

2021 Annual Results Conference Call Presentation

HBM HOLDINGS-B, 02142.HK

25 March 2022





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- 01** 2021 Overview and Highlights
- 02** Innovative and Differentiated Portfolio
- 03** Financial Results
- 04** Q&A

HBM Global Innovation Ecosystem Leads Next-Gen Therapeutics

HBM Innovation, Global Vision



3 Industry Leading
Technology Platforms



Worldwide Clinical Sites
(US, China, Europe, Australia, etc.)

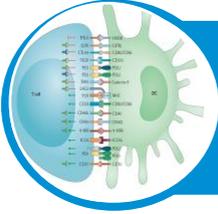
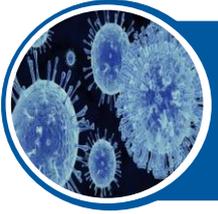
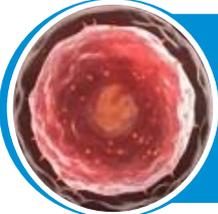
3 Global Research Centers

110+ Discovery Scientists



HBM Global Innovation Ecosystem Leads Next-Gen Therapeutics

HBM Next-Gen Innovative IO Therapy Strategy

	Immune Cell Engager	HBM7008 HBM7020 ...
	Novel Immune Evasion Pathway	HBM1020 HBM7008 ...
	Treg Depletion	HBM4003 HBM1022 ...
	Innovation in Novel Frontier NK/ADC	Undisclosed ...

Scientific Strategy is Warranted by Cutting-edge Technologies

1. T/NK cell infiltration/proliferation increasing via immune cell engager (HBICE, SBC, Fc engineering)
2. Innovative targets and pathways of the B7 family (H2L2, HBICE, mRNA/DNA immunization)
3. Depletion of regulatory T cells (eADCC, Afucosylation, HCAb)
4. Innovative products in novel frontier NK/ADC (HBICE, HCAb)

Significant Advancements were Achieved both in Portfolio Products and Business Development in 2021

Portfolio Products

2 Ph 3 Clinical Trials

10 Ongoing Clinical Trials

- HBM9161 *MG, TED, NMOSD, ITP*
- HBM9036 *DED*
- HBM4003 *mono trial*
- HBM4003 *combo trial for Melanoma*
- HBM4003 *combo trial for NSCLC*
- HBM4003 *combo trial for HCC*
- HBM4003 *combo trial for NEC/NET*

3 Clinical Studies Milestones

Data Readout

- HBM9161 *MG Ph 2*
- HBM4003 *mono trial Ph 1*

Data Analysis

- HBM9036 *Ph3 1st Interim Analysis¹*

7 IND Approvals

- HBM9161 *CIDP, PV*
- HBM4003 *combo trial for NSCLC*
- HBM4003 *combo trial for HCC*
- HBM4003 *combo trial for NEC/NET*
- HBM7008²
- HBM9378³

6 Global Academic Data Presentation

- HBM4003 *at ESMO*
- HBM9161 *MG at WCN*
- HBM9036 *at Int Ophthalmol⁴*
- HBM1020 *at AACR*
- HBM7022 *at AET*
- Immune Cell Engager *at CES*

Business Development

- Collaborated with **Dana-Faber**, a teaching hospital of Harvard Medical School, to develop novel oncologic drugs including bispecific antibodies and CAR-T
- Further advanced collaboration with **Mount Sinai**, received gains from COVID-19 product
- Entered into strategic partnership with Shanghai NK Cell Technology Limited (**NK Cell Tech**) as an incubator to develop novel NK cell therapeutics
- Collaborated with **BioMap** to research and develop novel antibodies with integration of AI technology



Further Expanded Global Leadership Team, Enhanced Corporate Advancement in 2021

Team Expansion



Amy Que
PhD

Chief Technology Officer

- Former Senior VP, Quality at Innovent Biologics
- Former Principal Scientist and R&D Lead at Pfizer, Genentech and Wuxi Biologics
- PhD, Indiana University Bloomington



Yingying Chen
PhD MBA

Chief Financial Officer

- Former Managing Director, Head of Healthcare at GF Investments HK and CMBC International
- Rich investment banking experience at Deutsche Bank and UBS Investment Bank
- Former Research Scientist, Pfizer
- MBA, University of Michigan; PhD, University of Minnesota



Weihao Xu
MPhil

Chief Strategy Officer

- Former Chief Finance Officer at Alphasab Oncology, CASI Pharmaceuticals, and 111 Inc.
- Former Portfolio Manager for Matthews Asia responsible for global equity investments



Corporate Advancement

Set-up 8500 m² facility in Suzhou in 2021
Enter into production in 2022



Enrolled into Hang Seng Composite Index



Enrolled into Shenzhen-Hongkong Stock Connect



01 2021 Overview and Highlights

02 Innovative and Differentiated Portfolio

03 Financial Results

04 Q&A



First-in-class and Best-in-class Clinical Assets



■ HBM
 ★ Registrational Clinical Trial
 ● In-license Program
 ● Program from Harbour Discovery Platforms

a. Melanoma, HCC, RCC, and Other Advanced Solid Tumors
 b. Melanoma, HCC, NEC/NET and Other Advanced Solid Tumors, HCC is in Ph 1
 c. NSCLC and Other Advanced Solid Tumors

1. HBM7008 IRB approval in Australia February 2022
 2. HBM9378 IND approval in China in February 2022

Tanfanercept (HBM9036): A Differentiated Therapeutics to Treat the Growing Prevalence of Moderate-to-severe Dry Eye Disease

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

HBM9036 Ph 3 Development Achievements

2021

- **Completed** first dosing of Ph 3 clinical trial in March 2021
- Target to recruit around 640 patients at 30+ sites
- **Completed** half of patients enrollment

2022

- **Completed** the first interim analysis of Ph 3 trial in January 2022

Excellent Safety Profile

Highly Comfortable

Similar drop comfortable score with placebo

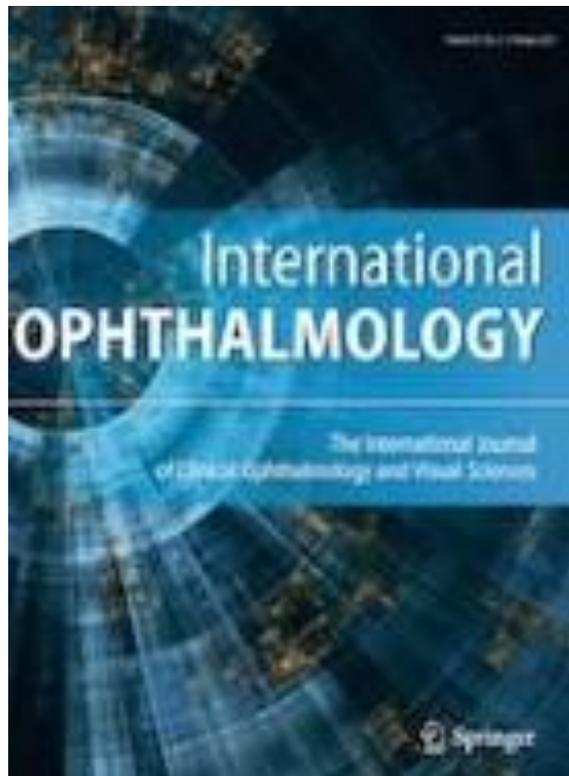
Rapid Onset

4 weeks vs. 3-6 months

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

Tanfanercept (HBM9036): A Differentiated Therapeutics to Treat the Growing Prevalence of Moderate-to-severe Dry Eye Disease

Positive Results of HBM9036 Ph 2 Clinical Data, Published on “International Ophthalmology”



Int Ophthalmol
https://doi.org/10.1007/s10792-022-02245-1

ORIGINAL PAPER

TNF- α inhibitor tanfanercept (HBM9036) improves signs and symptoms of dry eye in a phase 2 trial in the controlled adverse environment in China

Yanling Dong · Shuang Wang · Lin Cong · Ting Zhang · Jun Cheng · Nannan Yang · Xiaohong Qu · Dongfang Li · Xueying Zhou · Holly Wang · Michael Lee · Meng Wang · Stephen Chen · George W. Ousler · Xiaoliang Chen · Lixin Xie

Received: 28 October 2021 / Accepted: 10 February 2022
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Abstract
Purpose This study evaluated the clinical safety and efficacy of tanfanercept (HBM9036) ophthalmic solution as a novel treatment for dry eye disease (DED) in a controlled adverse environment (CAE) study conducted in China.
Methods In a single-center, double-masked, randomized, placebo-controlled study, 100 patients received 0.25% tanfanercept, or placebo, twice daily for eight weeks. A mobile international CAE[®] DE Model was used for patient selection with a standardized challenge endpoint. Primary efficacy endpoint was fluorescein inferior corneal staining score (ICSS) pre- to post-CAE challenge from baseline. Secondary endpoints included Schirmer’s Tear Test, Tear-Film Break-Up Time, Ocular Discomfort Score, Ora Calibra[®] Ocular Discomfort and 4-Symptom Questionnaire, total corneal staining score (TCSS), and drop comfort. Signs and symptoms were assessed both pre- and post-CAE to evaluate the efficacy of tanfanercept on both environmental and CAE endpoints.
Results The tanfanercept treatment group showed improvement in ICSS pre- to post-CAE change from baseline scores when compared to placebo (-0.61 ± 0.11 and -0.54 ± 0.11 , respectively; mean difference = 0.07 , $p=0.65$). TCSS pre-post-CAE change from baseline scores was also in favor of active when compared to placebo (-1.03 ± 0.21 and -0.67 ± 0.21 , respectively; mean difference = 0.37 , $p=0.23$). Schirmer’s score improvement was demonstrated in favor of active (1.87 ± 0.62 mm) as compared to placebo (1.28 ± 0.62 mm; mean difference = 0.59 mm, $p=0.50$). Change from baseline in mean Tear-Film Break-up Time favored active treatment over placebo (mean difference = 1.21 s, $p=0.45$). Notably, the tanfanercept showed more obvious benefits for each DED sign in a subgroup of subjects ≥ 35 years of age. Tanfanercept was well tolerated with no serious adverse events occurring during the study.
Conclusion Tanfanercept demonstrated improvements in favor of active as compared to placebo in the signs of DED, being safe and well tolerated. These data support further evaluation of tanfanercept for the treatment of DED in China.

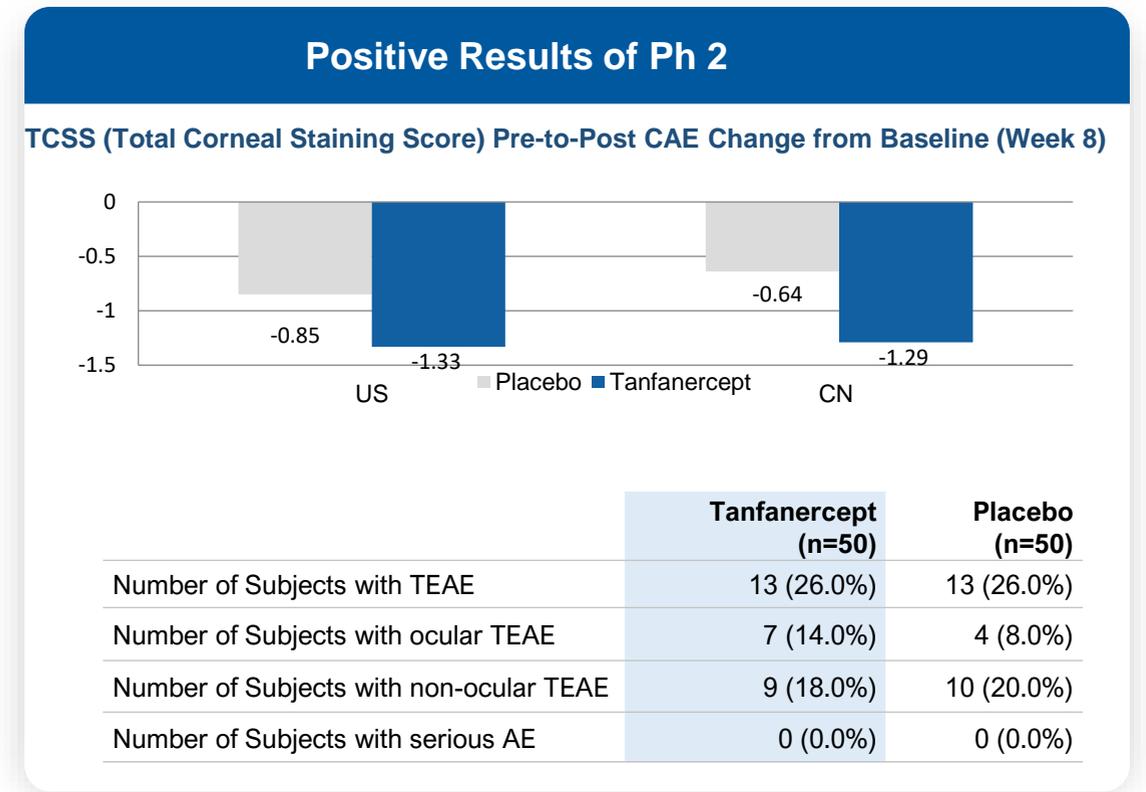
Y. Dong · S. Wang · L. Cong · T. Zhang · J. Cheng · N. Yang · X. Qu · D. Li · L. Xie (✉)
Qingdao Eye Hospital of Shandong First Medical University, State Key Laboratory Cultivation Base, Shandong Provincial Key Laboratory of Ophthalmology, Eye Institute of Shandong First Medical University, Qingdao, China
e-mail: lixin_xie@hotmail.com

X. Zhou · H. Wang · M. Lee · M. Wang · S. Chen · X. Chen
Harbour BioMed, Shanghai, China

G. W. Ousler
Ora Inc, Andover, MA, USA

Published online: 22 February 2022

Springer



Tanfanercept showed consistent and strong treatment benefits. It was well-tolerated without serious treatment emergent adverse events (“TEAEs”) or serious adverse events (“SAEs”)

Batoclimab (HBM9161): A Breakthrough Therapeutics for IgG Mediated Autoimmune Diseases with a Pipeline-in-a-product Approach

2021

- **MG**

Achieved positive Ph 2 data readout in July
 Achieved Ph 3 FPF in September, reflecting accelerated advancement following positive Ph 2 study

- **NMOSD**

Completed Ph 1b/2a data analysis

- CIDP IND approval
- PV IND approval

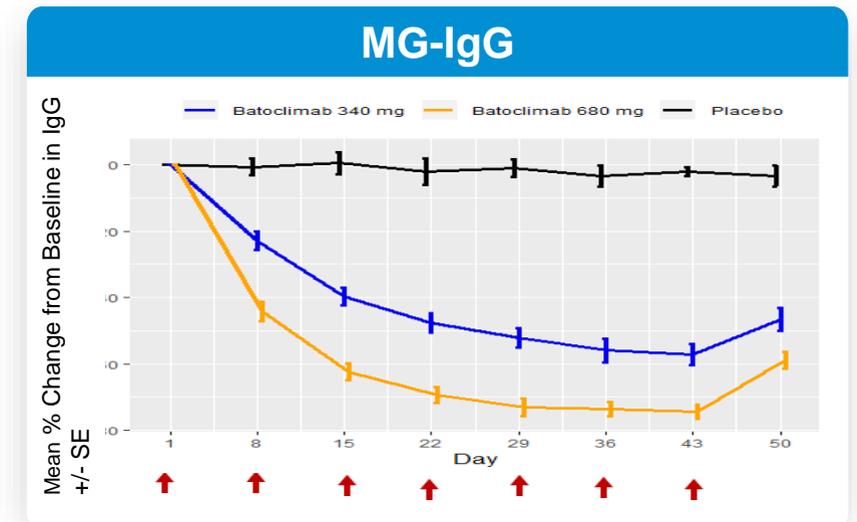
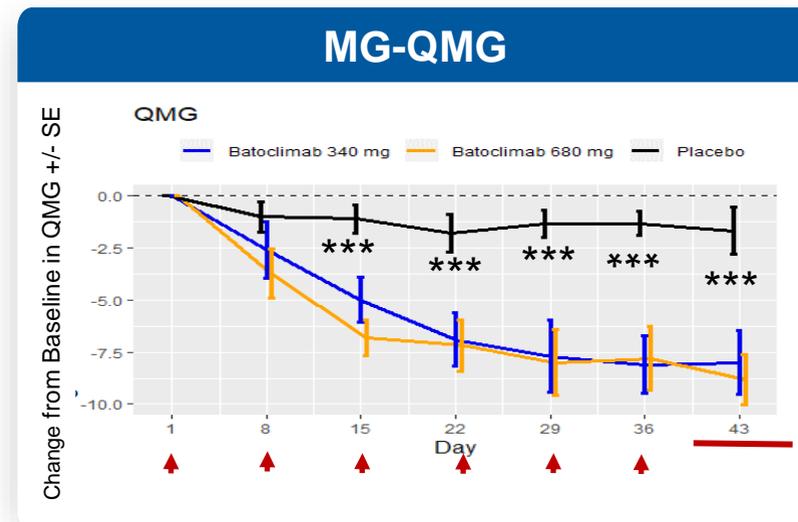
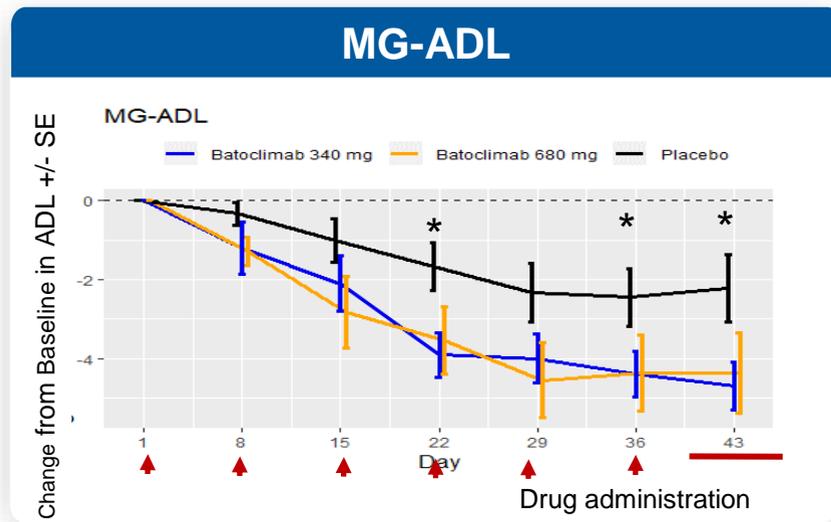
- **GO (TED)**

Initiated Ph 2/3 study and completed FPF in October

- **ITP**

Completed Ph 2 data analysis

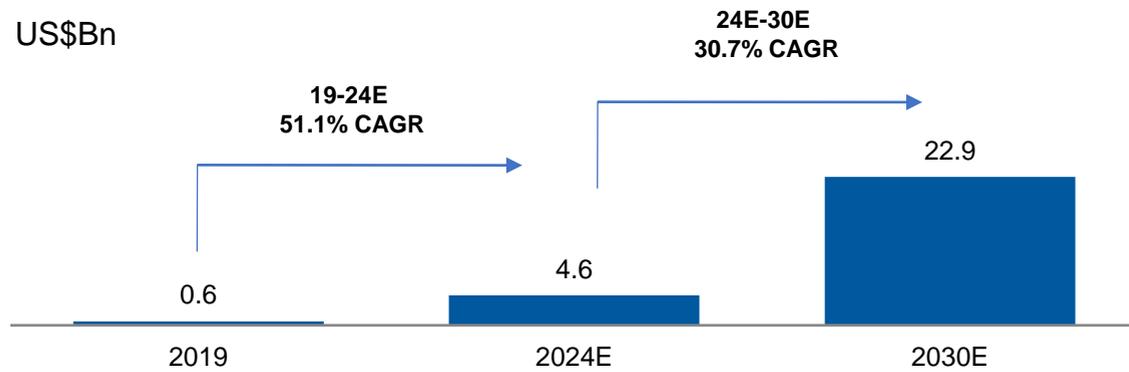
MG Positive Ph 2 Study Results, Presented at the 25th World Congress Neurology (WCN)



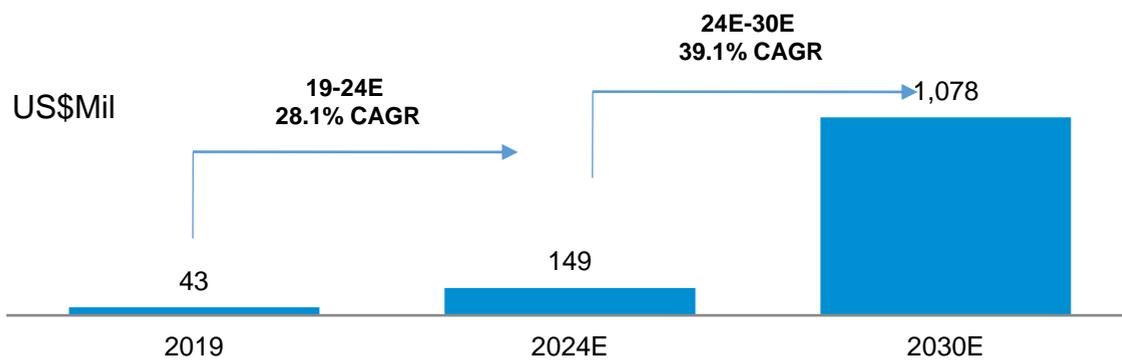
Batoclimab (HBM9161): A Breakthrough Therapeutics for IgG Mediated Autoimmune Diseases with a Pipeline-in-a-product Approach

Huge Market Potential

Pipeline-in-a-Product: 60~70 pathogenic IgG mediated autoimmune diseases



China Biologics for Immunological Diseases Treatment



China MG Market

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
- Well-tolerated, majority of AEs are mild and/or moderate



Convenient Treatment

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

HBM4003: Next-Gen HCAb Anti-CTLA4 Antibody with Potential to Become the Mainstream of Immuno-Oncology Therapy

HBM4003 is endorsed by global leading experts in IO therapeutics aiming 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



Dr. Robert Kamen

Venture Partner at Third Rock Ventures
Former President & Unit Head of Abbott Bioresearch Centre



Dr. Jon Wigginton

Chief Medical Officer, Cullinan Oncology; Advisor of MPM Capital
Former Therapeutic Area Head of Immuno-Oncology, Early Clinical Research at BMS
Former President of the Society for Immunotherapy of Cancer



Dr. Alexander Zukiwski

Chief Medical Officer at CASI Pharmaceuticals
Former Chief Executive Officer and Chief Medical Officer of Arno Therapeutics
Former Chief Medical Officer and Executive Vice President of Clinical Research at MedImmune



Dr. John M Kirkwood

Distinguished Service Professor Medicine, University of Pittsburg
Usher Professor of Medicine, Dermatology, Clinical and Translational Science at The University of Pittsburg School of Medicine
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

HBM4003: Next-Gen Anti-CTLA4 Antibody with Potential to Become the Mainstream of Immuno-Oncology Therapy

Global Development in 2021

Monotherapy

- Completed Ph 1a clinical trial, published at ESMO
- Completed Ph 1b/2 patient enrollment, submitted to ASCO

Combination Therapy

- 3 IND approvals
- Completed Ph 1a trials for Melanoma and NSCLC, submitted to ASCO and WCLC
- Initiated Ph 1b/2 trial for Melanoma
- Initiated Ph 1 trials for HCC, NEC/NET

HBM4003 Competitive Advantages

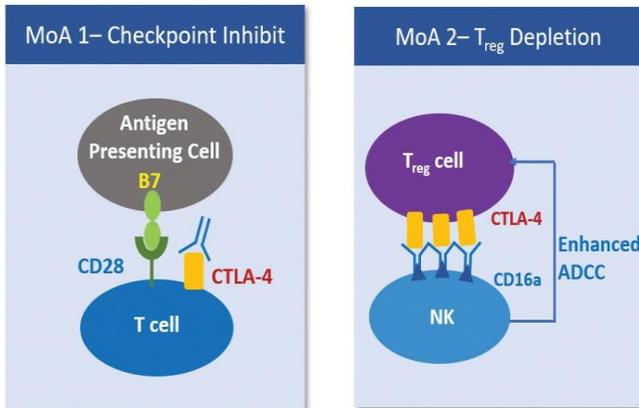
Deplete intra-tumoral Treg cells via enhanced ADCC strategy

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

Huge potential for combination therapies

■ HBM4003: Next-Gen Anti-CTLA4 Antibody with Potential to Become the ■ Mainstream of Immuno-Oncology Therapy

Strong Clinical Evidence to Demonstrate Next-Gen Treg MoA Therapeutics



Encouraging Results on HBM4003 Mono Therapy Phase I

- Initial efficacy indicating great potential to break the barrier of current IO therapy
- 2 patients with PD-1 refractory HCC (Australian, China) have been confirmed as PR, tumor reductions were over **60%** via RECIST, another CRPC patient from Australia had PSA response of more than **50%** reduction. All responses have been durable
- Well tolerated, majority of TRAE were G1/2; \geq G3 TRAE was 16.7%; diarrhea/colitis was the most frequent severe TRAE; no fatal TRAE

Positive Results on HBM4003 Combination Therapy Phase 1a

- Promising efficacy, Melanoma and Urothelial Carcinoma patients were confirmed as PR
- Well tolerated, \geq G3 TRAE was 13%, no fatal TRAE. No new signals or unexpected toxicities in combo therapy

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

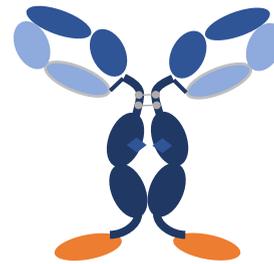
Obtained the IRB approval to commence Ph 1 trial in Australia in 2022

Competitive Advantages and Highlights

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

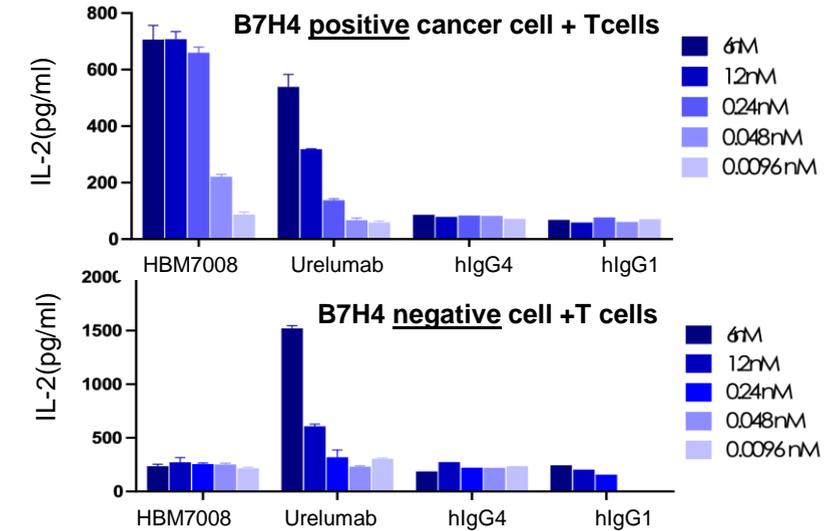
The world's first bispecific antibody against B7H4x4-1BB

'2+2' symmetric HBICE (S-HBICE)

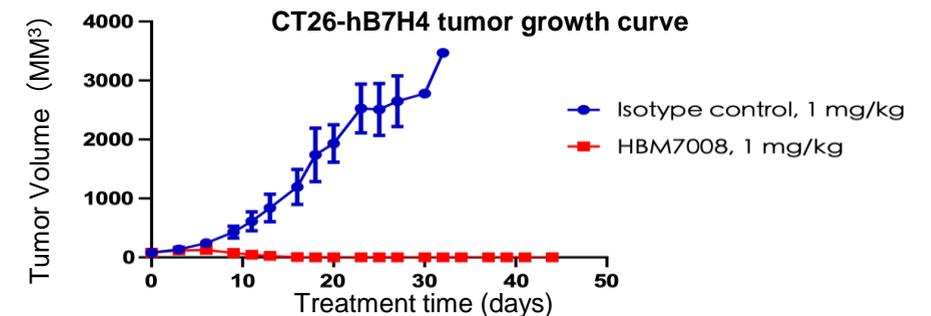


~175 KDa

B7H4 dependent 4-1BB activation and T cell stimulation



HBM7008 completely leads tumor regression in B7H4 positive syngeneic model



HBM9378 (TSLP): Next-Gen Immune Therapeutics with Potential to Break Current Treatment Limitation

IND Approval in February 2022, a fully human antibody targeting TSLP, for the treatment of moderate-to-severe asthma

Significant Clinical Unmet Needs for Moderate-to-severe Asthma

- 45.7 million adult asthma patients (≥20 years) globally, 1.2 million severe asthma in China¹⁻²
- 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



- High intensity treatment (23.5%)
- Difficult to treat asthma = poor asthma control + high intensity treatment (17.4%)
- Severe refractory asthma = poor asthma control + high intensity treatment + good adherence + correct inhaler technique (3.7%)

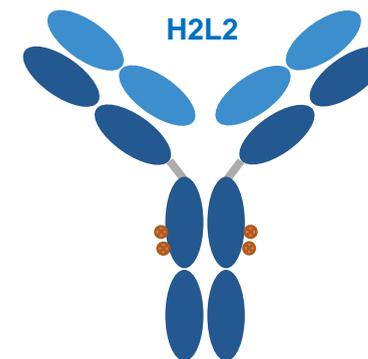


Figure based on data from the Netherlands ([Hekking et al. 2015](#))

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



First-in-class and Best-in-class Preclinical Assets

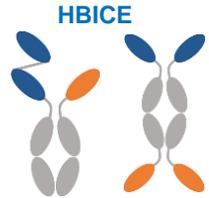
Project	Target	Indication	Commercial Rights	Status	
				Discovery	Pre-Clinical
HBM7020	BCMA×CD3	Multiple Myeloma	Ex-Greater China ¹	▶	
HBM1020	B7H7	Solid Tumors	Global	▶	
HBM1022	CCR8	Solid Tumors	Global	▶	
HBM1007	CD73	Solid Tumors	Global	▶	

(1) Greater China rights out-licensing to Hualan Genetics

Cutting-edge Fully Human Antibody Platforms with Global IP Enable

Sustained Invention of Novel Molecules

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



Advantages:
Unique and versatile geometric formats & flexibility

\$1.6 B \$3.2 B

HCAb – Next-Gen Heavy-Chain Antibody Platform



Advantages:
Unique fully human HCAb, versatile for broad applications

\$4.8 B \$2.5 B

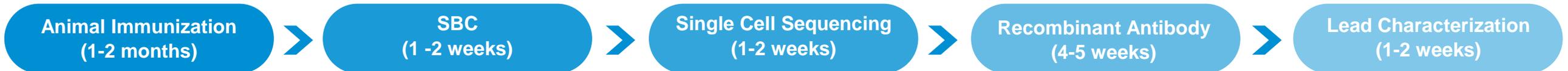
H2L2—Full IgG Antibody Discovery Platform



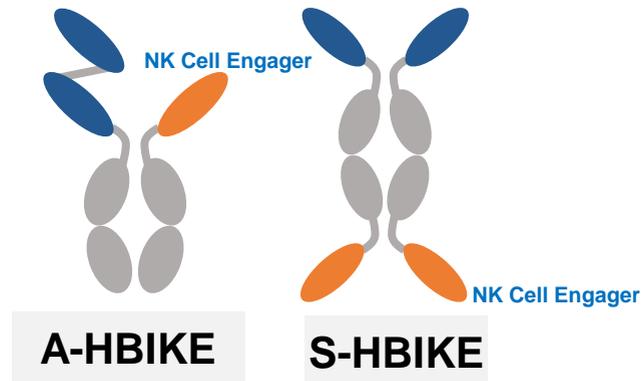
Advantages:
Robust and highly efficient, clinically validated

\$178M \$1.1 B

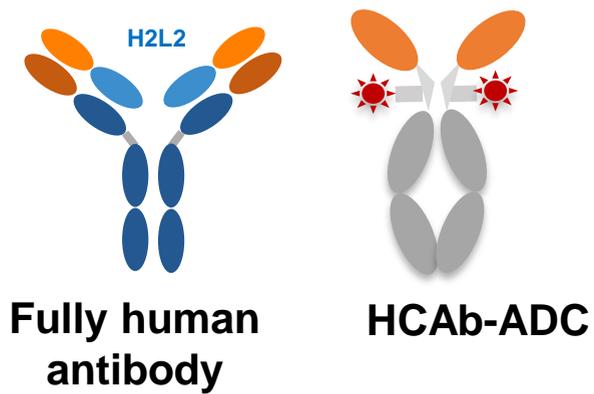
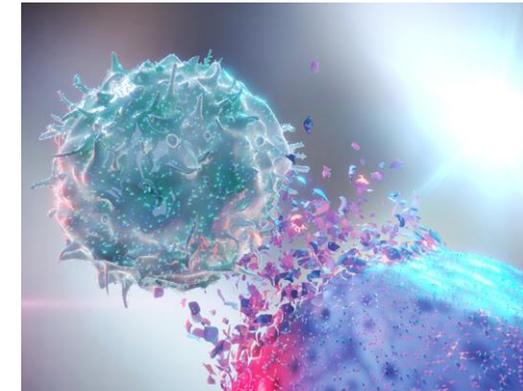
Antibody generation with Single B Cell cloning method in 3-5 months



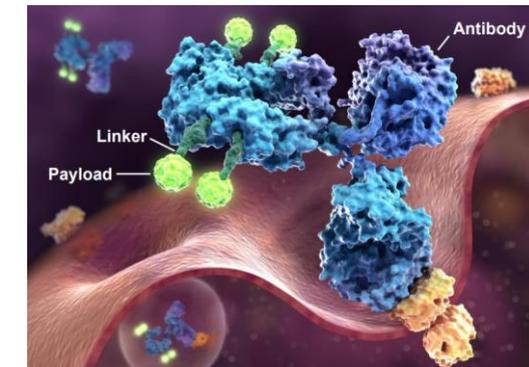
HBM Proprietary Antibody Technologies Continuously Drive Next-Gen of Therapeutics



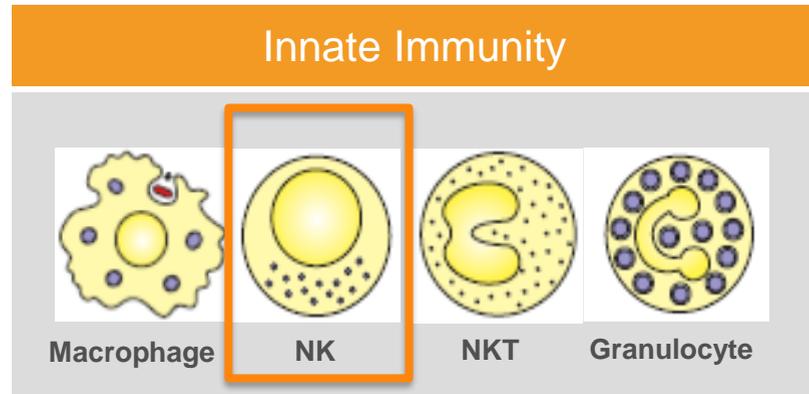
NK Cell Engager Bispecific (HBIKE)



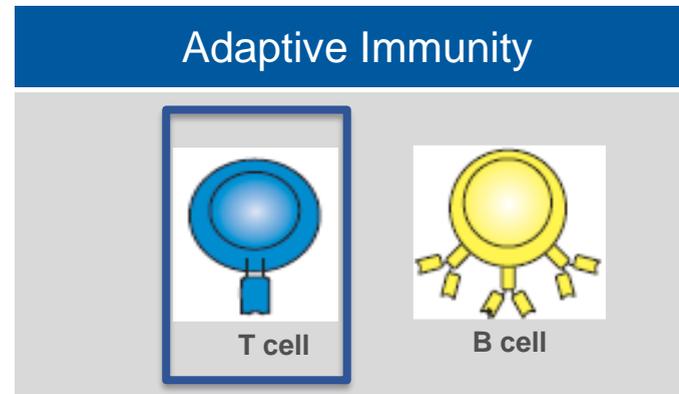
Next-Gen ADC



Innate Killer - NK Cell Engager is the Next Innovative Wave in Bispecific Field

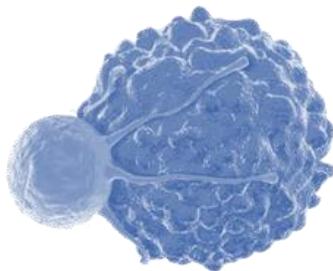


Immediate response (hours), whole body
 Selective but non-antigen specific
 Gatekeeper of adaptive immunity, also memory



Antigen specific
 Memory, days, from lymphoid organs

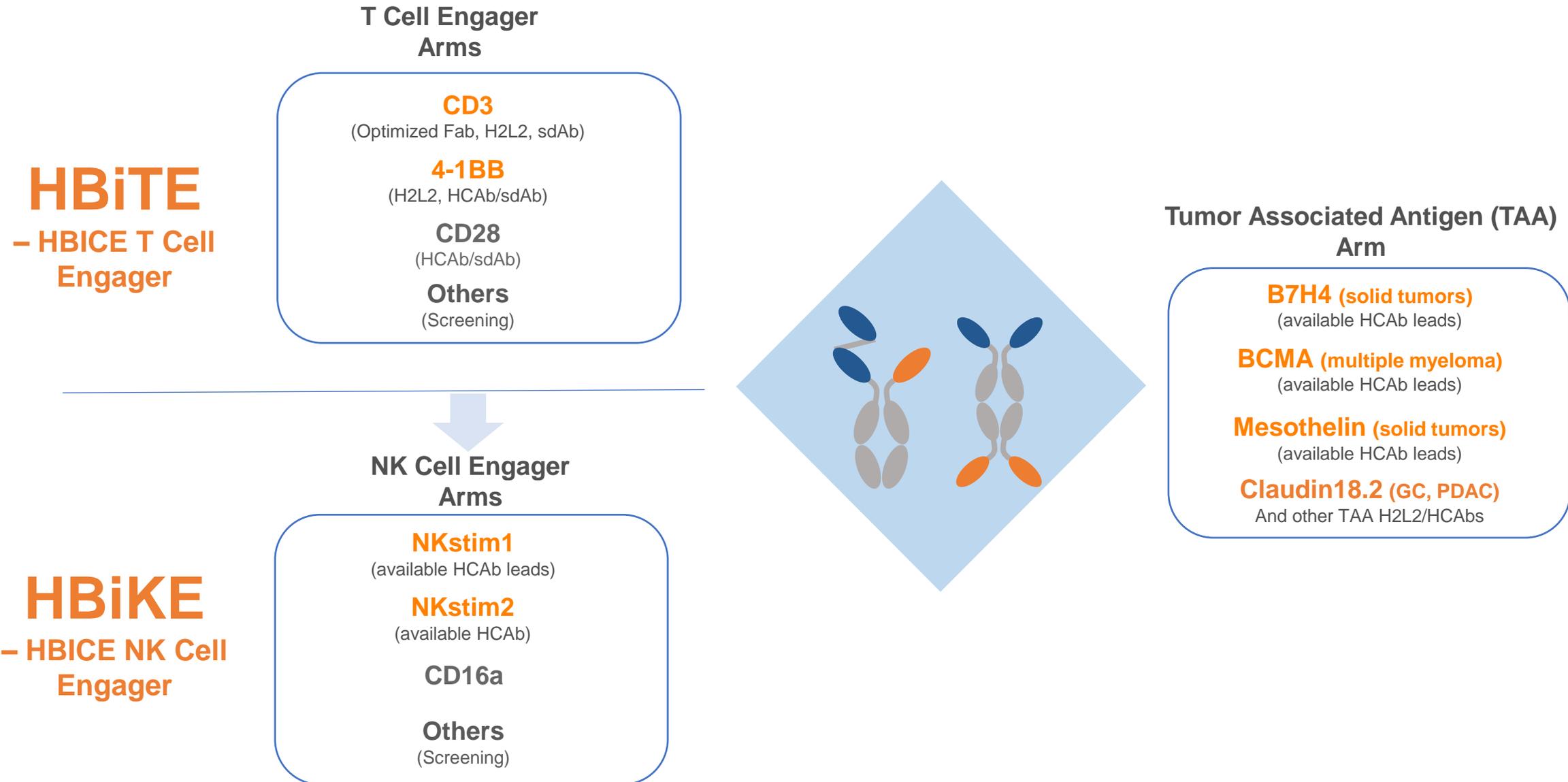
NK cell based approaches are becoming game-changing therapies with preliminary clinical POC results



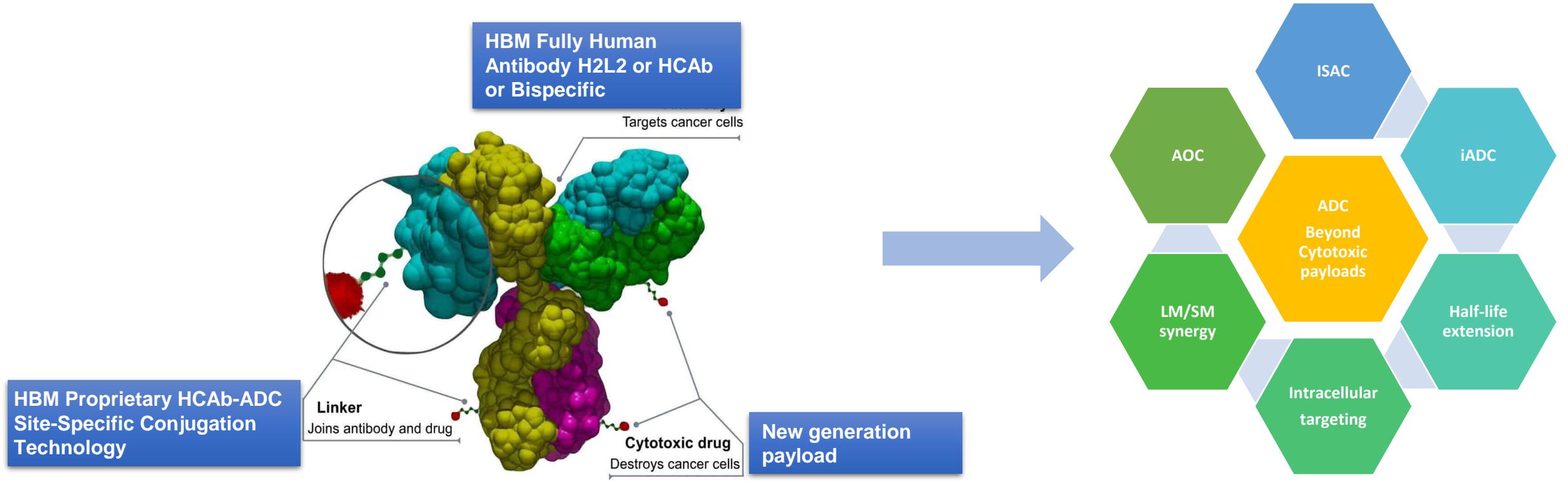
- Frontline defense system
- Kill tumor independent on MHCs, which can escape T lymphocyte detection
- Always switched on and rapid killing
- NK Accounts for 10-15% PBMC and cross-activate T cell via cytokines
- Amplify the effectiveness of T cells, acting as sentinel of immunity, broadening therapeutic window with less CRS

Roche
 TIGIT+PD-L1
 affimed
 CD16 NK Cell Engager
 AstraZeneca
 innate pharma
 the innate immunity company
 NKG2A
 THE UNIVERSITY OF TEXAS
 MD Anderson
 Cancer Center
 Making Cancer History®
 CAR-NK
 ROIVANT SCIENCES
 affimed
 SANOFI
 abbvie
 Kiadis pharma
 Dragonfly THERAPEUTICS

Innovation Upgrade from T Cell Engager (HBiTE) to NK Cell Engager (HBiKE) Leveraging Fully Human HBICE® Bispecific Platform



Next-Gen ADC at HBM is Empowered by Innovative Technologies



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

HBM7020: Next-Gen Bispecific Antibody Therapeutics from HBICE[®] Platform



Novel Bispecific Antibody from Immune Cell Engagers

• Highlights:

- 1) New generation BCMAxCD3, HBICE[®] -based bispecific T cell engager
- 2) 2+1 format and optimized anti-CD3 activity
- 3) High tumor killing specificity **with less cytokine storm risk**
- 4) Off-shelf convenience

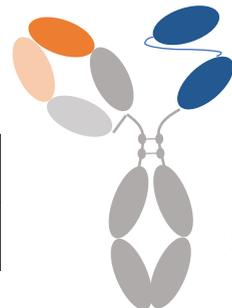
HCAb Based “2+1” Format A-HBICE

anti-CD3:

- Optimized activation of CD3, to balance the efficacy and minimized CRS

Cytokine release

	PR002895	PR003178	PR002953	TAB2
CD3 affinity(nM)	~30 nM	medium (~100nM)	Very weak (uM)	Very weak (uM)

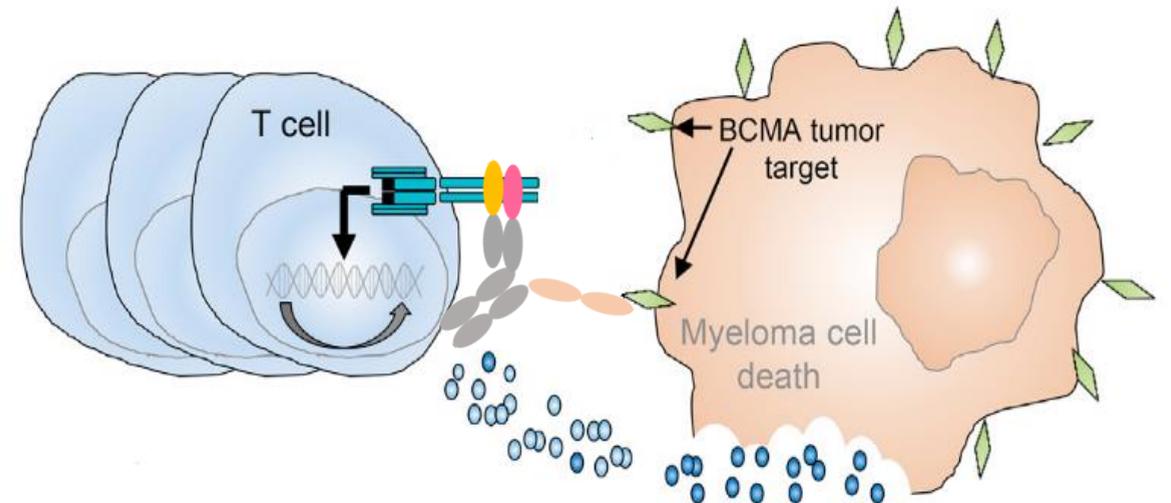


Dual anti-BCMA VH-VH

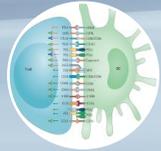
- High avidity binding to myeloma cells
- Cross reactive to cyno BCMA

Fc:

- Silenced the Fc effect
- Long half-life



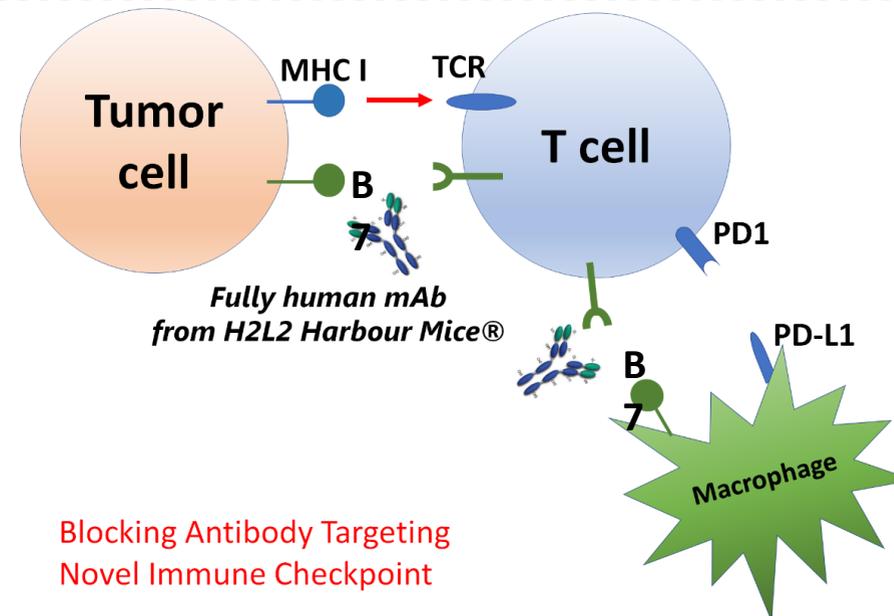
HBM1020: A Novel B7 Family Checkpoint Plays an Alternative Immune Escape Mechanism Beyond PD-L1



B7 Family Innovative First-in-Class Therapeutics

Highlights:

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



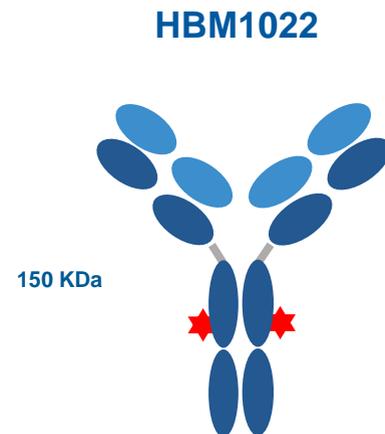
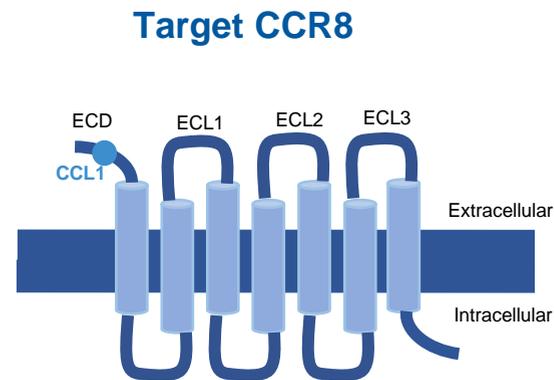
HBM1022: CCR8 is a Novel Target Expressed on Tumor Infiltrated Treg Cells



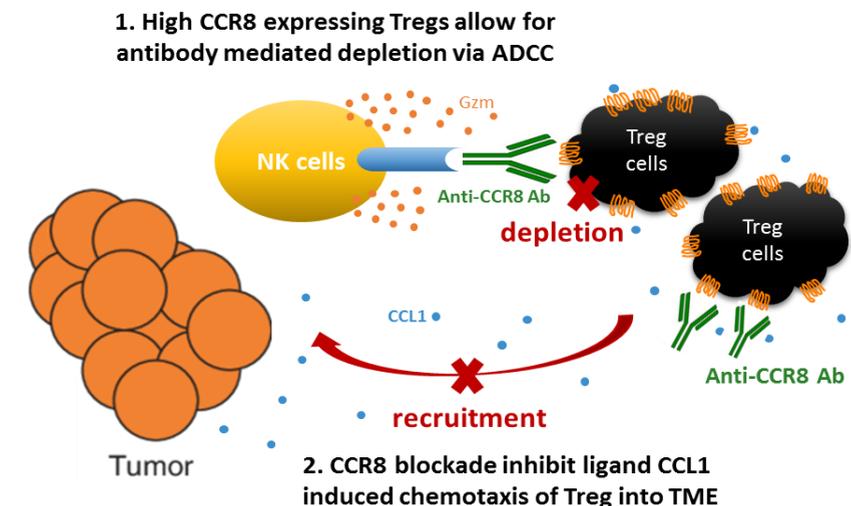
Nex-Gen Treg Depletion Therapeutics

Highlights:

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

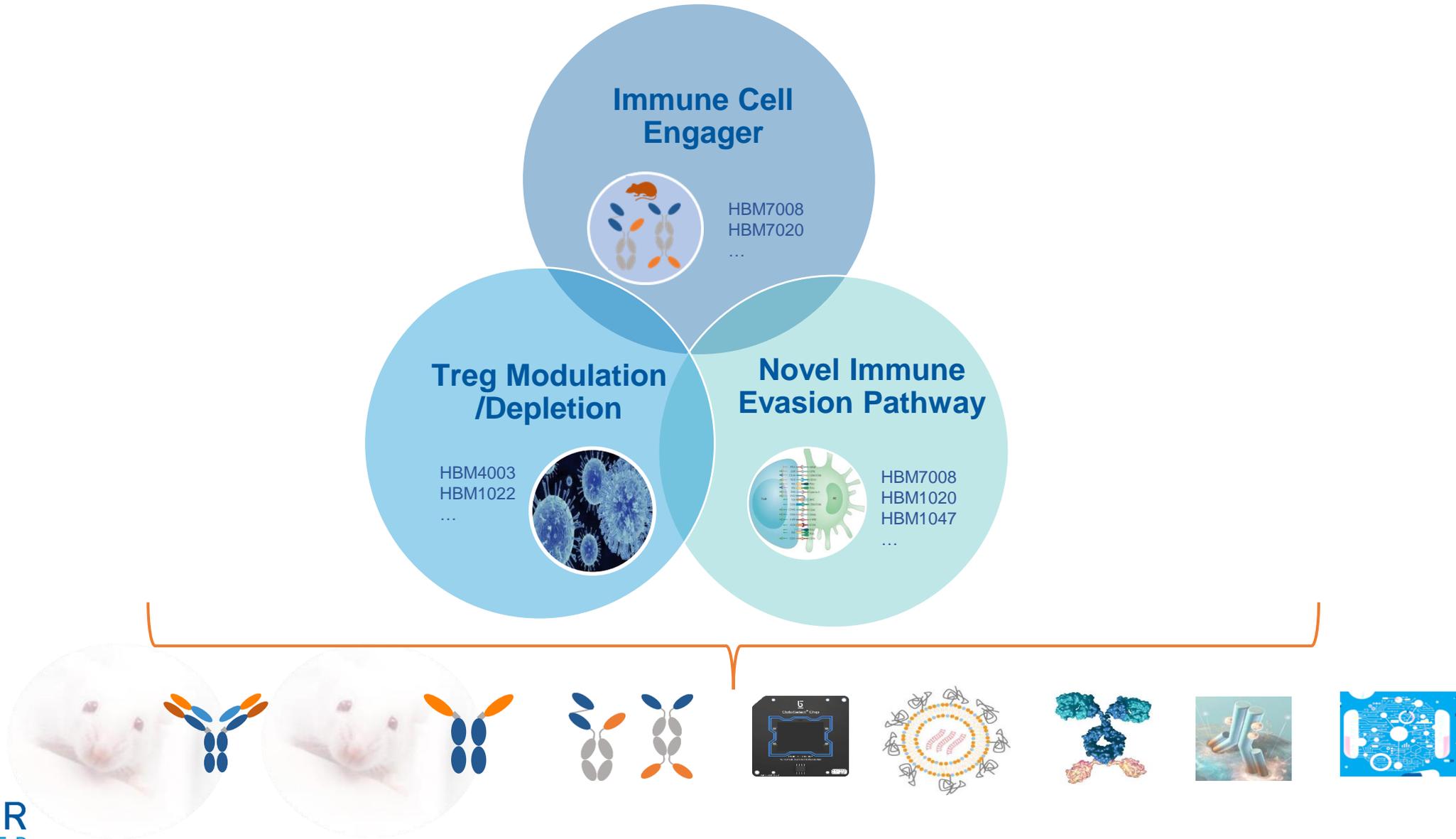


Mechanism of Action





HBM Antibody Technology Engine Drives the Next-Gen Therapeutics



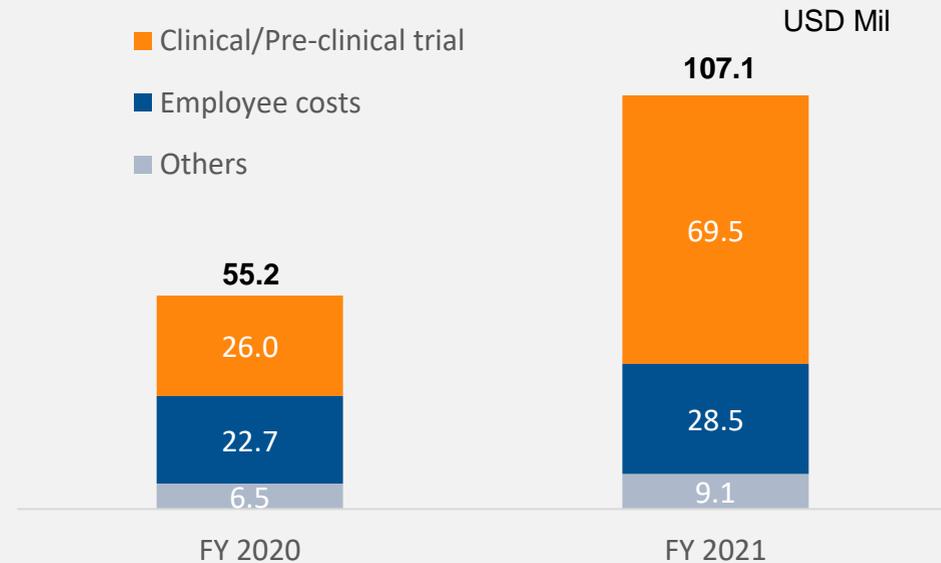
- 01** 2021 Overview and Highlights
- 02** Innovative and Differentiated Portfolio
- 03 Financial Results**
- 04** Q&A



Consolidated Statement of Profit or Loss

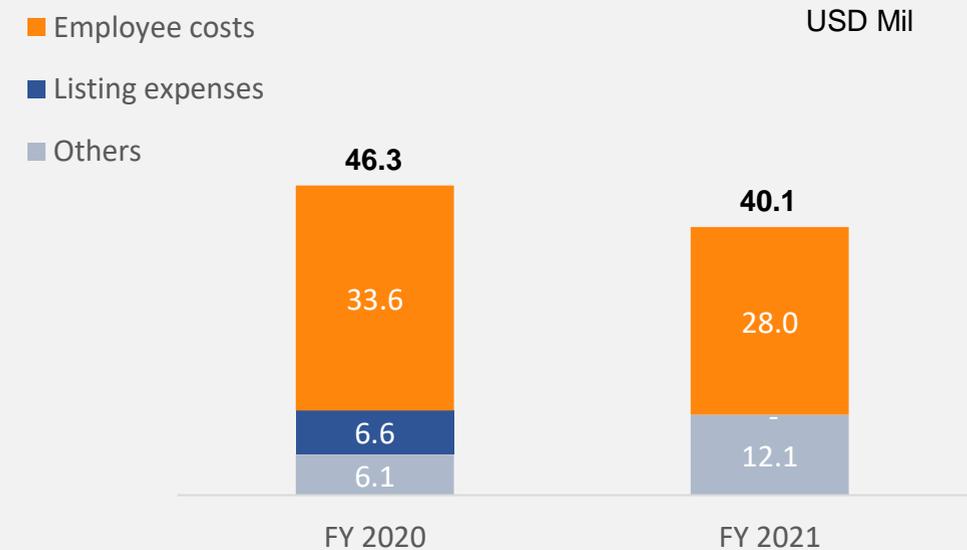
Research and development costs

R&D costs were US\$107.1 million, the increase was primarily attributable to the combined impacts of (i) an increase in materials and third-party contracting costs due to our increased investments in key clinical programs and molecule assets in discovery and pre-clinical stages; (ii) an increase in employee cost caused by an increase in the headcount of our research scientists and development clinician to support in driving our R&D programs



Administrative expenses

Administrative expenses decreased by US\$6.2 million to US\$40.1 million, primarily attributable to (i) listing expenses of the Company which were incurred in 2020; (ii) a decrease in employee cost caused by the decrease of share-based payment expenses in relation to our administration headcount; (iii) partially offset by increased expenses of consulting and professional services



Loss for the year

Loss for the year decreased from US\$296.5 million for the year ended 31 December 2020 to US\$137.9 million for the year ended 31 December 2021

Consolidated Statement of Financial Position

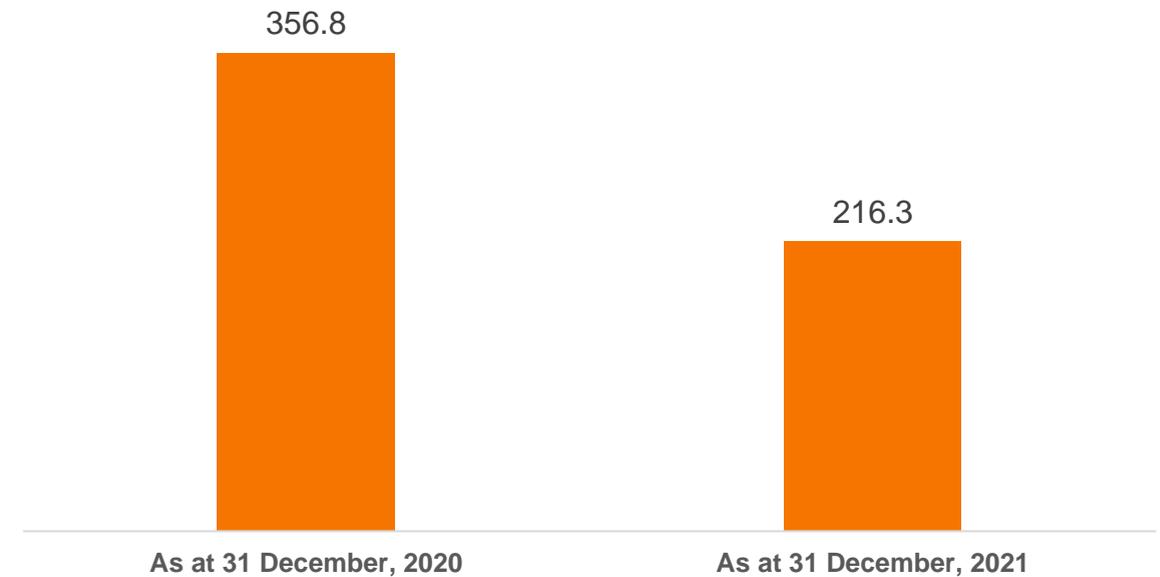
Summary of Consolidated Statements of Financial Position

USD Mil	As at 31 December	
	2021	2020
Non-current assets	41.5	19.4
Current assets	240.9	369.3
Include: Cash and bank balances	<u>216.3</u>	<u>356.8</u>
Current liabilities	41.1	25.6
Net current assets	200.0	343.7
Non-current liabilities	18.4	2.2
Net assets	222.9	361.0

Cash and bank balances

Cash and bank balances decreased from US\$356.8 million to US\$216.3 million, it was primarily as a result of R&D and administrative expenses, as well as investments in non-current assets

USD Mil



Rapid Progress of Key Assets Towards a Global Innovation Biotech Company

1. Major Advancements on Portfolio Development

- 2 Ph 3 Trials
- 10 Ongoing Clinical Trials
- 6 Highly Innovative New Assets

2. Novel Frontier Development – NK and ADC

- NK Cell Engager, NK Assets
- Next-Gen ADC

3. Global Collaboration



Global Leading Technology Platforms



• **Rapidly** develop clinical products, advancing for BLA



• **Quickly** advance 4+ pre-clinical assets into clinical stage



• **Consistently** deliver new differentiated and innovative assets



• **Continuously** expand global operation and collaboration

2022

2021

Q&A



THANK YOU



Harbour BioMed
WeChat Account

CONTACT US:

ir@harbourbiomed.com

www.harbourbiomed.com

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