HARBOUR BIOMED

2024 INTERIM RESULTS

August 28, 2024

HBM HOLDINGS-B

2142-HK

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HBM Holdings: Innovation Value Leads to High-Quality Sustainable Growth

HBM Holdings: 24H1 Business Highlights Fuel Sustainable Growth

Advance Innovative Pipeline and Platform

Rapidly advance differentiated assets and leverage innovative platform to expand global collaboration opportunities

Assets/Platform Progress

- **Multiple clinical-stage assets milestones**
  - **1 IND approvals from FDA: HBM9027**
  - **Batoclimab BLA re-submission**

Nona Platform Upgrading and Collaborations:

- ***HBICE®*** • ***mRNA-Encoding Engagers***
- ***HBICA®*** • ***H2L2/HCAb- ADC Toolbox***
- ***Blood–Brain Barrier Shuttle BsAb***

NONA BIOSCIENCES → Alaya.bio **CAR-T Cell Therapies**

NONA BIOSCIENCES → BOOSTIMMUNE **ADC against Novel Targets**

Global Collaboration Ecosystem Expansion

Strategize Global connections to build a diversified collaboration ecosystem, linking with lead pharma and biotech

Collaboration Ecosystem Expansion

Global License and Option Agreement with AstraZeneca, total $604 million including upfront $19 million, near-term milestone $10 million

AstraZeneca

2022:
CLDN18.2xCD3

2024:
Pre-clinical mAb

Consecutive Net Profit Validates Business Model

24H1 revenue ~$23.7 million (~RMB 168 million), further enhance financials and strongly support company business and strategic operation

High Quality financial Efficiency

- **3rd Consecutive Interim Net Profit**
- **Cash Position +30.3% vs. 12/31/23**
- **Improved operating efficiency, total cost down by -38.7% vs. 1H23**

NONA BIOSCIENCES **Revenue Growth of Core Business Doubled vs 1H23**

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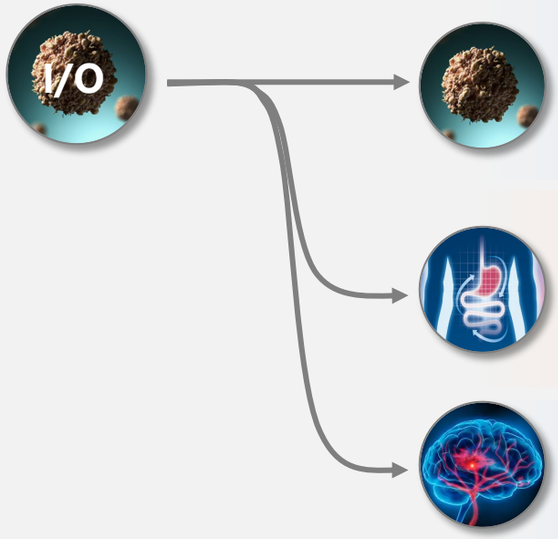
HBM Holdings: Focus on Oncology and Immunology, With Support from Technology Innovation

Therapeutics Area: From I/O to I&I

Pipelines focus on IO and I&I, expanding to new therapeutics area through strong R&D capabilities and experience



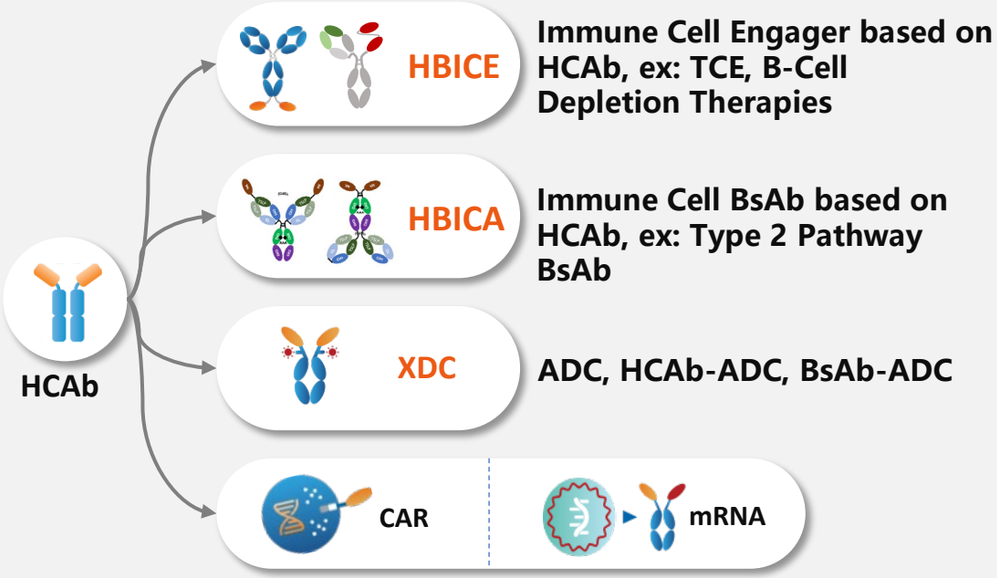
- Next-Generation IO Therapeutics
- XDC Platform
- Immune Cell Engager

- Type 2 Pathways for I&I
- Pathogenic B Cell Depletion for Autoimmune Diseases
- Other I&I Innovative Therapies

- New Therapeutics Area

Discovery Strategy: Innovation-Driven

HBICE+HBICA+XDC, power innovation more efficiently in multiple areas



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Harbour Therapeutics: Accelerate Innovative Pipeline Expansion

Leverage Leading Harbour Mice and XDC Platforms to Advance Novel and Highly Differentiated Potential Assets

	Project	Target	Indication	Commercial Rights	Status	Partner
mAb for Next-gen IO Therapeutics	Porustobart HBM4003	CTLA-4 [1]	Melanoma	Global	Combo with PD-1 Ph 1b/2 → Ph3 Preparing	
			CRC		Combo with PD-1 Ph 1b/2	
			HCC		Combo with PD-1 Ph 1b/2	
			NEN		Combo with PD-1 Ph 1b/2	
	HBM1020	B7H7/HHLA2	Solid Tumors	Global		
	HBM1022	CCR8	Solid Tumors	Global	US IND clearance	
	HBM9014	LIFR	Solid Tumors	Global		Yinuoke
Immune Cell Engager for Oncology	HBM7022	CLDN18.2xCD3	Solid Tumors	Global Out-license		AstraZeneca
	HBM7008	B7H4×4-1BB	Solid Tumors	Global		
	HBM7020	BCMA×CD3	Hematologic carcinoma	Ex-China	CN IND clearance	华兰生物 HUALAN BIO
	HBM9027	PD-L1xCD40	Solid Tumors	Global	US/CN IND clearance	
	HBM7004	B7H4×CD3	Solid Tumors	Global		
XDC Platform	HBM9033	MSLN ADC	Solid Tumors	Global Out-license		Pfizer
	ADC Program	Undisclosed	Solid Tumors	Global		
	RDC Program	Undisclosed	Solid Tumors	Global		

Status: Discovery | Pre-Clinical | IND | Phase I | Phase II | Phase III

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

Innovation in Inflammatory & Immunology Driven by Differentiated Biological Pathways and Molecular Properties

Project	Target	Indication	Commercial Rights	Status	Partner
FcRn-targeted Therapies for Autoimmune Disease					
Batoclimab HBM9161	FcRn	Myasthenia Gravis	Great China Rights Out-licensed[1]	BLA	CSPC
Type 2 Pathways for Inflammatory & Immunology					
HBM9378	TSLP	Asthma	Global	Ph1 Completed → Ph2 Preparing	
		COPD	Global	IND Enabling	
BsAb Programs	TSLP× Undisclosed	Inflammation disease	Global		
Pathogenic B Cell Depletion for Autoimmune Diseases					
HBM7020	BCMA×CD3	Autoimmune Diseases	Ex-China	IND Enabling	HUALAN BIO
TCE Program	CD19×CD3	Autoimmune Diseases	Global		
BsAb Program	Undisclosed	Autoimmune Diseases	Global		
TsAb Program	Undisclosed	Autoimmune Diseases	Global		

Status: Discovery | Pre-Clinical | IND | Phase I | Phase II | Phase III | BLA

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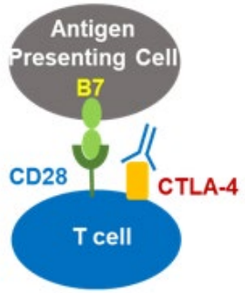
1. HBM in-license the Greater China Rights of HBM9161 from HanAll in 2017, and the rights is out-license to CSPC in Oct 2022

Porustobart (HBM4003): Next-Gen Anti-CTLA-4 Antibody with Potential to Be the Mainstream of IO Therapeutics

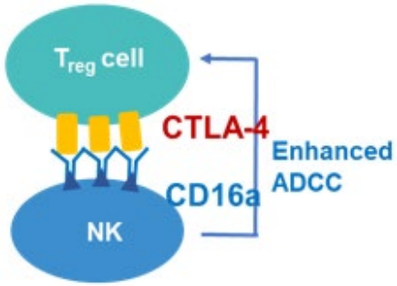
Highlights

- Deplete intra-tumoral Treg cells via enhanced ADCC strategy
- Great safety profile resulted from the reduced systemic drug exposure
- Huge potential for combination therapies

MOA1: Checkpoint Inhibit



MOA2: T_{reg} Depletion



Brianna M Lax., et al., Both intratumoral regulatory T cell depletion and CTLA-4 antagonism are required for maximum efficacy of anti-CTLA-4 antibodies. ***PNAS.*** *2023 Aug;120(31)*

Encourage efficacy observed for HBM4003 + Tislelizumab in Late-Line MSS CRC

Best Overall Response by RECIST 1.1, N (%)

Pts with tumor assessments	**9 (100%)**
ORR (CR + PR)	2 (22.2%)[1]
DCR (CR + PR +SD)	5 (55.6%)

- **Encouraging efficacy observed for HBM4003 combo with Tislelizumab in later line MSS CRC**
- **Continue to enroll Late-line MSS CRC patients**
- **Explore other combination opportunities, ex: combo with Toripalimab on 1L mucosal melanoma**

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1. 2 PR（including 1 unconfirmed）

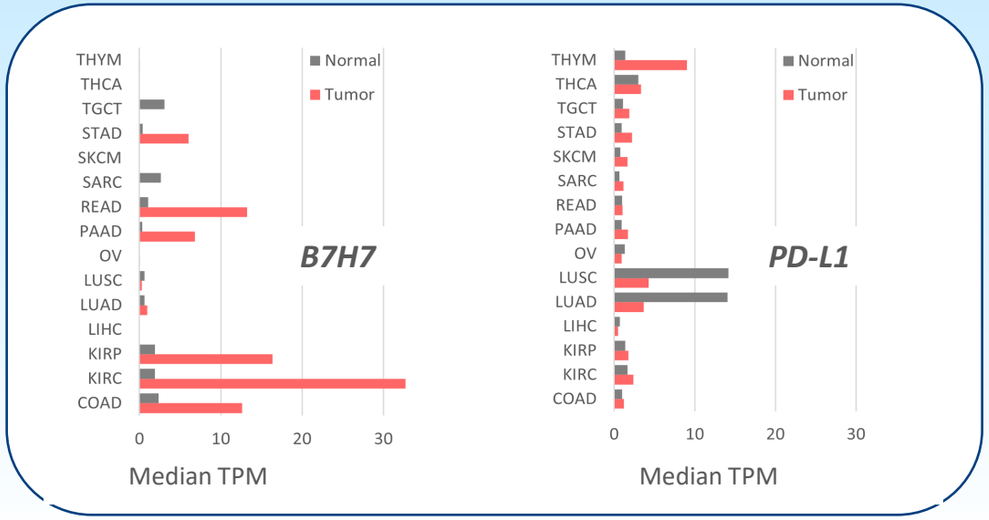
HBM1020 (B7H7): An Alternative Immune Escape Mechanism Beyond PD-L1, Potential Therapy for PD-L1 Negative/Refractory Patients

Highlights

- T cell and NK cell activation activity and excellent in vivo efficacy in humanized tumor models
- Widely Expressed in Various Solid Tumors & Reciprocal to the Expression of PD-L1
- Huge potential to treat PD-L1 negative or anti-PD1/PD-L1 refractory cancer patients
- HBM1020 is the first and only mAb entering clinical development worldwide
- Ph1 ongoing - multiple patients dosed in collaboration with top-tier US cancer centers

B7H7: Widely Expressed in Various Solid Tumors & Reciprocal to the Expression of PD-L1

- **Dose escalation of Ph1 study had been completed**
- **Excellent safety profile with no DLT or MTD identified**
- **Preliminary PK demonstrated typical IgG behavior**
- **The latest clinical data will be released at the ESMO Congress 2024**



Data re-edited from GEPIA database

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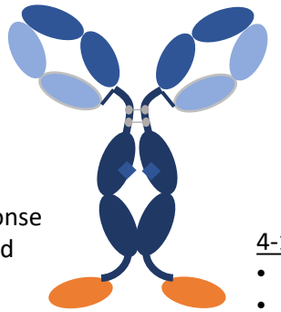
HBM7008 (B7H4x4-1BB): First-in-Class Bispecific Antibody from HBICE® Platform

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
- May 2022, first patient dosed in AU. Oct 2022, first patient dosed in US

HBM7008



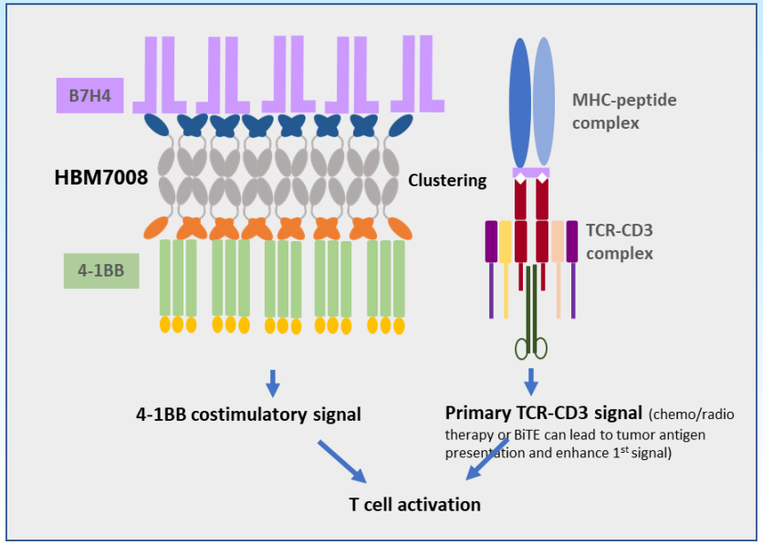
~175 KDa

B7H4 arm:
Human B7H4 H2L2 antagonist mAb

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

4-1BB arm:
- VH from HCAb,
- B7H4-dependent T activation

Primary MoA



Monotherapy dose escalation had been completed.

Preliminary PK of HBM7008 is generally linear across all tested doses.

Acceptable safety/tolerability with no DLT, no G3+ TRAE observed, no treatment related discontinuations.

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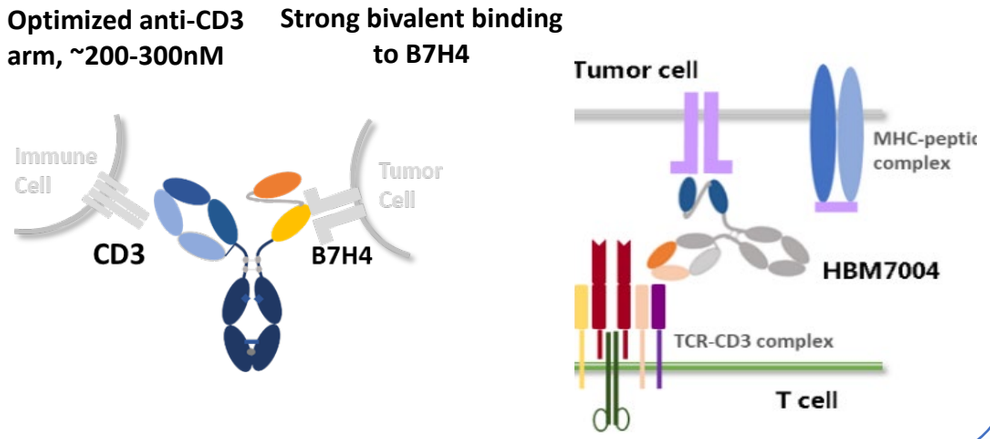
Study Record | ClinicalTrials.gov

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

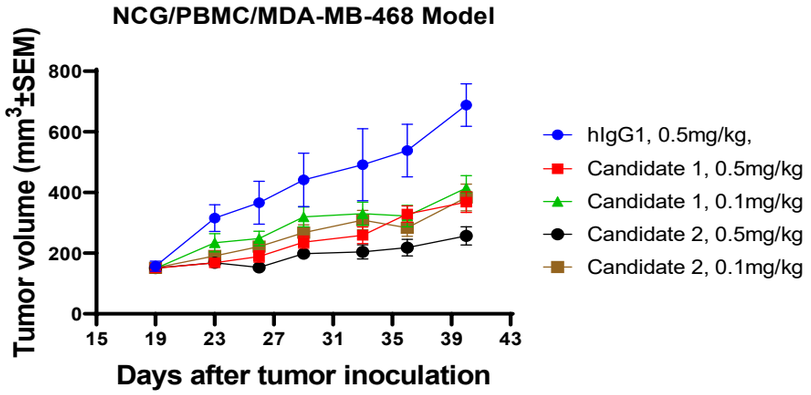
Highlights

- 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
- In the Dose-Range-Finding toxicity study in cynomolgus monkeys, well tolerated up to 30mg/kg
- Potentially combine with ADC or in-house assets to overcome unmet medical need beyond PD-1

Molecule Design and MOA



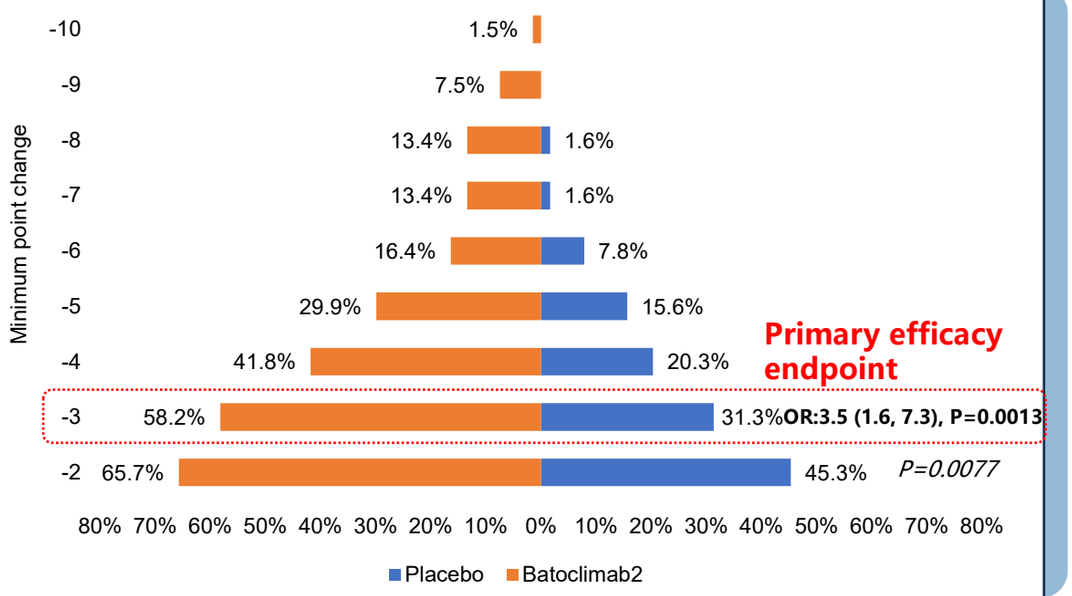
Strong Anti-tumor Activity in Mouse Tumor Model



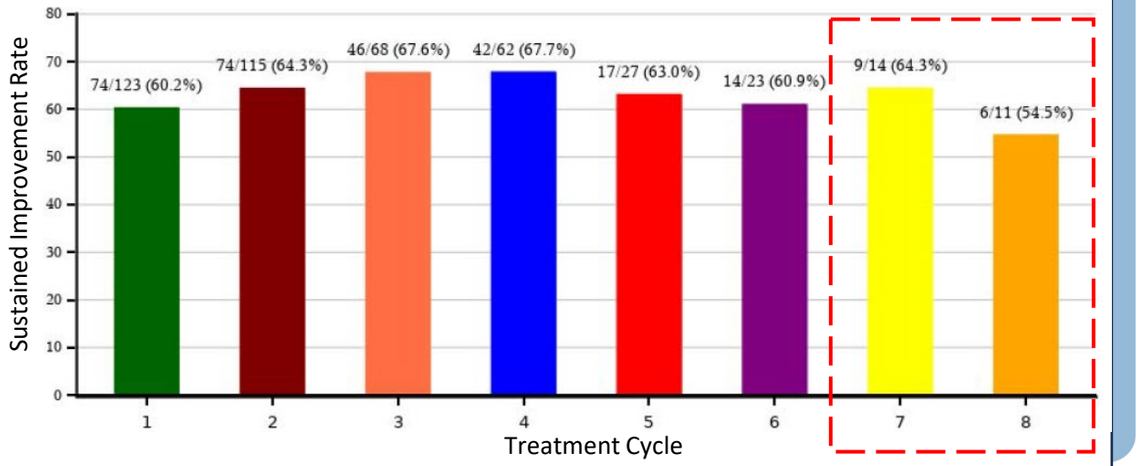
Batoclimab (HBM9161) Demonstrates Remarkable Therapeutic Benefits in gMG Patients

Highlights

- First and only innovative drug targeting FcRn that has completed phase I,II and III clinical trials in China
- First and only innovative drug that has achieved outstanding phase III positive results in China gMG patients
- Updated clinical data supports sustainable efficacy for long-term disease management, and has the potential to be a breakthrough treatment option for a wide range of autoimmune diseases



Updated Efficacy: Sustainable efficacy for long-term disease management



Note: Sustained improvement was defined as a >=3-point reduction from baseline MG-ADL score from day 1 to day 64 that persisted for 4 weeks.

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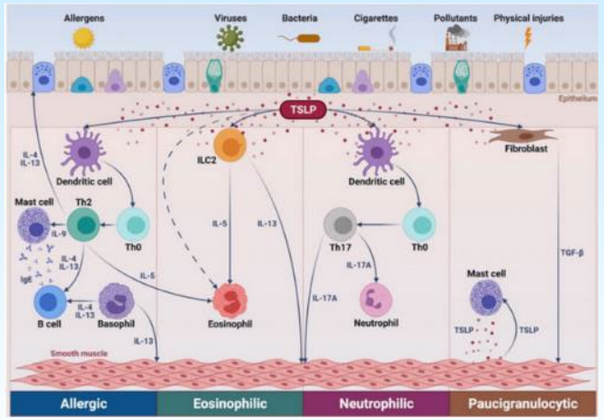
HBM9378 (TSLP mAb): Fully Human Anti-TSLP mAb with Extended Half-life

Highlights

- 2nd fully human anti-TSLP mAb in the world；
- **The half-life of HBM9378 is 2-3 times more than Tezepelumab in monkey and human**, which reduces the dosing frequency;
- Impressive pharmacological characteristics: strong stability at high concentration, desirable druggability, increased convenience of patient dosing through s.c. administration.
- High production: 7.7g/L

TSLP: A Target of Great Potential In Asthma Treatment

- TSLP gets produced mainly by epithelial cells at barrier surfaces (such as lung and gut), and will be upregulated when tissue injury is triggered by environmental insults (such as allergens).
- TSLP acts as a pro-inflammatory cytokine in various type of asthma:



The Clinical Trial of HBM9378 in China Proceed Smoothly

- **2022 – Phase I IND**
- **2023 – Completed Phase I**
- **2024 – Plan to initiate Phase II Asthma patient enrollment; 2nd indication (COPD) IND in preparation**

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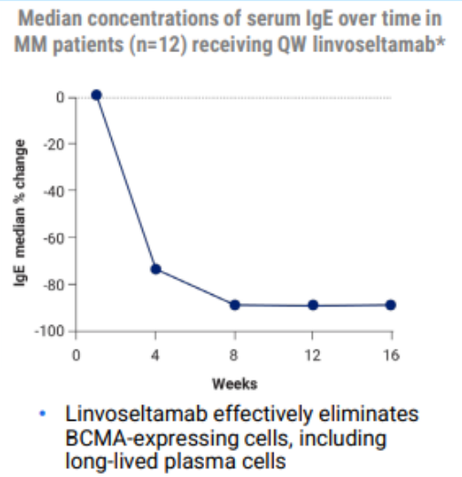
HBM7020 (BCMAxCD3): Great Potential in Autoimmune Disease

Highlights

- HBICE® technology grants asymmetric structure but less light chain mispairings
- Good monkey safety profile and druggability
- Clinical data from third party support, have great potential in autoimmune disease
- CN IND clearance in 2023.07, Ph1 in preparation

BCMA/CD3 effectively eliminates BCMA-expressing cells, including LLPC



Source: Regeneron deck in Jan 2024

BCMA CAR T had also achieved first POC in autoimmune disease

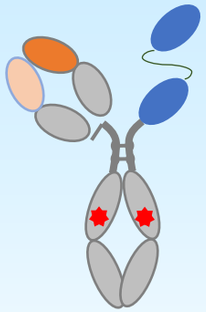
	All participants who completed treatment in part 2 (n=9)	By treatment group		By myasthenia gravis type		
		Group 1 (n=2)	Group 2 (n=7)	AChR antibody-positive (n=6)	MuSK antibody-positive (n=2)	Seronegative (n=1)
Mean score change (95% CI)*						
MG-ADL	-5·9 (-9 to -2·8)	-6, -8	-6 (-15 to 3)	-6 (-11 to -1)	-3, -4	-8
QMG	-7 (-11 to -3)	-5, -3	-8 (-20 to 4)	-5 (-10 to 0)	-9, -5	-17
MGC	-14 (-19 to -9)	-7, -11	-15 (-29 to -1)	-14 (-21 to -7)	-14, -7	-22
MG-QoL-15r	-9 (-15 to -3)	-8, 4	-11 (-23 to 1)	-8 (-17 to 1)	-10, -6	-14
Number of participants with improvement (%)						
MG-ADL decrease ≥2 points	8 (89%)	2 (100%)	6 (86%)	5 (83%)	2 (100%)	1 (100%)
MGC decrease ≥3 points	9 (100%)	2 (100%)	7 (100%)	6 (100%)	2 (100%)	1 (100%)
QMG decrease ≥3 points†	8 (89%)	2 (100%)	6 (86%)	5 (83%)	2 (100%)	1 (100%)
MG-ADL decrease ≥6 points‡	5 (56%)	2 (100%)	3 (43%)	4 (67%)	0	1 (100%)

Data are for participants in groups 1 and 2 of part 2 who completed all six infusions and 12-week follow-up. One group 1 participant withdrew from the study before the first assessment after treatment. Clinical efficacy outcomes for the single group 3 participant are shown in figure 1. AChR=acetylcholine receptor. *Individual values are presented for groups of ≥2 participants. †All participants who had the prespecified ≥2-point improvement in QMG also had a ≥3-point improvement. ‡Post-hoc analysis of depth of response.

Table 3: Measures of disease severity at week 12

Granit V, et al. Lancet Neurol 2023.

Molecule Design based on HBICE Technology



BCMA: KD ~0.02 nM
CD3: KD ~950 nM

- High binding with BCMA, low binding with CD3.
- Design with improved safety profile.
- Great Potential with deeply Plasma Cell depletion.

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Nona Biosciences : Platform Linking Global Ecosystem

Cutting-edge Innovation and Technology Platform Continue to Power Global Ecosystem, Fuel High-quality Business Growth

Deepen Global Innovation Collaboration Ecosystem

1H24 Total Revenue **>$23 Million**

1H24 Total Net Profit **>$13 Million**

NONA BIOSCIENCES + AstraZeneca

2nd Collaboration on innovative asset with MNC AstraZeneca

Total **$604 Million**

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Strong Business Results Fueling High-quality Growth

Continuous global business expansion and collaboration stickiness

Net profit margin of core business increased 13%

Platform-based collaboration with 2 MNCs

Global Collaboration Accelerating expansion, up 25% vs. 1H23

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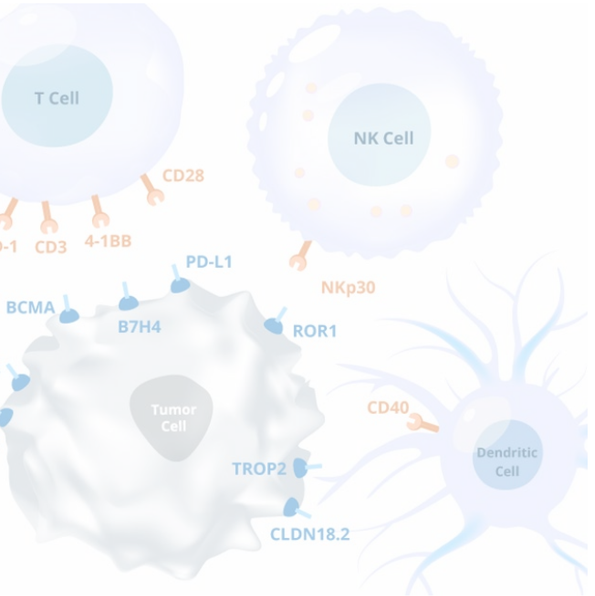
Note: As per Nona 1H24 Management accounts

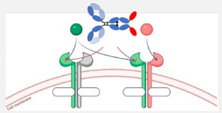
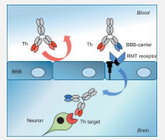
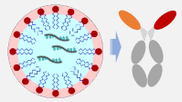
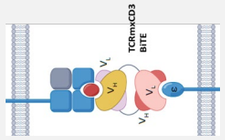
Leading BsAb Platform Creates Innovation Engine of Nona

HBICE® Immune Cell Engager Platforms



- **B7H4×4-1BB HBICE®**
  HBM7008
  Phase I
  HARBOUR BIOMED
- **CLDN18.2×CD3 HBICE®**
  HBM7022(AZD5863)
  Phase I
  AstraZeneca
- **BCMA×CD3 HBICE®**
  HBM7020(HL17)
  CN IND
  HARBOUR BIOMED / 華蘭生物 HUALAN BIO
- **PDL1×CD40 HBICE®**
  HBM9027
  US&CN IND
  HARBOUR BIOMED
- **B7H4×CD3 HBICE®**
  HBM7004
  IND-enabling
  HARBOUR BIOMED

Explore New Application Opportunities

Inflammation & Immunology Diseases	*HCAb based Bispecific Immune Cell Antagonist* 
CNS Diseases	*Blood–Brain Barrier Shuttle BsAb* 
New Modalities	*mRNA-Encoding Engagers*  *https://nonabio.com/mrna*
Tumor Antigen	*TCRm BsAb Engagers*  *https://nonabio.com/tcrm-antibody*

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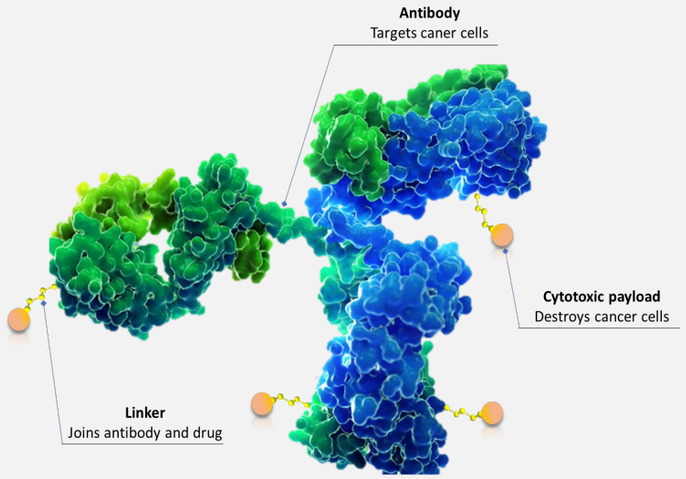
ADC Technology Platform Continue to Upgrade

Support from ADC Target Nomination to IND



Pfizer

Seagen

HBM9033

ADC 2.0 Platform

Linker Payload

- Self-developed linker and payload from Nona
- ADC design based on target biology

Site Specific Conjugation

- IP-protected site-specific conjugation technology

New Target/Dual Target

- Fully human antibody toolbox for tumor targets
- Universal bispecific ADC platform

Next-generation ADC innovation

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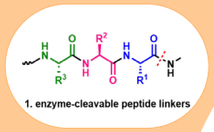
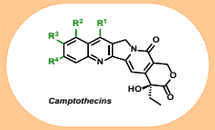
Validation of Self-innovation ADC Linker and Payload Technology

Carefully designed enzymatic cleavable linker allowing specific release of payloads only in tumor environment

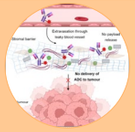


Novel CPT derivatives with optimized potency and properties to adapted with extracellular releasing MoA

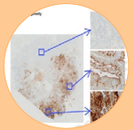


Improved efficacy with great safety: Superior efficacy comparing with competitors

Internalization-independent LDs

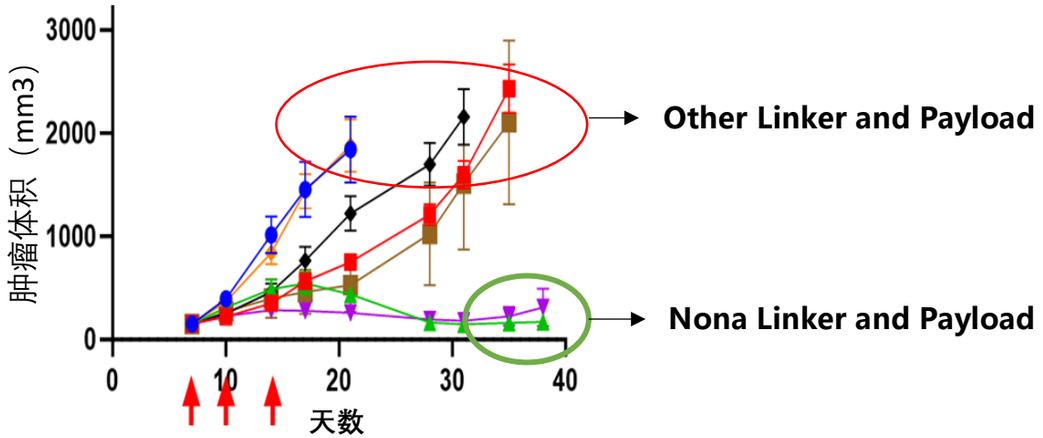


Free payload diffusion allow the better tumor penetration/ enrichment of drugs

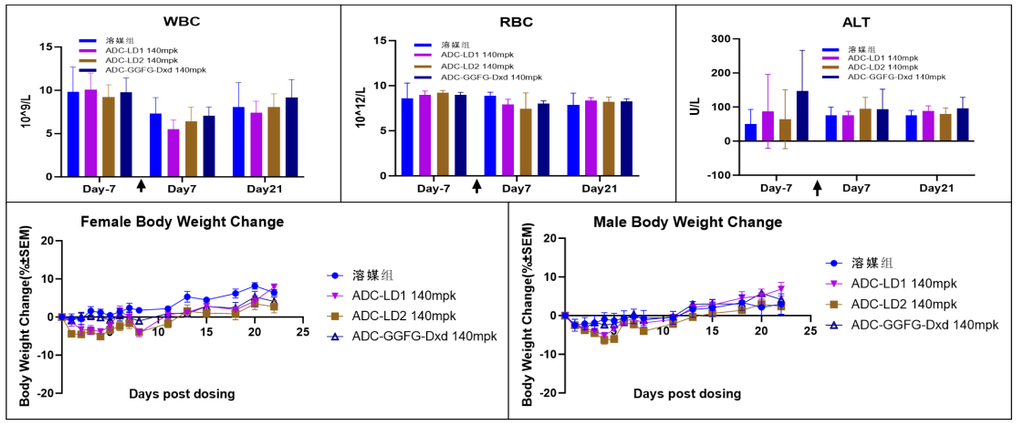


Tumor killing without requirements of internalization, better efficacy for heterogenous tumors

Targets on stroma or ECM, or even soluble targets could also be selected for some unreachable tumor



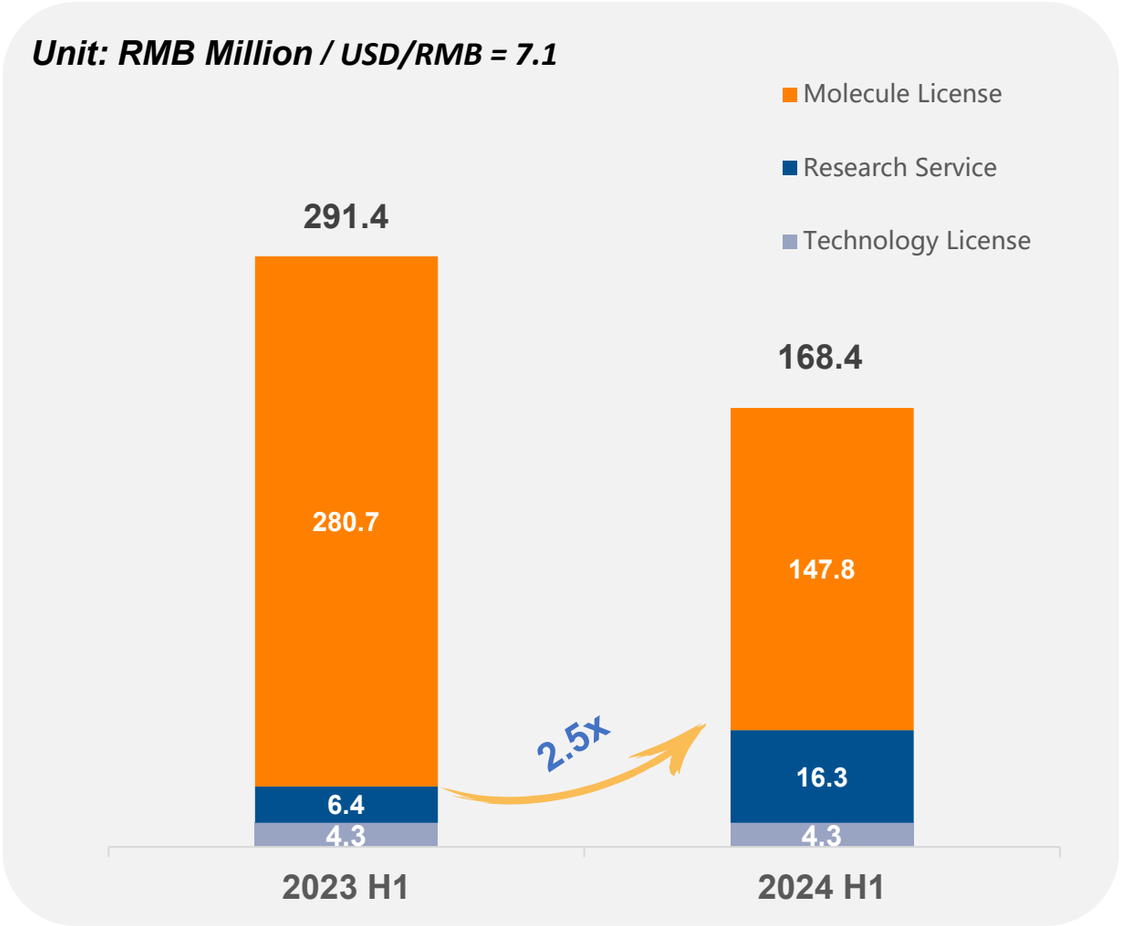
Nona Linker and Payload Show Comparable Safety Profile with GGFG-Dxd at 140mpk



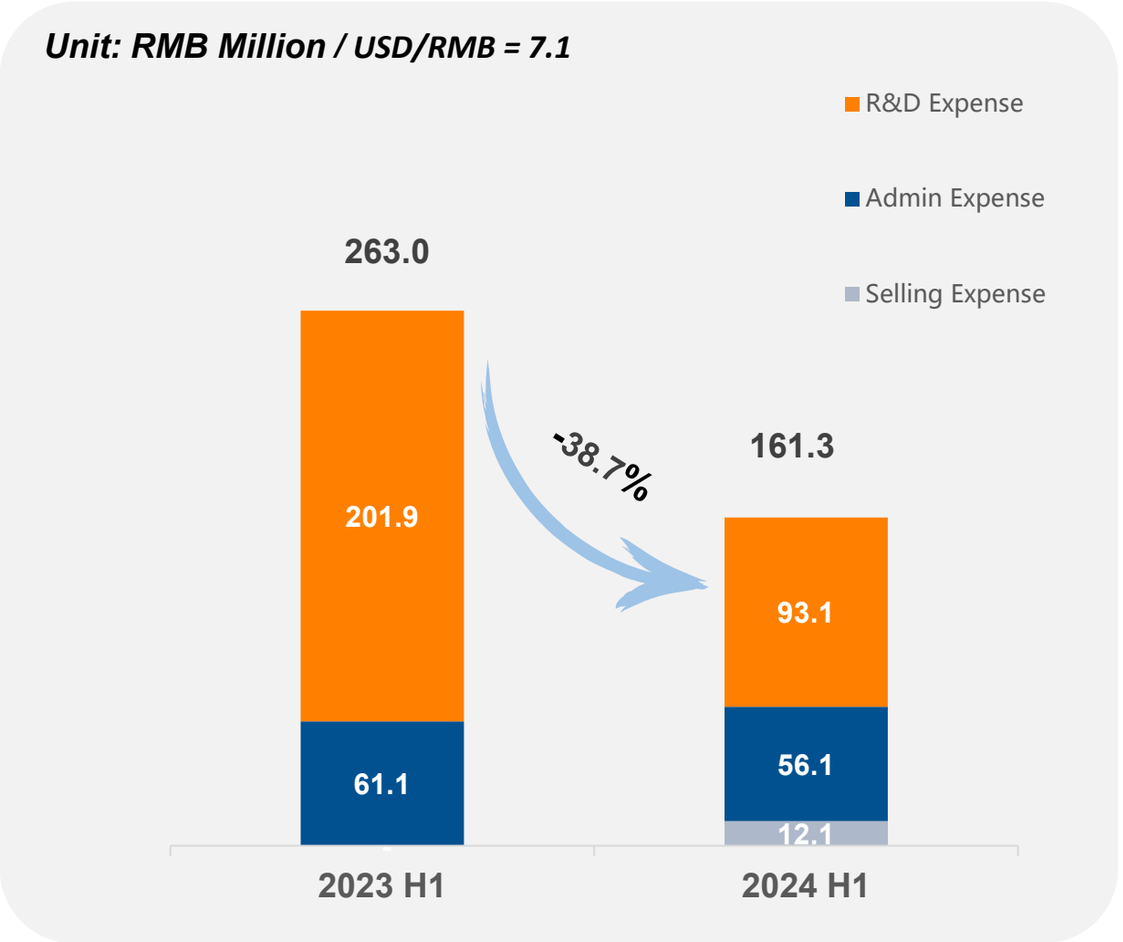
Financials:
Continue Net Profits with Strong Growth of Core Business

Continue Reporting Net Profits, Strong Growth of Nona Core Business Strengthens Financial Position

Diversified Revenue Resource with Core Business Revenue Doubled



R&D Strategic Optimization improved Operating efficiency



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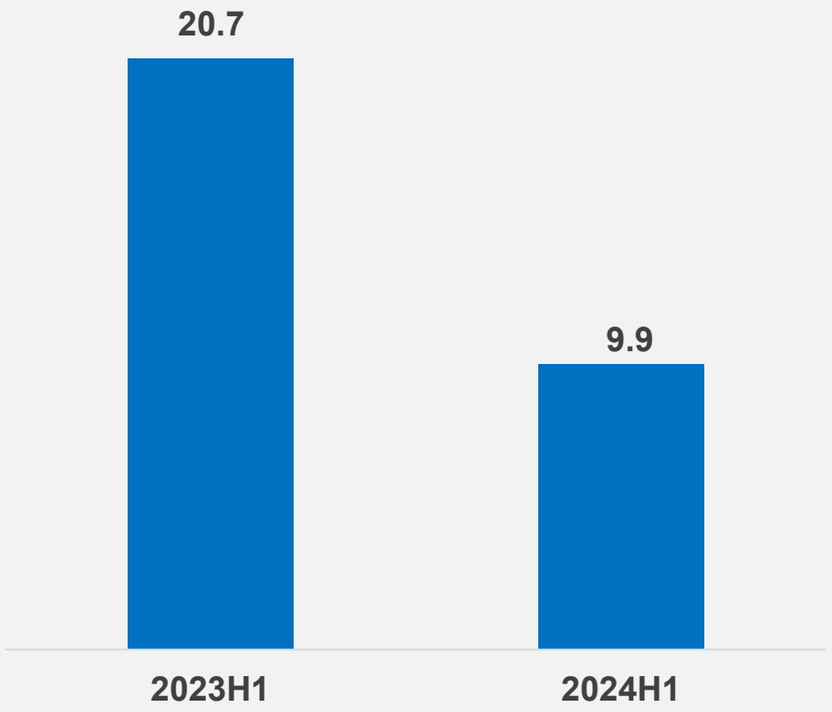
R&D Strategic Optimization to Improve Operating Efficiency, Pave the Way for High-Quality Growth

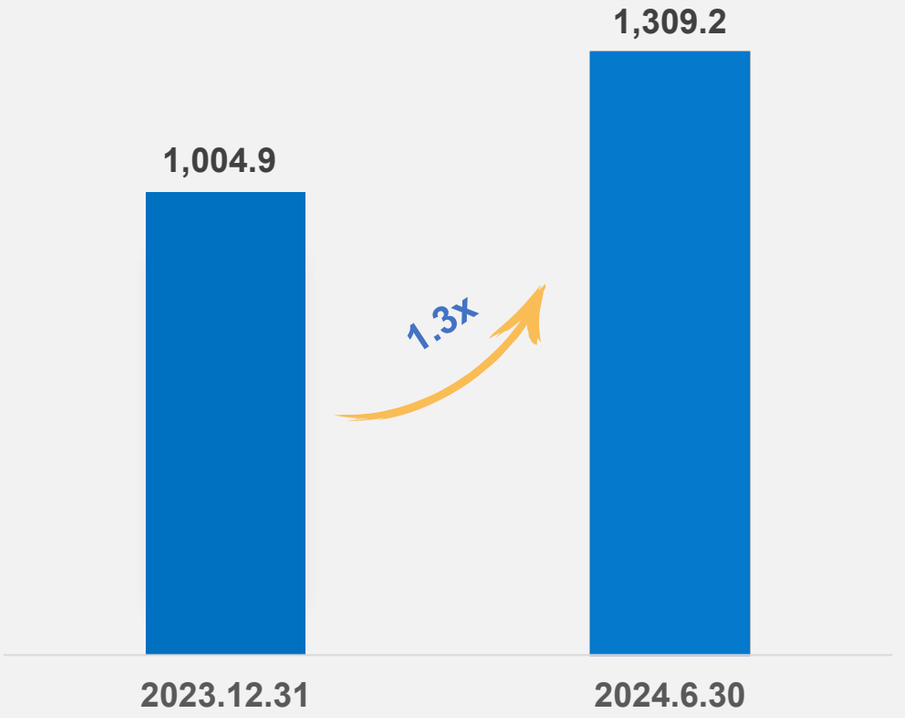
Consecutive Interim Net Profits

Unit: RMB Million / USD/RMB = 7.1



Cash Position Increased By 30.3%

Unit: RMB Million / USD/RMB = 7.1



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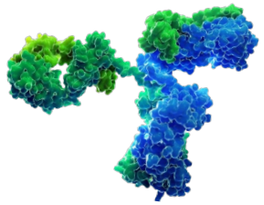
Corporate Development: Innovation Validated By Global Collaboration

Outlook of 2H24 and Beyond: Continue to Motivate Innovation and Expand Global Collaboration Footprint



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Global Collaborations Continue to Validate Innovative Pipeline

- R&D strength transforming into differentiated pipeline, with innovative therapies on IO and I&I
- Deepen diversification and global collaboration ecosystem, explore new pathways for asset value realization

Nona Biosciences

Unique Growth Model Validated by Robust Cash Inflow

- Actively expand global business, to fuel sustainable growth through strong connection with ecosystem
- Take full advantage of unique platform as innovation engine, improve application for multiple areas

Q&A

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