cutting Edge Technology

03 Accelerated Growth: Business Model Expansion

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05 Outlook: Deliver Value Through Sustainable Growth

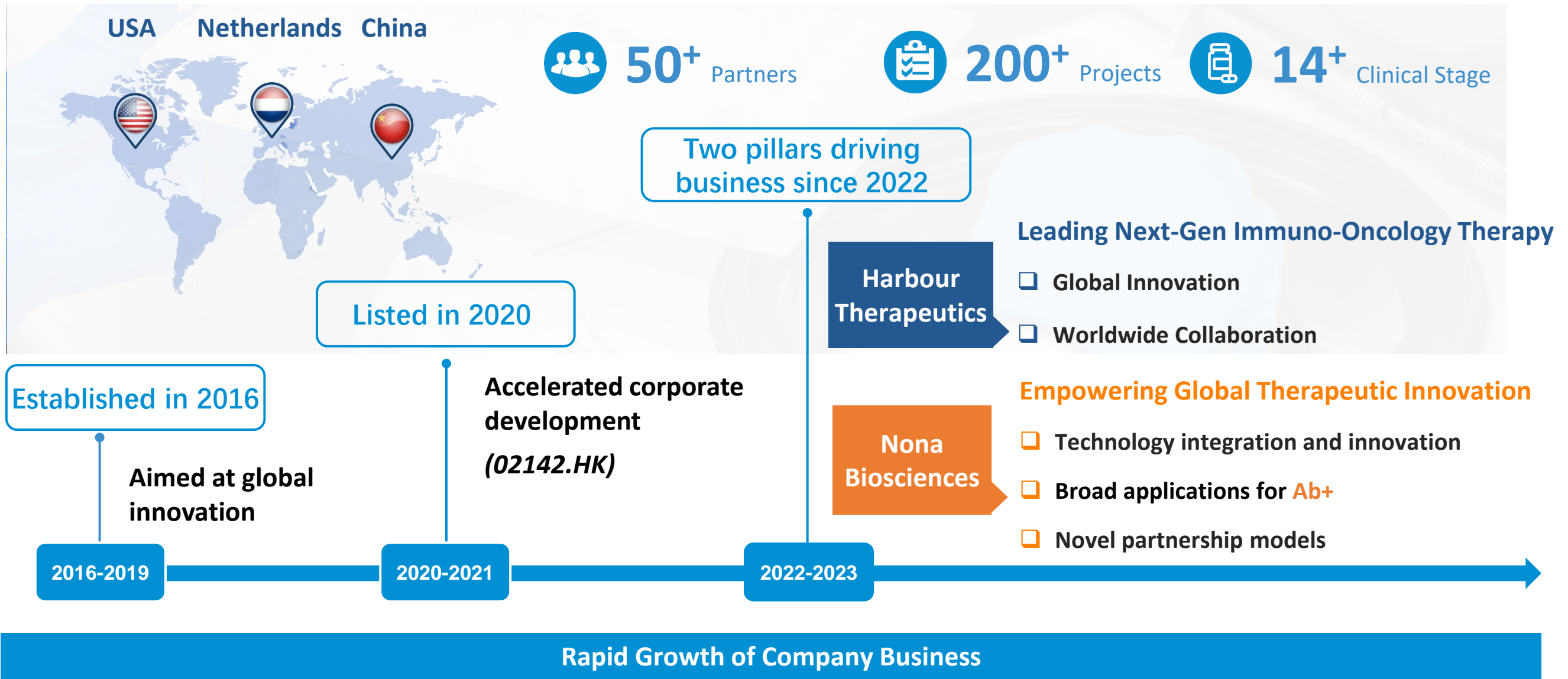


Full Year 2022: A Landmark Year






Dr. Jingsong Wang

Founder, Chairman of the Board and Chief Executive Officer

Harbour BioMed: Next-Generation Global Biotech Company



Highly Innovative and Differentiated Global Pipeline

Project	Target	Indication	Commercial Rights	Status						
				Discovery	Pre-Clinical	IND	Phase I	Phase II	Phase III	BLA
Batoclimab HBM9161	FcRn	Myasthenia Gravis	Greater China Rights Out-licensed ¹	Ph 3 Completed						
		Thyroid Eye Disease							Ph 2/3	
Porustobart HBM4003	CTLA-4 ²	Solid Tumors ^a	Global						Monotherapy Ph 1b/2	
		Solid Tumors ^b							Combo with PD-1 Ph 1b/2	
		Solid Tumors ^c							Combo with PD-1/PD-1+Chemo Ph 1	
HBM7008	B7H4×4-1BB	Solid Tumors	Ex-U.S. ³				Ph 1			
HBM9378	TSLP	Asthma	Global				Ph 1			
HBM1020	B7H7/HHLA2	Solid Tumors	Global				US IND clearance in January 2023			
HBM1007	CD73	Solid Tumors	Global				US IND clearance in January 2023			
HBM1022	CCR8	Solid Tumors	Global				US IND clearance in February 2023			
HBM7022	CLDN18.2×CD3	Solid Tumors	Global Out-license							
HBM9027	PD-L1×CD40	Solid Tumors	Global							
HBM9033	MSLN ADC	Solid Tumors	Global							
HBM7004	B7H4×CD3	Solid Tumors	Global							
HBM1047	CD200R1	Solid Tumors	Global							
HBM9014	LIFR	Solid Tumors	Global							

New Stage with Numerous Milestones

Harbour Therapeutics

Multiple Major Milestone
Achievements in Advancing
Global Product Portfolio

Batoclimab (HBM9161): Near commercial stage

- ✓ Positive outcome for gMG in Ph3 pivotal trial
- ✓ BLA submission in preparation

Porustobart (HBM4003): Pivotal trial enabling stage

- ✓ Exciting PoC data in multiple indications
- ✓ Pivotal-Enabling for neuroendocrine carcinoma

Established as the global leader in bispecific antibody field

- ✓ Endorsed by MNCs
- ✓ Extensive immune cell engager portfolio
- ✓ Global patent protection proprietary platform

Transformational Engine for New Growth

Mission

Leveraging industry leading technology platforms, Nona Biosciences is committed to provide integrated discovery solution for biotech and pharmaceutical companies from **Idea to IND (I to I)**.

Leading Technology

- Innovation
- License
- Service

Integrated Solution

- Form Idea to IND
- Quality Project

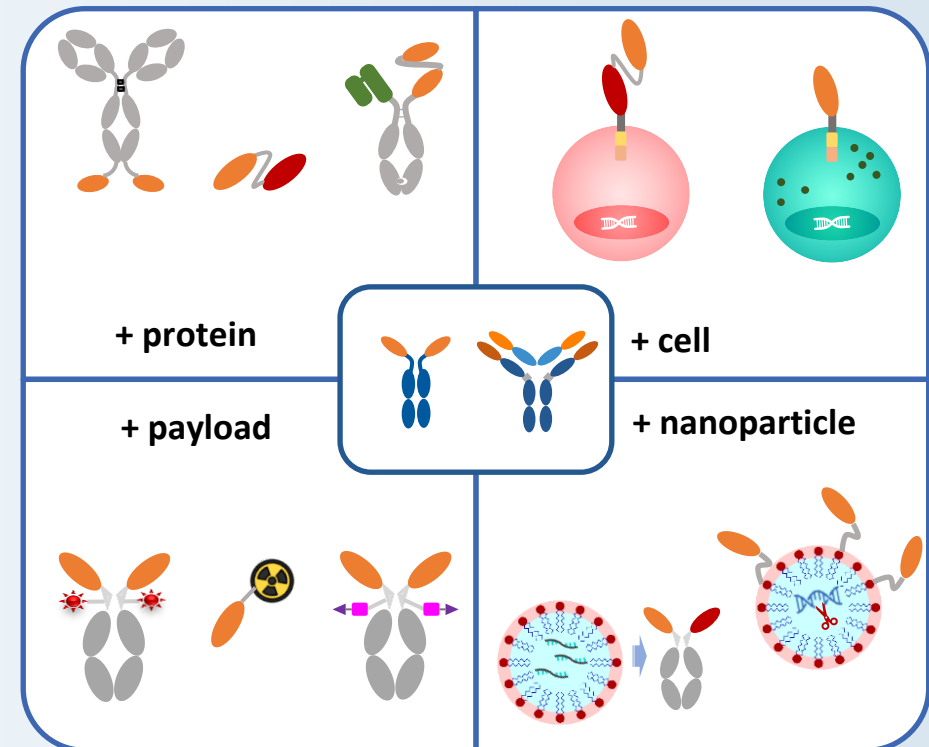
Business Model

- Transformational
- Open access
- Flexible solutions

Broaden the Business Models of Global Collaborations



Antibody PLUS



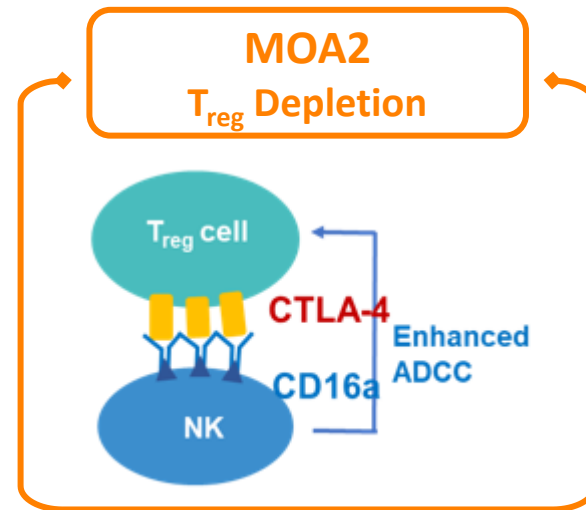
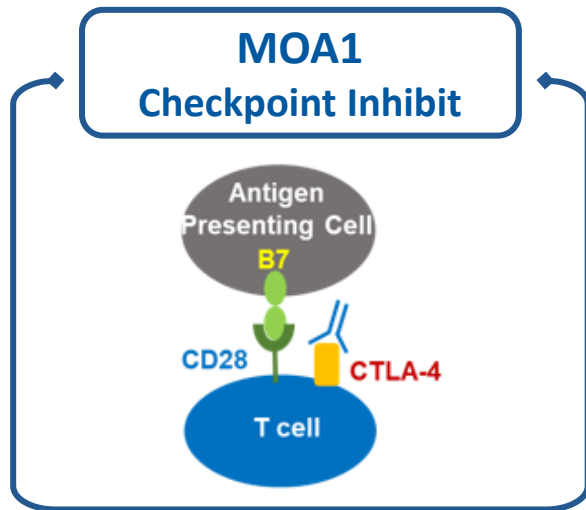
Innovation: Robust Portfolio & Cutting Edge Technology

Dr. Yiping Rong

Chief Scientific Officer

Porustobart (HBM4003)

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

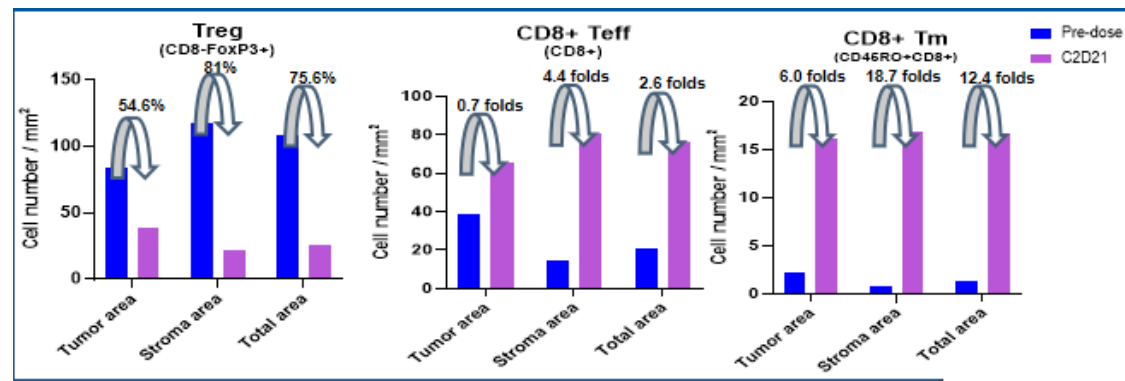


- Competitive Advantages**
- 1 Deplete intra-tumoral Treg cells via enhanced ADCC strategy
 - 2 Great safety profile resulted from the reduced drug exposure in the serum
 - 3 Huge potential for combination therapies

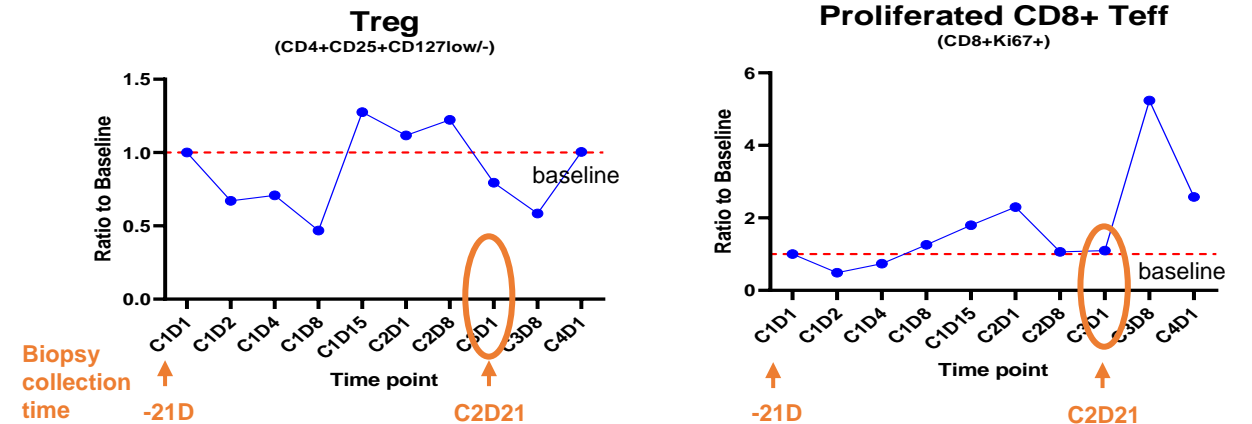


Selective Intratumor Treg Depletion and CD8+ Stimulation

Tumor Biopsy



Peripheral Blood



■ Porustobart (HBM4003)

■ Favorable Safety Profile with Promising Efficacy

As of August 31, 2022, a total of **173** patients had been treated with Porustobart in clinical studies, including:

- **67** patients were treated with Porustobart monotherapy, and
- **106** patients were treated with Porustobart in combination with anti-PD-1 antibody



Favorable Safety Profile

- All the Porustobart-related AEs were manageable and recoverable.
- No new signals or unexpected toxicities in combo therapy
- Most common TRAE is rash



Promising Efficacy

- Objective responses were observed in pts with HCC, CRPC, melanoma and NEN treated with Porustobart monotherapy or combination therapy.
- Porustobart plus anti-PD-1 antibody showed improved response rate in mucosal and acral melanoma, hepatocellular carcinoma and neuroendocrine neoplasms compared with currently available anti-CTLA-4 antibodies.

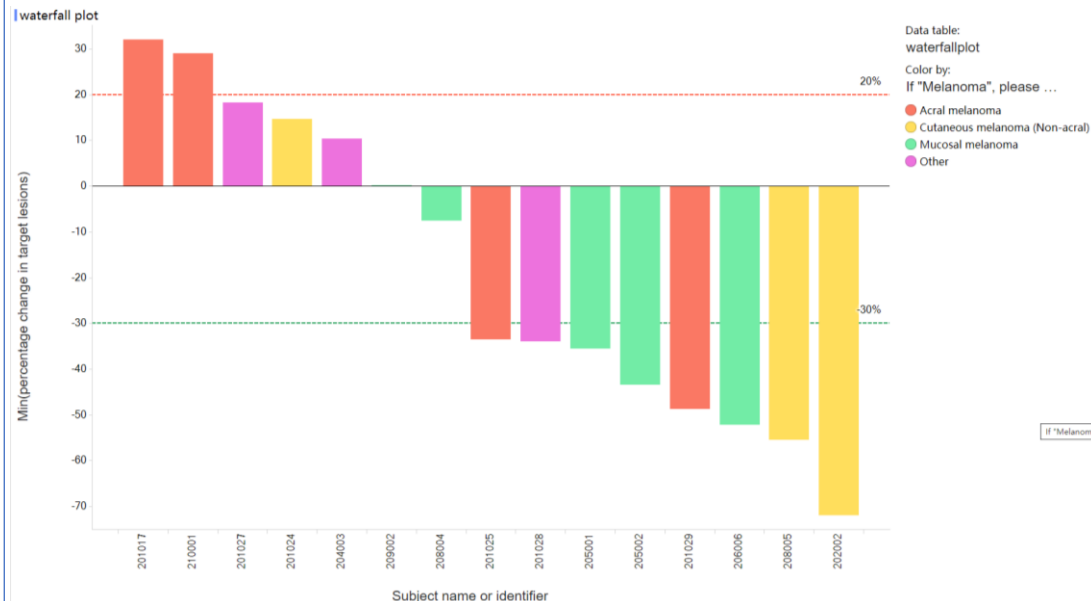
Porustobart (HBM4003)

Unprecedented Clinical Benefit in Chinese Melanoma Patients

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

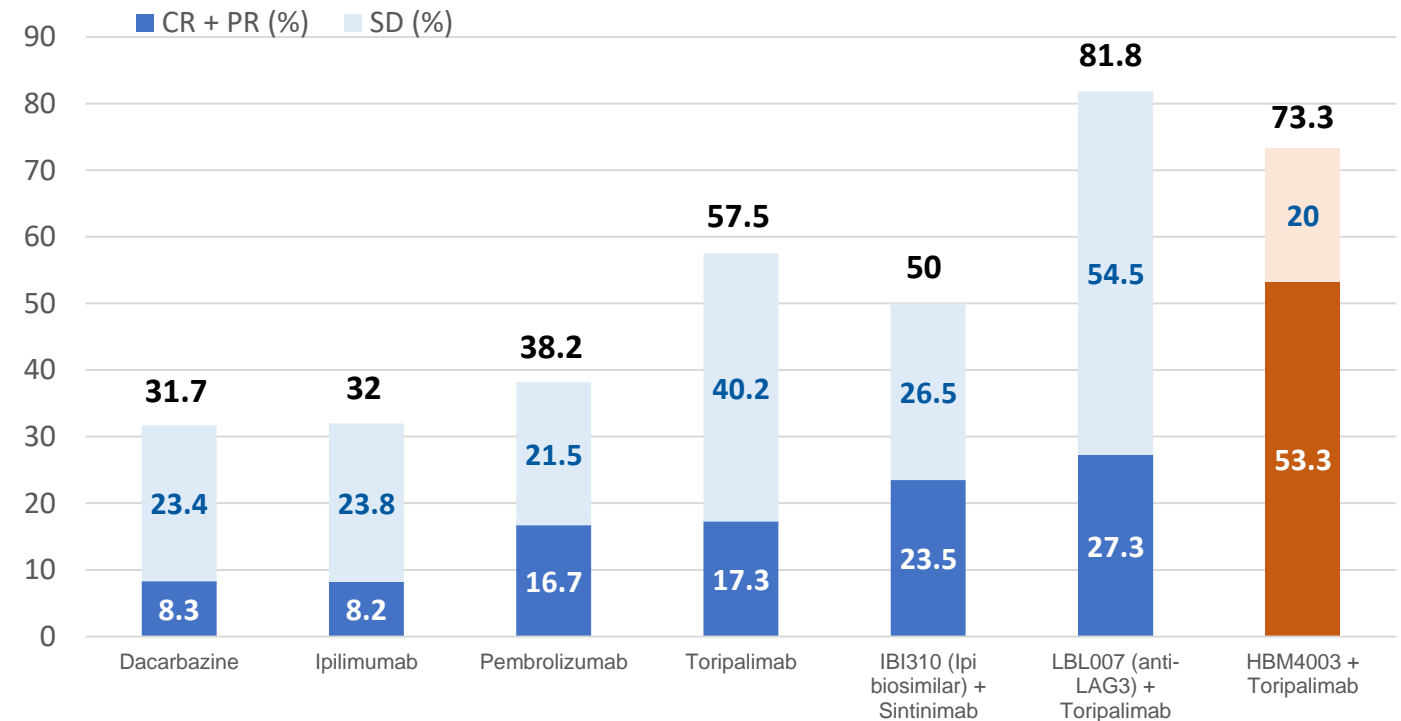
Best Overall Response by RECIST 1.1, N (%)

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%)



HBM4003 + Toripalimab elicited the highest response rate in Chinese melanoma patients

ORR and DCR of various treatments in Chinese melanoma patients



- 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

■ Porustobart (HBM4003)

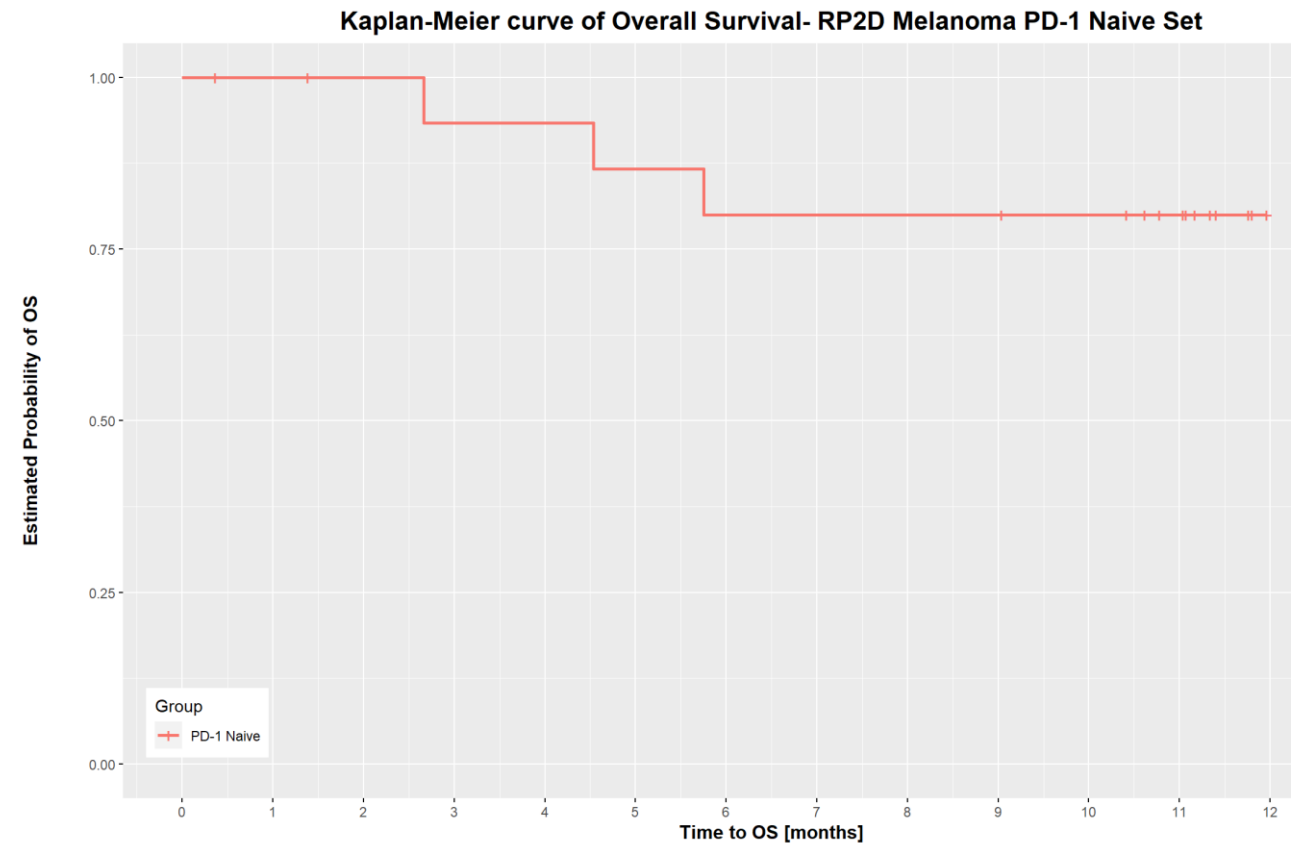
■ Promising OS Data with Significant Improvement

As of March 6 in combo therapy PD-1 Naïve Melanoma Cohort,

- 6-month OS rate was **80%** and
- median OS data collection *in progress*

OS Rate	PD-1 Naïve Cohort
3 month survival rate	0.93
4 month survival rate	0.93
5 month survival rate	0.87
6 month survival rate	0.8
8 month survival rate	0.8
Median Survival (months)	NR

Data cutoff 6 Mar 2023, 17 evaluable patients



■ Porustobart (HBM4003)

■ Great Opportunities in High-grade Neuroendocrine Neoplasm (NEN)

Study Design of 4003.6

Cohort 1

HBM4003 0.3mg/kg + Toripalimab 240mg High-grade NEN, N=8

Cohort 2

HBM4003 0.45mg/kg + Toripalimab 240mg High-grade NEN, N=13

▪ **Primary endpoint:**

- ORR

▪ **Secondary endpoints:**

- DOR, DCR, DDC, OS, PFS, safety

Poorly differentiated NEC represents a high unmet medical need

- Poorly differentiated NEC represents 10%~20% of all NENs and leads to a poor prognosis.
- Platinum-based chemotherapy was in the first line setting for advanced extra-pulmonary poorly differentiated NEC.
- No established standard treatment in second line setting.
- Single agent or combination chemotherapies were commonly used with a median ORR of 18% and median OS of 7.64 months.
- The presence of Treg cells has been shown to be more abundant in high-grade pNET.

Clinical Progress and Upcoming Milestone

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



American Association
for Cancer Research

HBM1020 (B7H7/HHLA2)

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



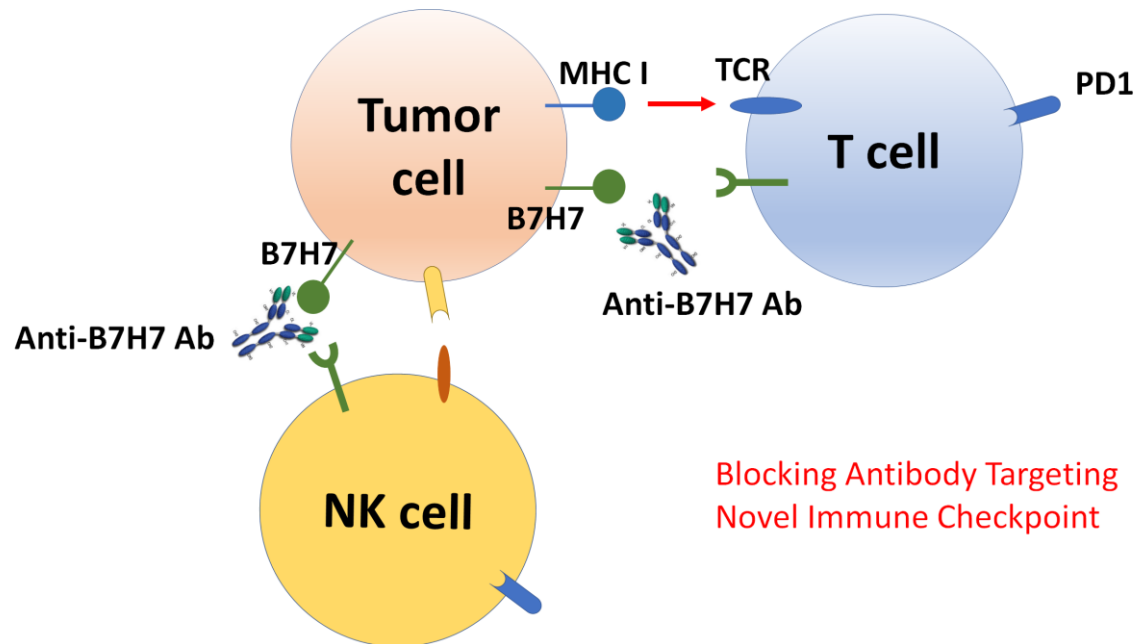
Highlights

- ❑ B7H7/HHLA2 is a first-in-class target potentially serving as an alternative immune escape pathway
- ❑ T cell and NK 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
- ❑ **Ph1 trial initiation in 2023**

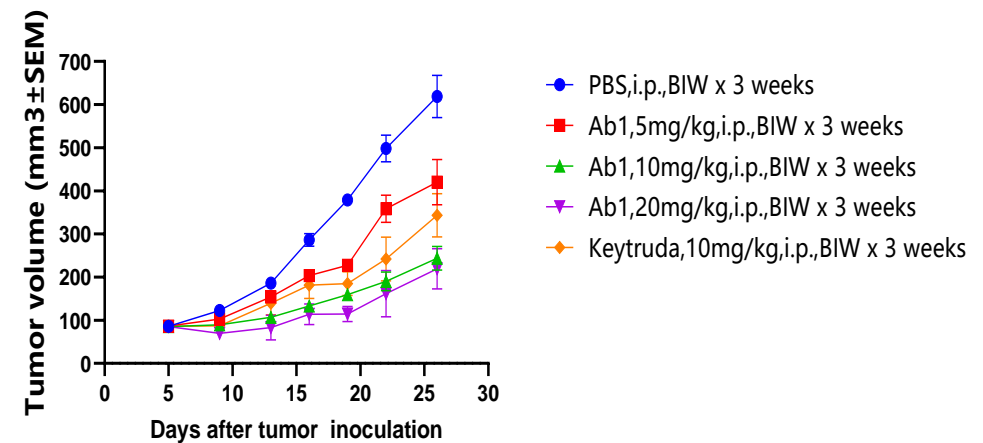


First and only mAb at clinical stage Targeting B7H7/HHLA2

Strong Anti-tumor Activity in Breast Cancer Model through Activation on T Cell and NK Cell



Breast Cancer Human PBMC Model



Ab1 represent HBM1020

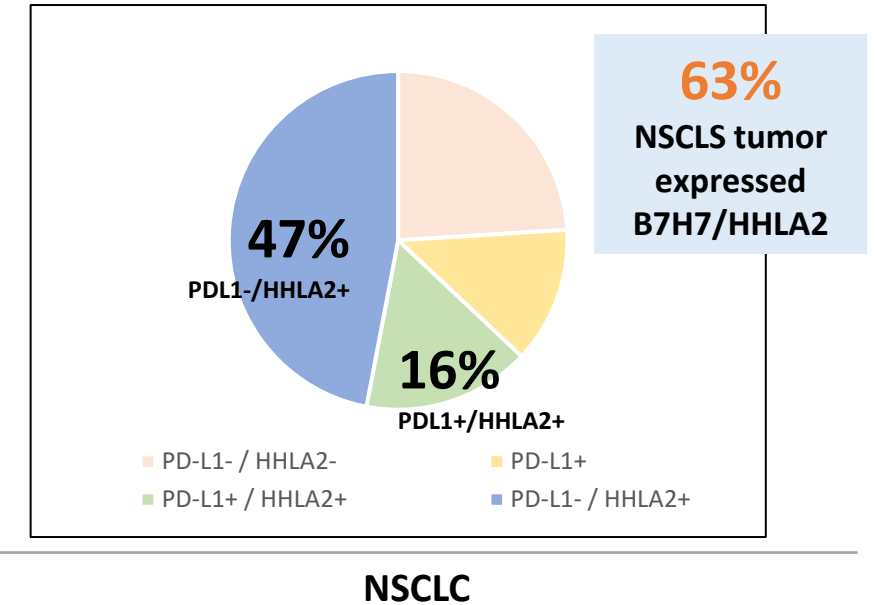
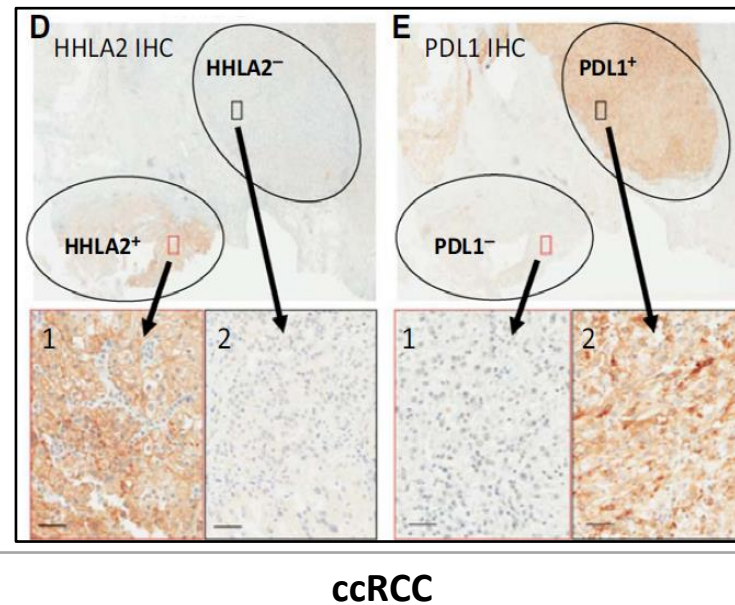
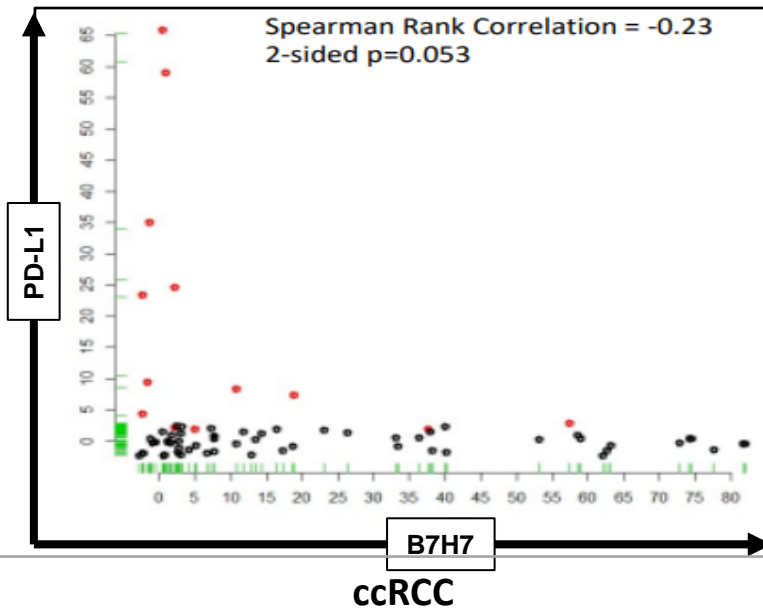
HBM1020 (B7H7/HHLA2)

Potential on Various Solid Tumors and Non-overlapping with PD-L1

Widely Expressed in Various Solid Tumors & Reciprocal to the Expression of PD-L1

Gastric cancer Clear cell renal cell carcinoma Bladder urothelial carcinoma Pancreatic ductal adenocarcinoma Colorectal carcinoma Breast cancer Intrahepatic cholangiocarcinoma Lung cancer

A potential therapy for PD-L1 negative/refractory patients or combination with PD-1/PD-L1 mAbs



B7H7 and PD-L1 expression in ccRCC
Cancer Immunol. Res., 9(2): 156-169, 2021

Distinct and non-overlapping expression
of B7H7 and PD-L1 in the same tumor

B7H7 and PD-L1 expression in NSCLC
WO 2019204057A1

HBM7022/AZD5863

Novel 2+1 Format from HBICE® Platform Validated by MNC

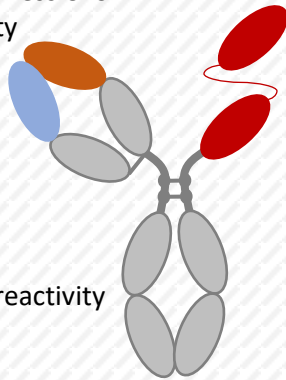


Highlights

- 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

Anti-CD3:

- Optimized anti-CD3 for less CRS
- Monkey cross-reactivity



Fc domain:

- Eliminated FcγR reactivity
- Knob into hole

Tandem anti-CLDN18.2 VH:

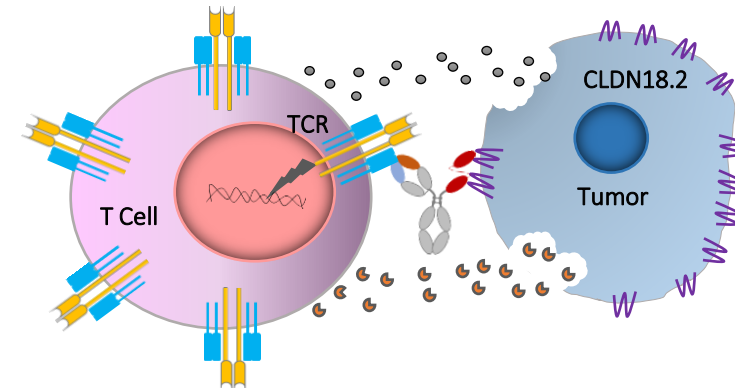
- High avidity binding
- Heavy chain only
- Fully human

HARBOUR BIOMED

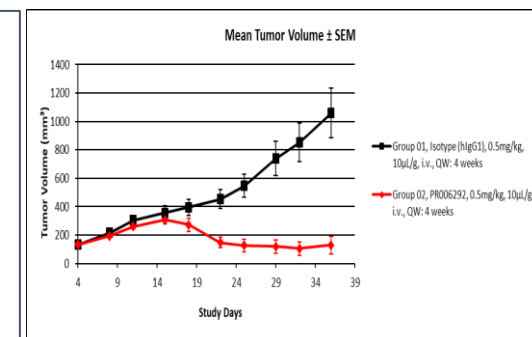
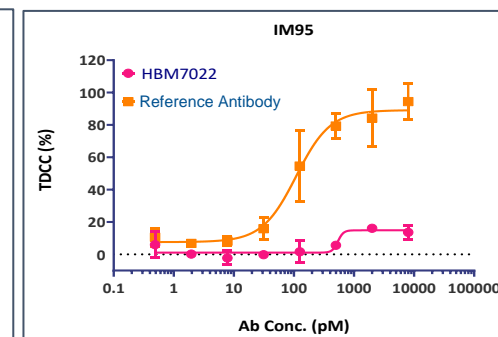
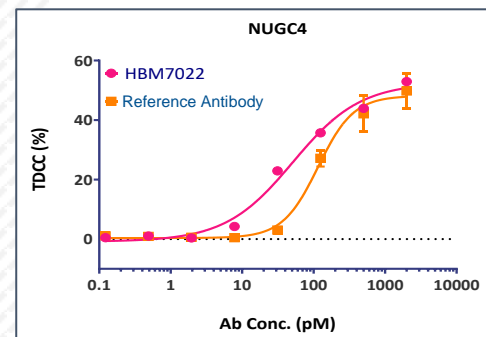


AstraZeneca

MOA of HBM7022



HBM7022 Pre-clinical Data



HBM7008 (B7H4x4-1BB)

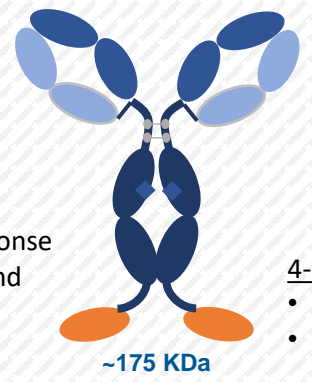
First-in-Class Bispecific Antibody from HBICE® Platform



Highlights

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

HBM7008



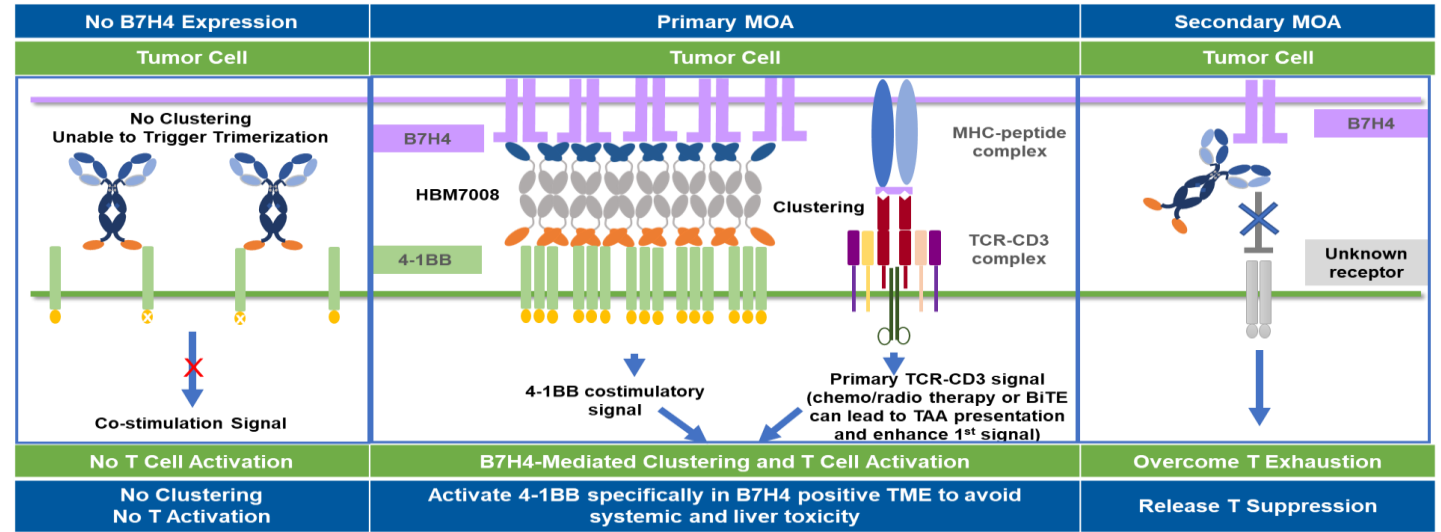
B7H4 arm:
Human B7H4 H2L2 antagonist mAb

4-1BB arm:

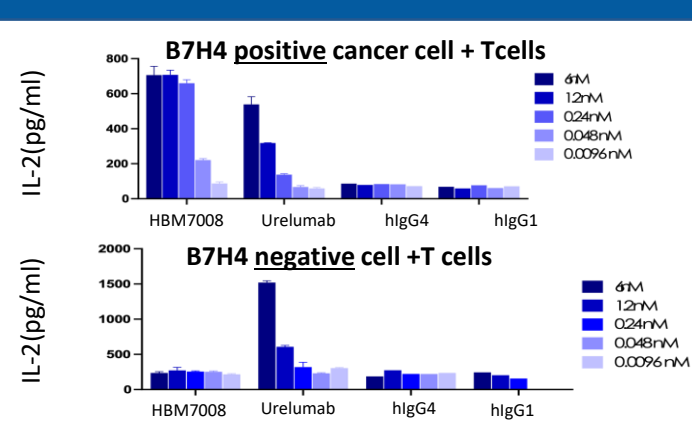
- VH from HCAb,
- B7H4-dependent T activation

Fc domain:
LALA mutation to reduce systematic immune response by crosslinking with Fc and ADCC effect

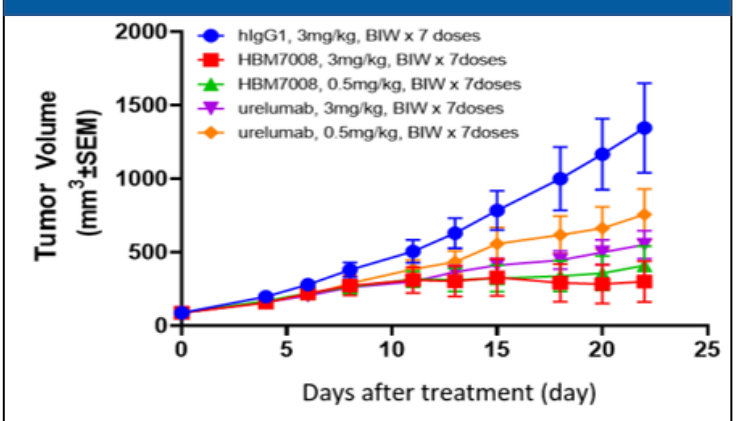
~175 KDa



B7H4 dependent 4-1BB activation and T cell stimulation



Mouse Tumor Model Efficacy



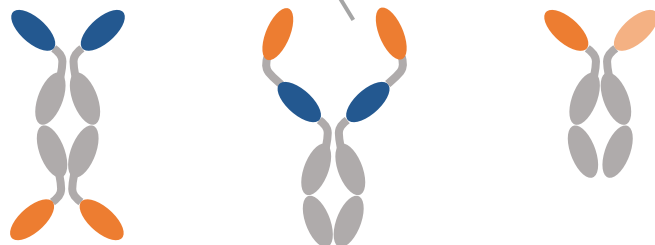
HBICE[®]: Optimized Molecule Generation with Rigorous Scientific Design

HBICE[®] – HCAb-Based Bispecific Platform for Immune Cell Engagers

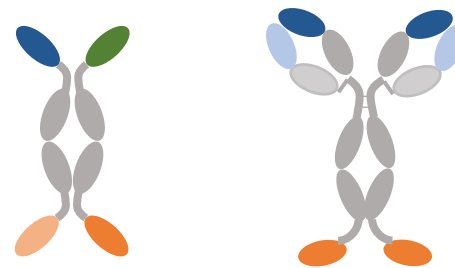
Advantages:
Unique and versatile geometric formats & flexibility

- ❑ Rational bispecific molecular design based on specific target binding/immune synapse charities
- ❑ Smaller size for better tissue penetration
- ❑ Fully human sequences with reliable CMC developability

02
Tandem VH improve specificity, accessibility and avidity



01
Flexible geometry adapts to crosslinking/clustering/dual binding/immune synapse formation



03
2 +1 format confers cooperative binding to tumor antigen

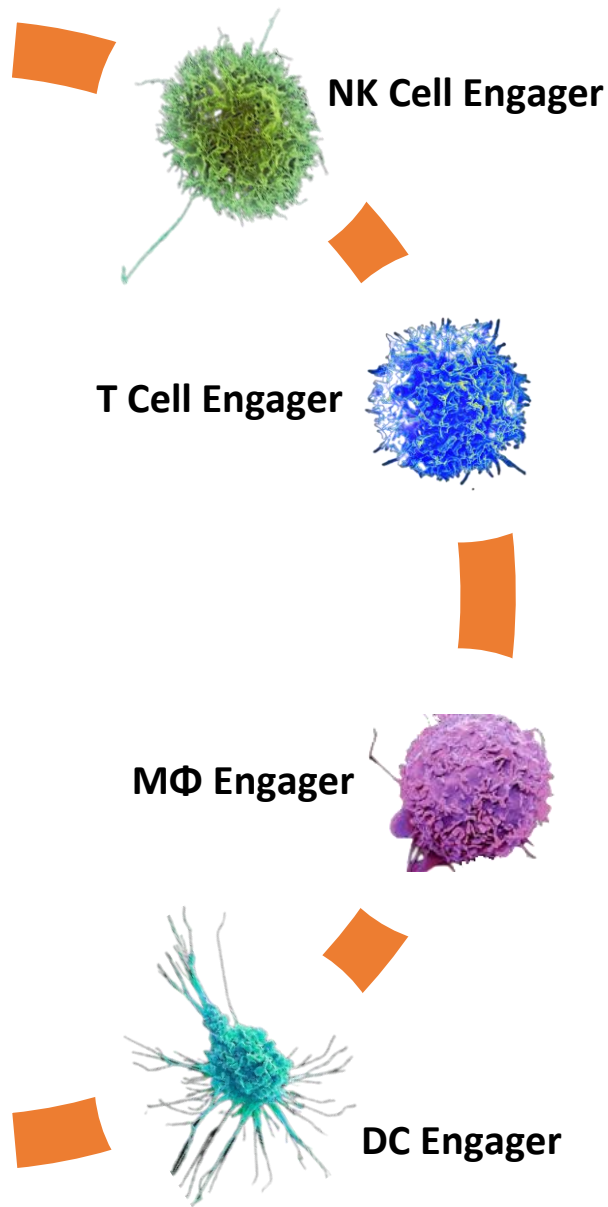


04
Fully human from mouse, less risk on developability and immunogenicity

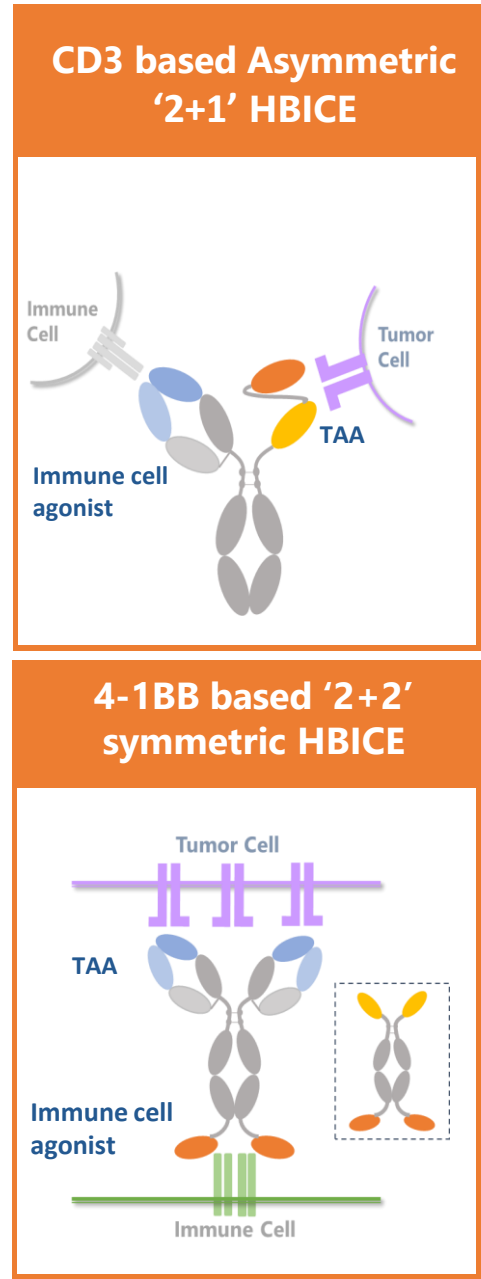
05
Intact silent Fc extends half-life, avoid Fc crosslinking and ADCC

Building Immune Cell Engager Bispecifics with Cutting Edge Technology

HBICE[®] targeting various types of immune cells



NKp30 HBICE [®]	TAAxNKp30 HBM7025
CD3 HBICE [®]	BCMAxCD3 HBM7020 華蘭生物 HUALAN BIO
	B7H4xCD3 HBM7004
	CLDN18.2xCD3 AZD5863/HBM7022 AstraZeneca
4-1BB HBICE [®]	B7H4x4-1BB HBM7008 cullinan ONCOLOGY
	MSLNx4-1BB HBM7021
CD28 HBICE [®]	PDL1xCD28 HBM7024
CD40 HBICE [®]	PDL1xCD40 HBM9027
	TAAxCD40 HBM7023



Accelerated Growth: Business Model Expansion

Mr. Weihao Xu

Chief Financial Officer and Chief Business Officer

Value Creation Through Business Development

Cash Received
2022 - 2023

> \$ 80 M

Collaborations achieved
from 2022 to 2023

Potential Milestones

~ \$ 2 B

Potential milestones generated
from collaborations since 2023

Royalties

Tiered royalties on
potential net sales



Harbour Therapeutics: Diversified Business Model to Advance Our Portfolio

INTERNAL DEVELOPMENT

- ✓ Retain the max value of products
- ✓ Comprehensive accumulation on experience and expertise

HBM4003 HBM1020 HBM1022...

CO-DISCOVERY / CO-DEVELOPMENT

- ✓ Retain strategic value of asset in certain territory/rights and provides potential ongoing revenue stream
- ✓ Pre-defined commercial arrangements

HBM7008
cullinan
ONCOLOGY

HBM9014
Yinuo

HBM9378
KELUN
BIOTECH

JOINT VENTURE

- ✓ Selected partners on special diseases or technology area
- ✓ Leverage breakthrough sciences and develop innovative programs

HBMAT



恩凯赛药
NK CELLTECH

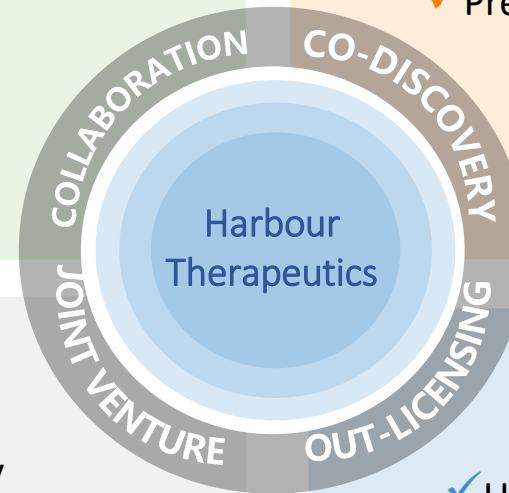
OUT-LICENSING

- ✓ Upfront payment, fees and milestones
- ✓ Royalties based on net sales

HBM7022
AstraZeneca

3 Assets
HUALAN BIO

HBM9161
CSPC



■ Collaboration with Cullinan In 2023

■ Co-development on HBM7008 Drives Speed and Delivers both Short/Long Term Values

Principal Terms

HARBOUR
BIOMED


cullinan
ONCOLOGY



Upfront Payment

• **\$25 million**



Milestone Payment

• **Up to \$600 million**



Royalties

• **Up to high teens**



Collaboration and Co-development

- US development and commercial rights
- Access to EU & Australia Patient population



Validation of the assets and company's platform



Integrate the internal and external resources

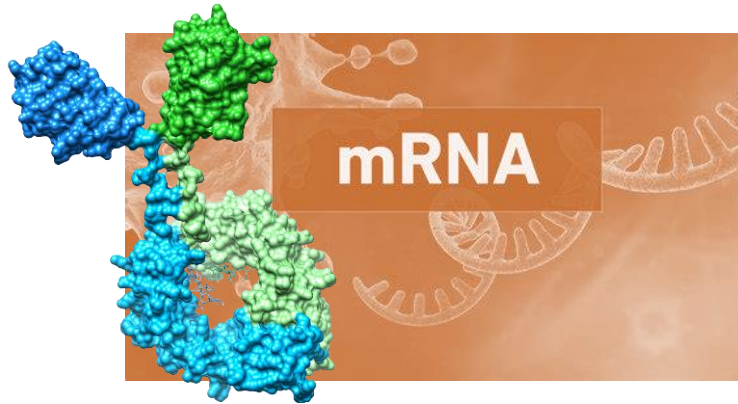


Expand cooperation network with global strategic perspective

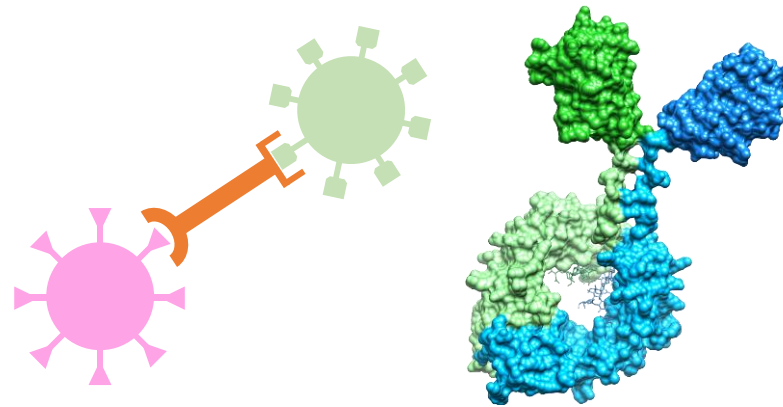


Nona's Technology Platforms Have been Endorsed by Renowned Partners

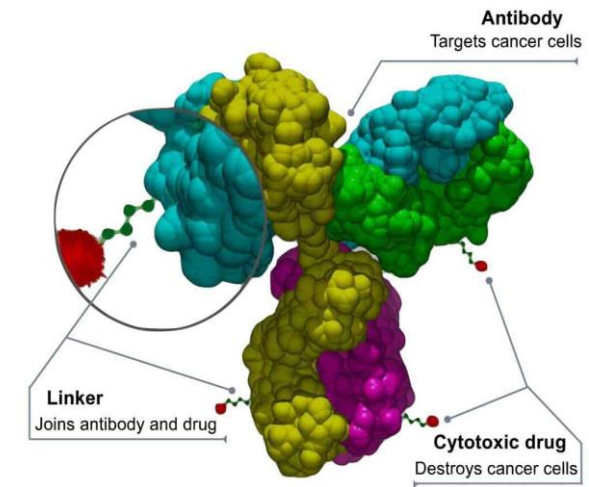
moderna



Dragonfly



MYTHIC THERAPEUTICS



Moderna's appetite for antibody tech spurs \$6M bet on Nona's heavy chain only platform

By Nick Paul Taylor • Nov 11, 2022 07:30am

Moderna Harbour BioMed antibody messenger RNA



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

Published: Nov 21, 2022



Nona Biosciences Enters into HCAb Based Antibody Discovery Collaboration Agreement with Mythic Therapeutics



Financial Results

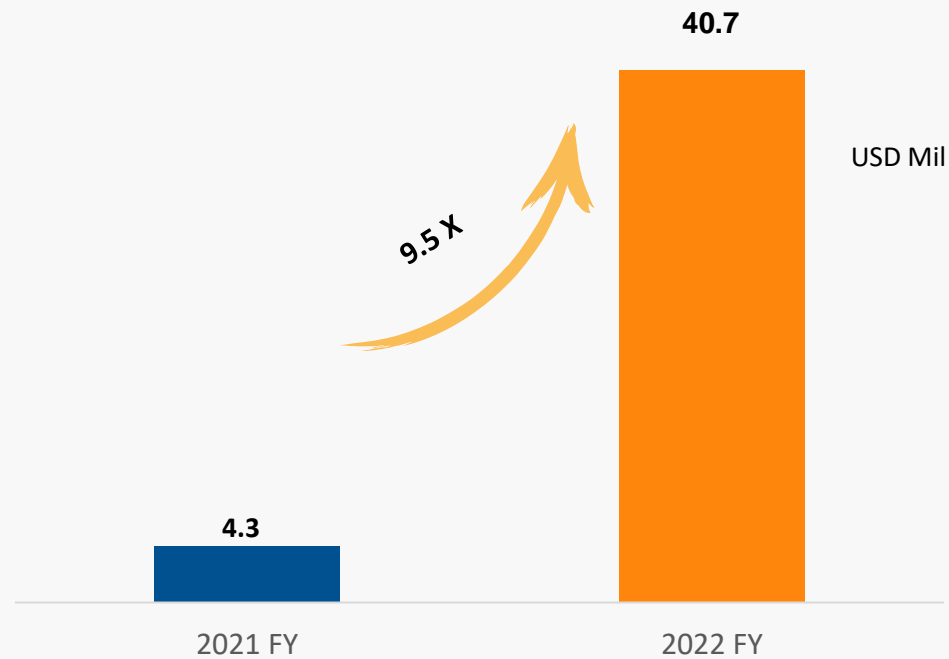
Mr. Weihao Xu

Chief Financial Officer and Chief Business Officer

Revenue Significantly Increased in 2022

Revenue

Total revenue significantly increased from US\$4.3 million for the year 2021 to US\$40.7 million for the year 2023



Abundant cash generated from company's assets and platform, primarily due to:

Upfront payment from :

AstraZeneca 


CSPC

Robust business growth in Nona:



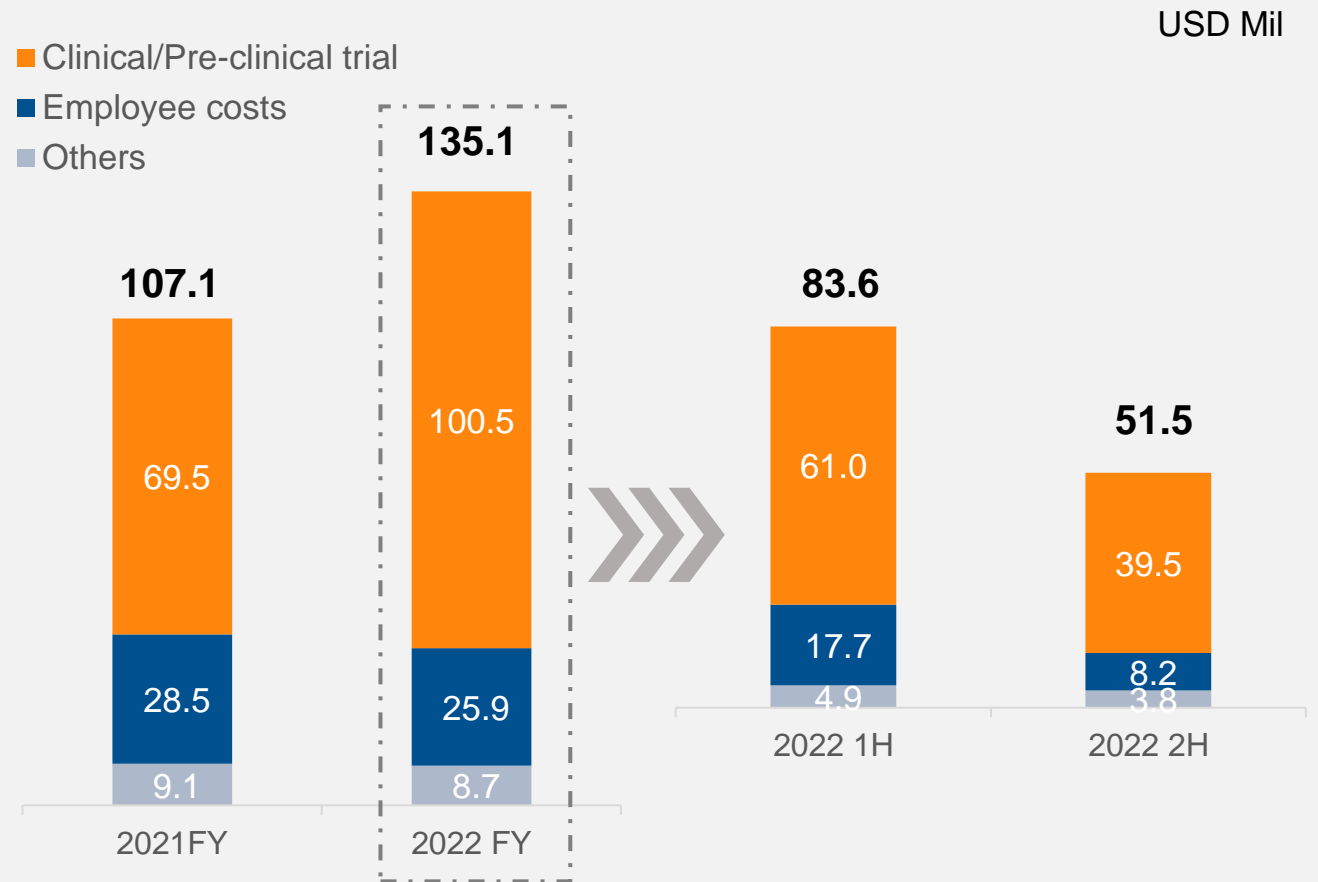
Multiple ADC collaborations

Committed to R&D for Sustained Business Growth

Research and development costs

R&D expenses increased from US\$107.1 million for 2021 to US\$135.1 million for 2022, was mainly due to increased investments in our key clinical programs.

R&D expenses decreased significantly from US\$83.6 million for 2022 1H to US\$51.5 million for 2022 2H

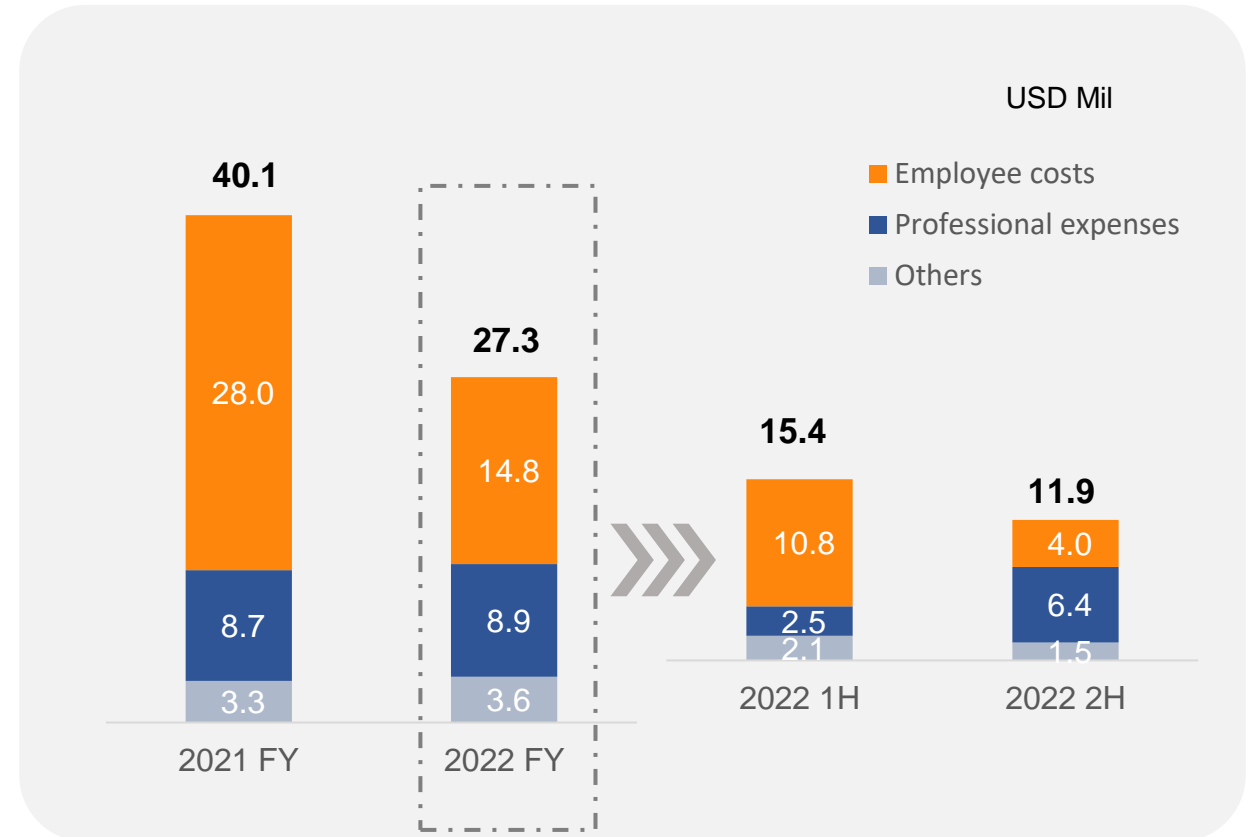


Control on Administrative Expenses to Enhance Operational Efficiency

Administrative expenses

Administrative expenses continued to decrease

- (i) a decrease in employee cost from US\$28.0 million for the year ended 31 December 2021 to US\$14.8 million for the year ended 31 December 2022
- (ii) a decrease in employee cost from US\$10.8 million for the six months ended 30 June 2022 to US\$4.0 million for the six months ended 30 December 2022



Loss for the period

- ☐ Loss for the period decreased US\$ 0.6 million from US\$137.9 million for 2021 to US\$137.3 million for 2022.

Healthy Cash Position to Drive Value Creation

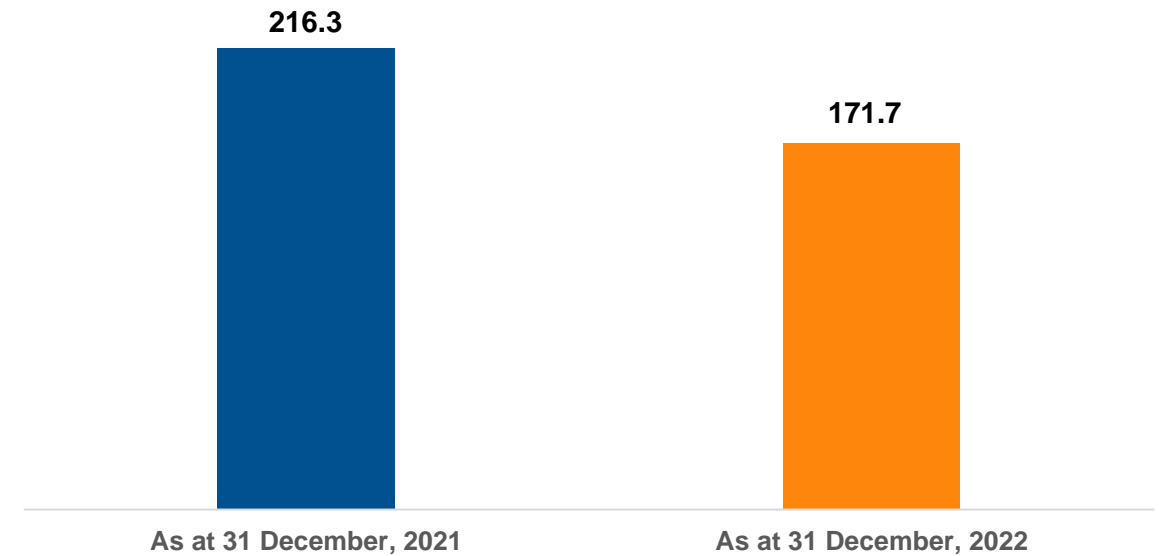
Summary of Consolidated Statements of Financial Position

USD Mil	31 December	31 December
	2022	2021
Non-current assets	23.1	41.5
Current assets	209.0	240.9
Include:		
Cash and bank balances	<u>171.7</u>	<u>216.3</u>
Current liabilities	75.0	41.1
Net current assets	133.97	199.8
Non-current liabilities	64.6	18.4
Net assets	92.5	222.9

Cash and bank balances

Cash and bank balances decreased from US\$216.3 million to US\$171.7 million.

USD Mil



Outlook: Deliver Value through Sustainable Growth

Dr. Jingsong Wang

Founder, Chairman of the Board and Chief Executive Officer

Harbour BioMed: Strong Growth with Multiple Catalysts in 2023

Harbour Therapeutics

□ HBM9161 Near Commercial Stage

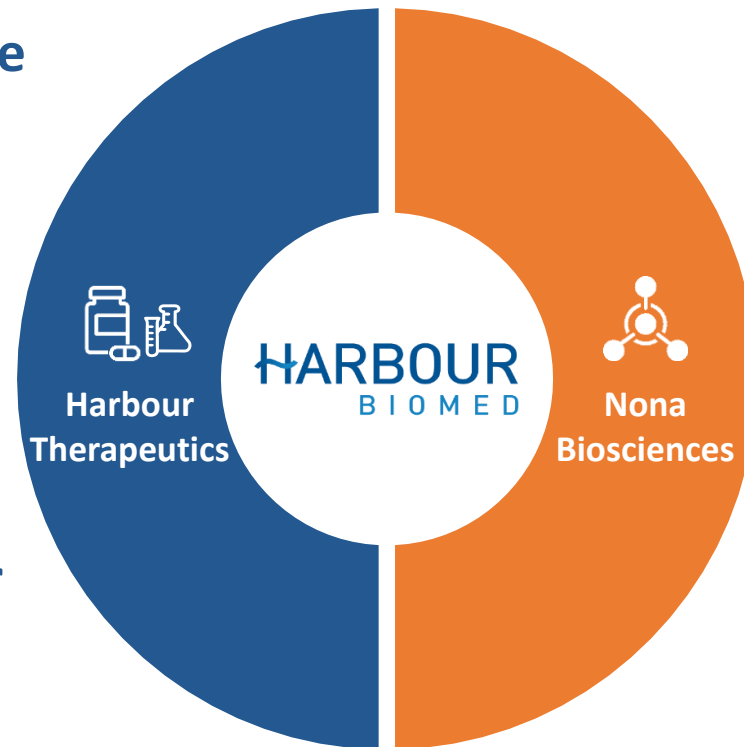
- Positive results of pivotal trial
- BLA submission in 2023

□ HBM4003 Enabling Pivotal Trial

- Potential BIC therapy on melanoma and NEC
- Pivotal trial design and regulatory pathway discussion with regulatory agencies

□ A Leader in Immune Cell Engager

- Validated by MNCs
- Robust portfolio
- Patent protection proprietary platform



Nona Biosciences

□ Advance Breakthrough Technology Innovation

- Antibody PLUS
- Next generation therapeutics

□ Expand Global Collaboration network

- MNCs
- Start-ups & biotech
- Academic institutions

□ Execute Transformational Business Model

- Open access
- No barrier entry
- Global innovation enabler

Q & A



THANK YOU

