BIOCYTOGEN

Stock code:02315.HK

Your partner from targets to therapeutics

RenBiologics

BioMice

Beijing

Heidelberg

Jiangsu

Shanghai

Boston

San Francisco

Our Vision

To become a global headstream of new drugs

Our Mission

To discover, develop and deliver new medicines through innovative technologies that benefit human health
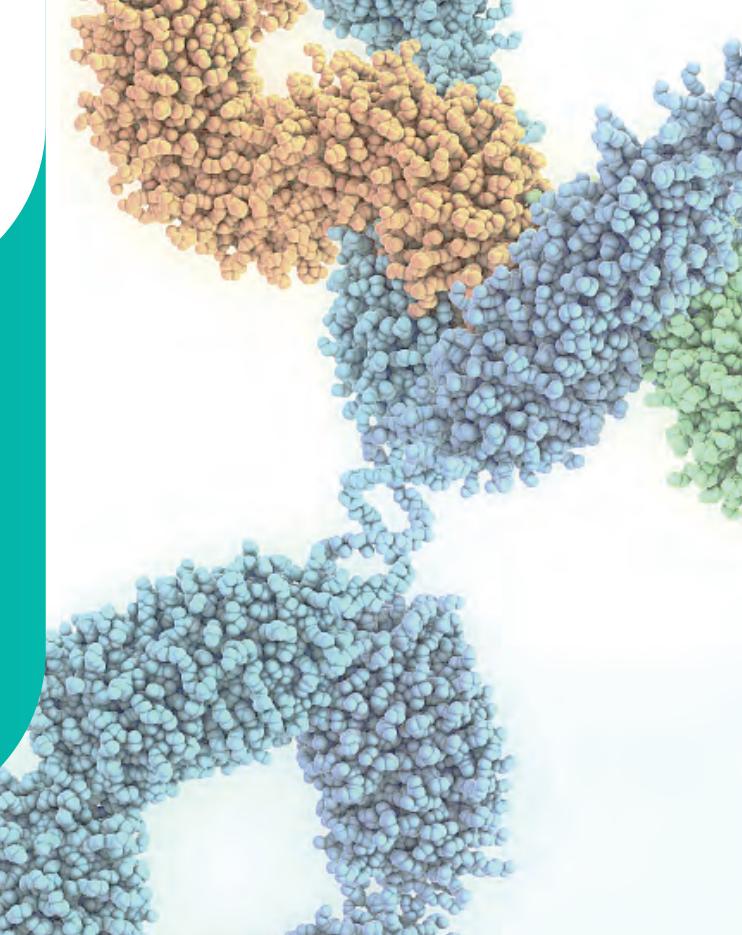
BioMice: Innovative models to accelerate drug discovery

BIOMICE

- **Animal & Cell Models**
- **Pharmacology Services**
- **Gene Editing Services**
- **Animal Center Related Services**
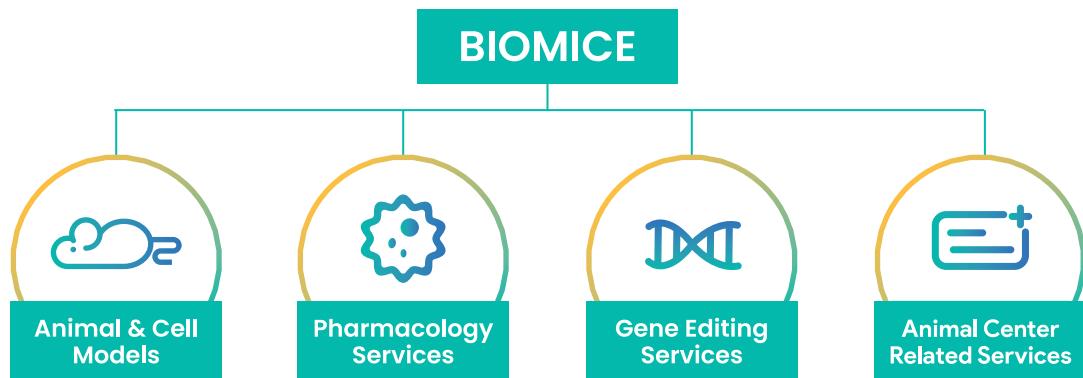
Partnerships with all of the Top **10** MNCs

BioMice's innovative animal models sold in **20+** countries and regions

Gene editing services

Stem cell lines in C57BL/6 background established in Biocytogen

Increase the efficiency of knock-in by 10-20 fold than CRISPR/Cas9

Unique chromosome editing at Mb level

ESC/HR	CRISPR/EGE	SUPCE

Three gene-editing technologies

1200+ publications used our gene editing service/gene edited models

4900+ Gene editing projects delivered for clients

Animal & cell models

3300+ Gene-edited animal and cell models developed

800000+ Animal models annual supply capacity

150000+ Cages in animal center with AAALAC

900+ Target humanized mice

> Humanized GPCR models

A2AR	C5AR1	CCL1	CCR2	CCR7	CX3CR1	CXCR6	FZD7	GPR40	LGR4
ADGRG2	C5AR2	CCL2	CCR3	CCR8	CXCR2	ETAR	GCGR	GPR55	MC4R
ADORA2B	CALCRL	CCL20	CCR4	CCR9	CXCR3	F2RL1	GLP1R	GPR75	S1PR1
BDKRB2	CB1	CCL22	CCR5	CGRP	CXCR4	FSHR	GPR20	GPRC5D	SUCNR1
C5	CB2	CCR1	CCR6	CRTH2	CXCR5	FZD5	GPR35	HCAR1	VPAC1

› Humanized immune-checkpoint models

4-1BB	CD112	CD24	CD24	CD4	CD79B	DLL1	GPC3	LILRB1	NKG2D	RAGE	VSIG4
4-1BBL	CD155	CD248	CD248	CD40	CD80	DLL3	HVEM	LILRB2	NKP46	RANKL	VSIR
ADRB1	CD160	CD27	CD27	CD40L	CD89	DR4	ICAM1	LILRB3	NOTCH1	ROBO4	
ALCAM	CD16A	CD28	CD28	CD43	CD93	EBI3	ICAM3	LILRB4	NRP1	RTN4R	
AMHR2	CD16B	CD30	CD30	CD44	CD94	F11R	ICOS	LRRC33	OX40	SELE	
ANTXR2	CD180	CD32A	CD32A	CD45	CDCP1	FAP	ICOSL	LY6E	OX40L	SELL	
AXL	CD19	CD32B	CD32B	CD47	CEACAM1	FGL1	ITGB3	MADCAM1	PD-1	SELP	
B2M	CD2	CD33	CD33	CD48	CLEC10A	FGL2	ITGB8	MERTK	PDGFB	SIGLEC10	
B7-H3	CD20	CD36	CD36	CD5	CLEC14A	FOLR1	KAAG1	MICA	PDGFRA	SIGLEC15	
B7-H4	CD200	CD37	CD37	CD52	CLEC9A	FOLR2	KLRG1	MRC1	PDGFRB	SIGLEC7	
BAMBI	CD200R	CD38	CD38	CD6	CSPG4	FOLR4	LAG3	NCR2	PD-L1	SIGLEC9	
BCMA	CD22	CD39	CD39	CD69	CTLA4	GARP	LAIR1	NCR3	PDPN	SIRPA	
BST2	CD226	CD3E	CD3E	CD70	CX3CL1	GAS6	LGALS9	NKG2A	PSGL-1	TF	
BTLA	CD23	CD3EDG	CD3EDG	CD73	DDR1	GITR	LIGHT	NKG2C	PVRIG	TGFB1	

› Humanized cytokines models

ADIPOQ	CCL4	CSF3	GDF8	IGFBP2	IL15RA	IL21R	IL33	INHBE	MIF	TFPI
ADM	CCL5	CXCL1	GEP	IGFBP7	IL17A	IL22	IL36A	KIT	OSM	TNFA
AFP	CCN1	CXCL10	GFRAL	IL10	IL17B	IL22RA1	IL36R	KITLG	OSMR	TSLP
ANG2	CCN2	CXCL13	GHRL	IL10RA	IL17F	IL23A	IL4	KLK2	PAI1	TSLPR
ANGPTL3	CCN4	CXCL16	GRP	IL10RB	IL17RA	IL25	IL4RA	KLK3	PCSK9	TWEAK
ANGPTL4	CD14	CXCL3	IFNAR1	IL11	IL17RB	IL26	IL5	LAIR1	PTHrP	VEGFA
ANGPTL8	CD59	CXCL4	IFNAR2	IL11RA	IL17RC	IL27	IL5RA	LIF	RNASE4	VEGFR1
APRIL	CD5L	CXCL7	IFNB1	IL12A	IL18	IL27RA	IL6	LPA	RSPO1	VEGFR2
BAFF	CETP	DKK1	IFNG	IL12B	IL18BP	IL2RA	IL6R	LTA	RSPO3	VWF
BAFFR	CFB	EPO	IFNGR1	IL12RB1	IL19	IL2RB	IL6ST	LTB	S100A8	WNT3A
C3	CFD	FCER1A	IFNGR2	IL12RB2	IL1B	IL2RG	IL7R	LTBR	S100A9	
CCL11	CSF1	FGF21	IgE	IL13	IL1RACP	IL3	IL8	LYPD3	SOST	
CCL24	CSF1R	FGFR3	IGF1R	IL13RA1	IL2	IL31	IL9	MAG	SPP1	
CCL3	CSF2RB	GDF15	IGF2R	IL15	IL20	IL31RA	IL9R	MASP2	TEK	

› Other humanized models

ADA	C1Q	CD9	DPP3	FXII	ITGA5	HLA-G	MET	ORAI1	SEMA7A	TGM2	XDH
ADAM15	CAIX	CD95	EGFL7	GFRA1	ITGA6	LAT1	MFGE8	P2RX3	SERPINF2	TIMP1	α4β7
ADAM17	CD105	CD98HC	EGFR	GFRA3	ITGA9	LGALS3BP	MMP9	PGLYRP1	SHH	TLR3	
ADAM9	CD133	CDH1	EMP2	GPC1	ITGAL	LRP10	MSLN	PLXNB2	SIGLEC8	TLR4	
ADAMTS5	CD147	CDH17	EPCAM	HAMP	ITGAV	LRP5	MST1R	PLAUR	SLAMF7	TLT1	
ALB	CD151	CDH3	EPHB3	HBEGF	ITGB1	LRP6	MUC1	POSTN	SLC16A3	TLT2	
AMIGO2	CD163	CFP	EREG	HER2	ITGB7	LRRC15	MUC17	PSCA	SLC43A2	TNC	
AOC3	CD1D	CLDN2	EVA-1	HER3	JAG1	LSR	NECTIN4	PSMA	SLPI	TPBG	
APOC3	CD209	CLEC5A	FcRn	HMMR	JAG2	LUCA2	NGAL	PTH	SRB1	TROP2	
APOE2	CD300A	CLU	FGB	IBSP	JAM3	MARCO	NGF	PTK7	SSTR2	TTR*V30M	
APOE4	CD55	CSPG5	FGFRL1	ILT7	L1CAM	MCAM	NPR1	RETN	TCIRG1	TYRO3	
AREG	CD63	CTSG	FLT3LG	ITGA1	HLA-A11.1	MDK	NTRK1	RGMA	TDGF1	UPA	
BDCA2	CD68	DLK1	FSHB	ITGA2	HLA-A24.2	MDR1	NTRK2	ROR1	TEM7R	UPAR	
BPIFA1	CD79A	DLL4	FSTL3	ITGA4	HLA-A3.1	MELTF	NTRK3	SEMA4D	TFR1	VLDLR	

60+ Immunodeficient mice	800+ Gene-edited mice	200+ Cell lines
• B-NDG series of immunodeficient mice • Other immunodeficient mice & Rats	• Cre mice • Target knock-out mice • Other gene edited mice • Aged mice	• Humanized cell lines • Reporter cell lines

B-NDG mice	B-NDG B2m KO mice plus	B-NDG hIL15 mice	B-NDG HLA-A2.1 mice
B-NDG hIL6 mice	B-NDG hTHPO mice	B-NDG hCSF1/hTHPO mice	B-NDG MGMT3 mice
B-NDG hFcRn mice	B-NDG MHC I/II DKO mice plus	B-NDG hSIRPA mice	B-NDG hSIRPA/hCD47 mice

hCLDN18.2 MC38	hHER2 MC38	hDKK1 MC38	hCD47 MC38	hHER2 EL4	hROR1 MC38	hLILRB4 MC38
hFAP MC38	hAMHR2 MC38	hGPC3 MC38	hTF MC38	hAMHR2 ID8	hFN14 MC38	hTROP2 MC38
hGPRC5D MC38	hBCMA MC38	hMSLN ID8	hNECTIN-4 MC38	hCXCR4 MC38	hTPBG MC38	hTPBG B16-F10

Pharmacology and Translational Research Services

4500+ Pharmacology programs for our clients

> *In vivo* Pharmacology Platform

Tumor (Allograft & xenograft model)	
Target humanized models	**Immune system humanized models**
Syngeneic model (Subcutaneous/ Orthotopic)	PBMC reconstitution model
Spontaneous tumor model	CD34+ HSC reconstitution model
	NK reconstitution model
Autoimmune disease & inflammation models	
RA (Rheumatoid Arthritis) / CIA (Collagen Induced Arthritis) model	IBD (Inflammatory Bowel Disease) model
	SLE (Systemic Lupus Erythematosus) model
Osteoporosis Model	DTH (Delayed Type Hypersensitivity) model
EAE (Experimental Autoimmune Encephalomyelitis) model	CKD(Chronic Kidney Disease)/(5/6 Nephrectomy) model
AD (Atopic Dermatitis) model	Pulmonary fibrosis model
Asthma model	Itchiness model
Pneumonia model	Alopecia areata model
Psoriasis model	
Metabolic disease models	
Obesity and diabetes model	Acute liver injury model
NAFLD/NASH model	Atherosclerosis model
Liver fibrosis model	Hyperuricemia model

> PD/PK Platform

Receptor occupancy (RO) analysis	Blood concentration analysis
Immune cell analysis	Immunogenecity analysis
Tumor infiltrating lymphocytes analysis	Tissue distribution analysis
Multiple cytokine analysis	
Tumor microenvironment analysis	

> Non-GLP Toxicology Platform

Histopathology toxicology tests	Clinical observation(Score)	Blood toxicology tests
Toxicokinetic (TK)	Cytokine release syndrome (CRS)	

> *In vitro* Pharmacology Platform

Model Validation	Screen	MOA	Toxicology
Binding assay	Killing assay	ADCC/ADCP/CDC	Inflammation/ Cytokines assay
Blocking assay	Internalization	MLR/Polarization	
Bioactivation assay			

> Large animal (canine) translational research platform

In vivo efficacy	PK/PD	Non-GLP toxicology

RenBiologics： Our Fully Human Library. Your Pipeline.

| mAb platform	BsAb platform	BsADC platform	Nanobody platform	TCR platform	TCR-mimic platform	GPCR platform
RenMab™	**RenLite®**	**RenLite®**	**RenNano®**	**RenTCR™**	**RenTCR-mimic™**	**RenMice® KO**
• Target KO strategy • Great diversity & affinity • Novel binding epitopes • Multi-species cross-reactivity	• Common light chain • Convenient assembly • High purity and good developabilities	• 200+ TAA targets • Good developabilities • Increased potency & reduced toxicity	• Good permeability • Small and good building blocks for bi-/multi-specific Ab, CAR-T, etc.	• Good T-cell immune response • Discovery of high-affinity antigen-specificTCR • Novel epitope discovery	• Intracellular TAAs • High specificity to the target/HLA complex	• Targeting challenging GPCRs • Targeting complex transmembrane structure

Streamlined Antibody Discovery

A large-scale antibody drug development project for 1000+ potential drug tardets using target knockout RenMice.

Target Identification — Antibody library development — *In vitro* Tests — *In vivo* Efficacy — PCC production and CMC — PK/PD/Tox — Collaborative clinical trial

Obtain cross-reactive antibodies to human, mice and large animals

Antibody Discovery
Target Identification
In vivo efficacy

1000+ Target KO RenMice → Mouse Preclinical → Large Animal Translation (Improve Clinical Translation) → Human Clinical

Fully Human Antibody Library Against 1000+Targets

400k	**40+**	**~150**
Fully-human antibody sequences	PCC	Partnerships

|		
20+	**Dual-TAA targeting BsADCs** SEZ6×B7-H3, PTK7 x TROP2, FOLR1 x MUC1, etc.	
30+	**Autoimmune projects** OX40 x OX40, CD40, TNFSF15, OSMR, etc.	
200+	**TAA-targeting antibody backbones** GUCY2C, CDCP1, PTK7, CDH17, SEZ6, B7-H3, etc.	
10+	**TCR-mimic antibodies targeting** CD3e x GP100, WT1, KRAS, AFP, NY-ESO-1, etc.	
200+	**Nanobodies targeting** TFR1, 4-1BB, CD3, BCMA, etc.	
70+	**mAb/BsAb programs targeting GPCRs** CCR8, GPRC5D, LGR5, CCR2 (Metabolism), etc.	

Nanobody Platform
RenNano to develop heavy-chain-only antibodies (HCAbs) or nanobodies

Advantages

Antigen A

RenNano

Target A screening

Antigen B

RenNano

Target B screening

sdAb

Bispecific antibody
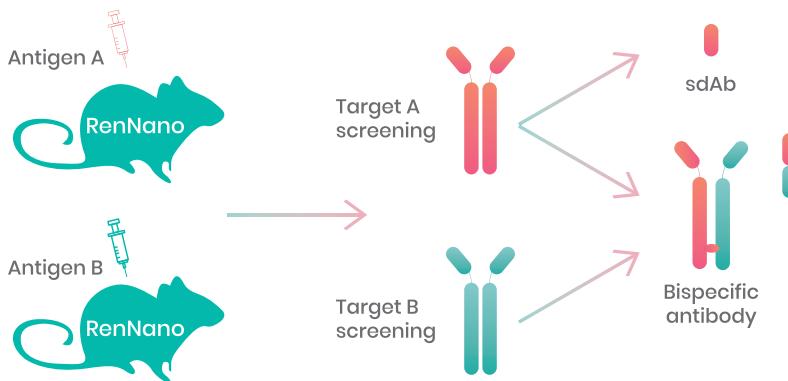
- Recognizing hidden epitopes
- Good hydrophilicity and penetration ability
- Robust immune response
- Diversified heavy chain repertoire
- High binding affinity at nanomolar range

Nano 100 Project

The "Nano 100 Project" aims to develop fully human nanobody drugs using RenNano mice for more than 100 targets, including tumor associated antigens (TAAs), GPCRs, immune-checkpoints, cytokines, and factors related to neurological diseases.

RenNano

HcAb/ sdAb

BsAb/ engager

Multi-specific Ab

CAR-T/ CAR-NK

Radionuclide antibody conjugate (RAC)

Nano-drug
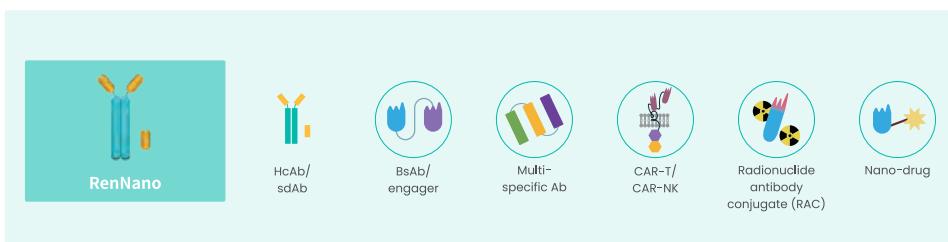
Nano 100

TCRmimic Antibody Platform

TCRmimic Antibody for the detection of intracellular tumor associated antigens

T-cell

TCR mimic Ab (fully human)

T-cell receptor (TCR)

MHC-I   MHC-I
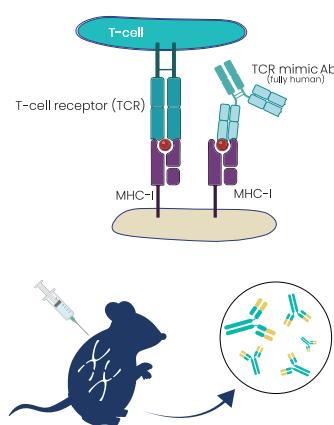
Immunization of HLA/RenMice

Progress of TCRm Antibodies

TAA	WT1/HLA-A02
	GP100/HLA-A02
	AFP/HLA-A02
	Survivin2B/HLA-A24
CTA	NY-ESO-1/HLA-A02
	MAGE-A4/HLA-A02
Mutation	KRAS(G12V)/HLA-A03
	KRAS(G12V)/HLA-A11
	P53(R175H)/HLA-A02
Virus	LMP2/HLA-A02
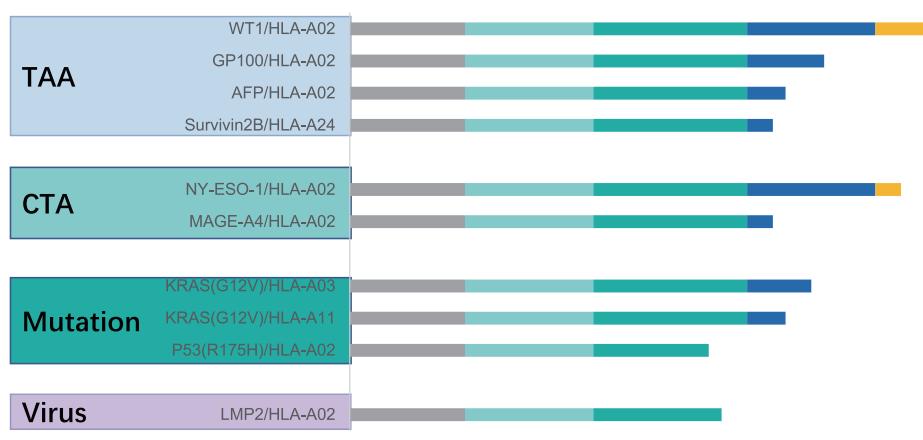
■ Target identification ■ Immunization ■ Sequence-based screening ■ In vitro tests ■ In vivo efficacy

Biocytogen's BsADC Platform

Advantages of bsADC

| Antigen 1 | Antigen 2 | Ligand 1 | Ligand 2 | Signaling activity | Signaling blockage | Payload |
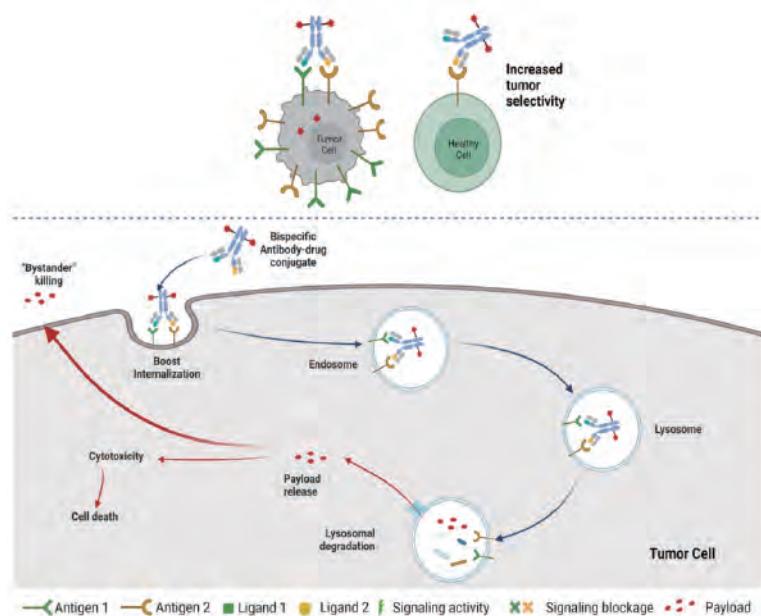
Advantages of Biocytogen's bsADC platform

01

Common light chain antibodies from RenLite are easy to assemble bsAbs with good stability making it convenient for further drug development.

02

RenLite mice with target gene knockout generate antibodies that bind to more epitopes of the target protein with similar affinities across different species.

03

There are plenty of targets for combinations and the ability to do multi-species drug efficacy and toxicity tests increases the success rate and reduces the time of drug development.

Construction of bsADC using RenLite

Antigen A — RenLite
Antigen B — RenLite

RenLite common light chain + knobs-into-holes

Payload conjugation

BsAbs → BsADCs
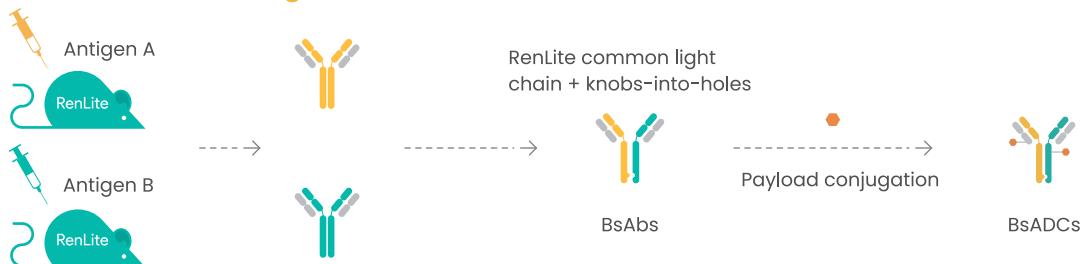
200+ TAA-targeting backbones for plug & play

MUC1	5T4	PTK7
GUCY2C	SEZ6	HER3
FOLR1	CEA	PSMA
HLA-G	LIV-1	ROR1
B7-H3	CDH3	MUC16

etc.

20+ Ongoing bsADC programs

Target(s)	Immunization	Discovery			Preclinical	IND	Phase I	Status
		Hits selection	Leads selection	Candidate selection				
HER2 x TROP2 (YH012)								Partnered
EGFR x MET (DM005)								Partnered
TROP2 x EGFR (DM001)								Partnered
HER3 x MUC1 (DM002)								Partnered
EGFR x MUC1 (BSA01)								Partnered
PTK7 x TROP2								
HER3 x MET								
PTK7 x EGFR								
EGFR x HER3								Exclusive MTA evaluation ongoing
B7-H3 x PTK7								Partnered
EGFR x 5T4								
FOLR1 x MUC1								
5T4 x MUC1								
SEZ6 x B7H3								
FOLR1 x MUC16								
Nectin-4 x TAAs								
FAP x TAAs								
CD71 x TAAs								
CDCP1 x TAAs								
ADAM9 x TAAs								
CDH6 x TAAs								
ITGB6 x TAAs								
MSLN x TAAs								
FOLR1 x SLC34A2								

Clinical Assets Available for Partnership

	Product candidate	Target(s)	Combination	Indication	Pre-clinical	IND	Phase I	Phase II	Phase III	Rights	Partner
Clinical-stage Drug Candidates	⭐ YH001	CTLA-4	PD-1	Solid tumors	Australia					Global	
			Monotherapy	Solid tumors	China						
	YH002	OX40	YH003+YH001	Intratumoral immunotherapy	Investigator Initiated Trials						Syncromune, Inc.
	⭐ YH003	CD40	PD-1+chemo	Pancreatic ductal adenocarcinoma (1L&2L)	Global MRCT					Global	
			PD-1+chemo	Mucosal melanoma	China						
			PD-1+YH001	Solid tumors	Global MRCT						
	YH004	4-1BB	Monotherapy	Solid tumors	Australia and China					Global	
	YH008	PD-1 x CD40 BsAb	Monotherapy	Solid tumors	China					ex-Greater China	Chipscreen NewWay (Greater China)

Notes: ⭐ Core Product Candidate | ⋯⋯ Out-licensing/Co-development | ▇ Oncology

Global partnerships for antibody therapeutics R&D

~150 asset-based collaborations

~50 target-nominated RenMice licensing projects

Assets-based partners

GILEAD | Merck KGaA | ablbio | NEUROCRINE BIOSCIENCES You Deserve Brave Science | ADC Therapeutics

ONA | Radiance | Sotio | IDEAYA BIOSCIENCES | PHEON THERAPEUTICS

BIOCOPY | LihuaThera | Manhattan BIOSOLUTIONS | 华润生物医药 CR BIOPHARM | 华北制药

NJCTTQ 国药正大天晴 | 翰森制药 | RemeGen 荣昌生物 | KELUN-BIOTECH 科伦博泰 | CTMBio concept to medicine

上海生物制品研究所有限责任公司 SHANGHAI INSTITUTE OF BIOLOGICAL PRODUCTS CO., LTD. | Fineimmu | CLON ORGAN 中科奥格 | DOMA 多玛医药 | 星奕昂生物科技 Neukio Biotherapeutics

RenMice® platform-based partners

Merck KGaA | Janssen | Xencor | BeiGene | Innovent

君实生物 TopAlliance
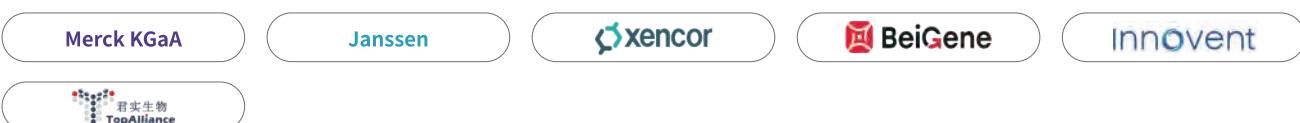
Clinical pipeline-based partners

syncromune | RemeGen 荣昌生物 | 微芯新域 NEWWAY CHIPSCREEN

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