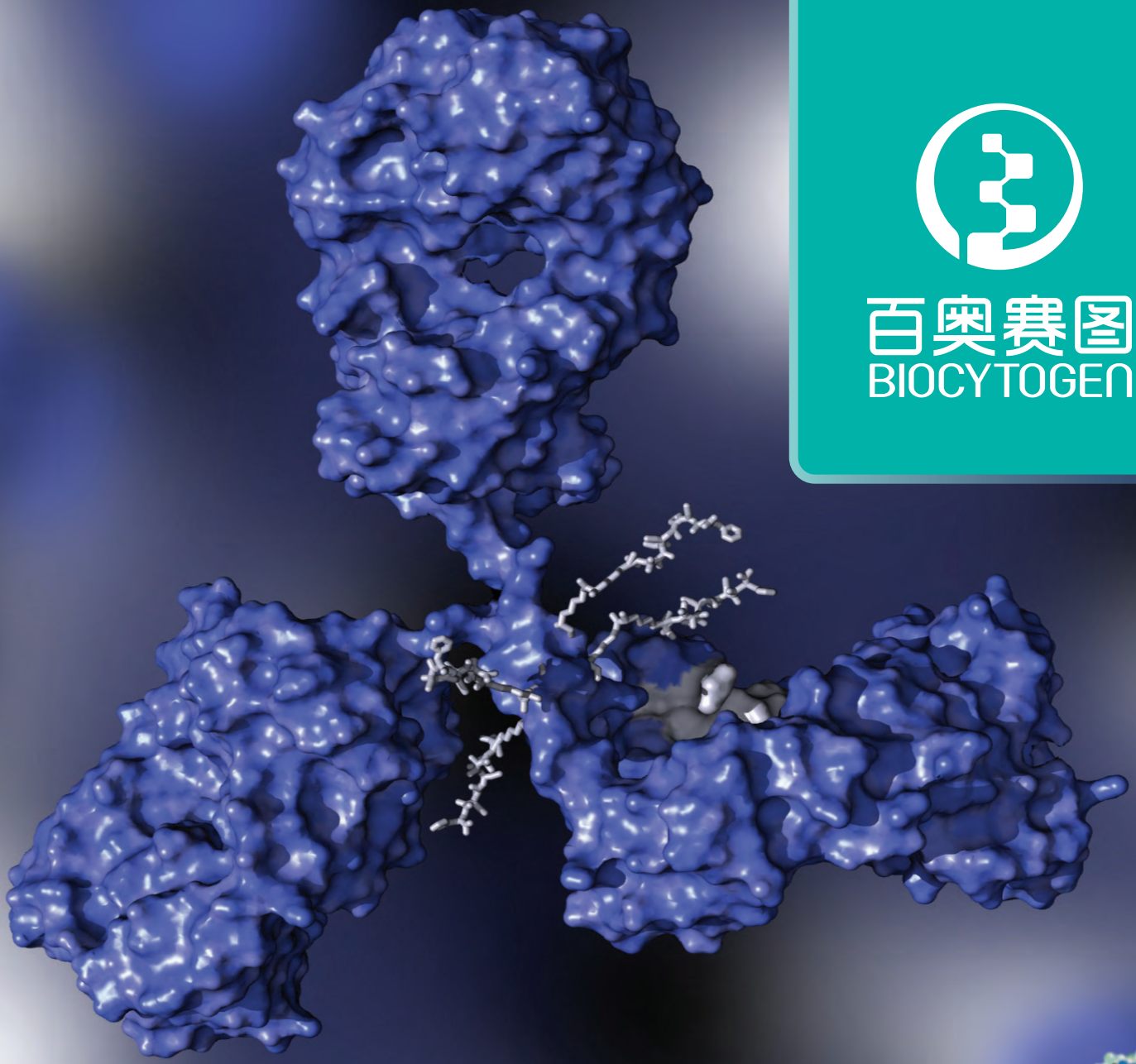
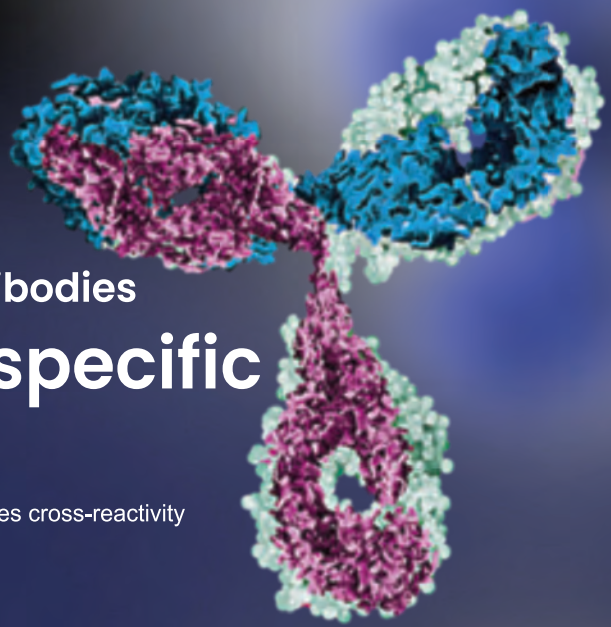
百奥赛图
BIOCYTOGEN





Based on RenLite common-light chain antibodies

Bispecific Antibody & Bispecific ADC Development

- RenMice KO strategy: fully human antibodies with increased diversity and species cross-reactivity
- Proprietary linker/payload system BLD1102
- 200+ TAA-targeting antibody backbones available for flexible plug & play

BISPECIFIC ANTIBODY PLATFORM

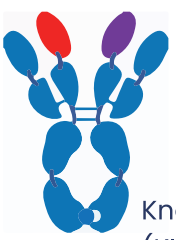
Types of Bispecific Antibodies (BsAbs)

IgG-ScFv Bispecific Antibody

Single chain variable fragment (ScFv)

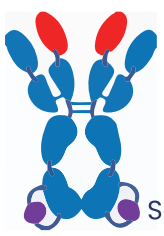
Common Light Chain-KIH Bispecific Antibody

Common light chain



Knob into hole (KIH)

3A Bispecific Antibody

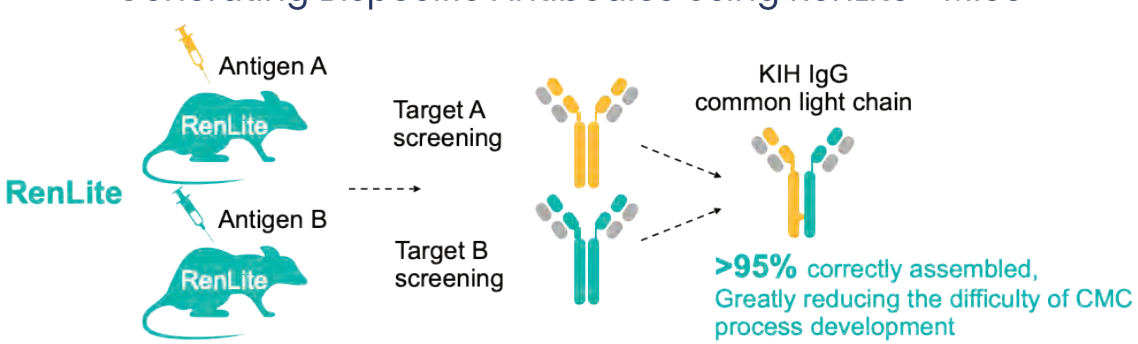


ScFv Inserted in CH3 domain (3A)

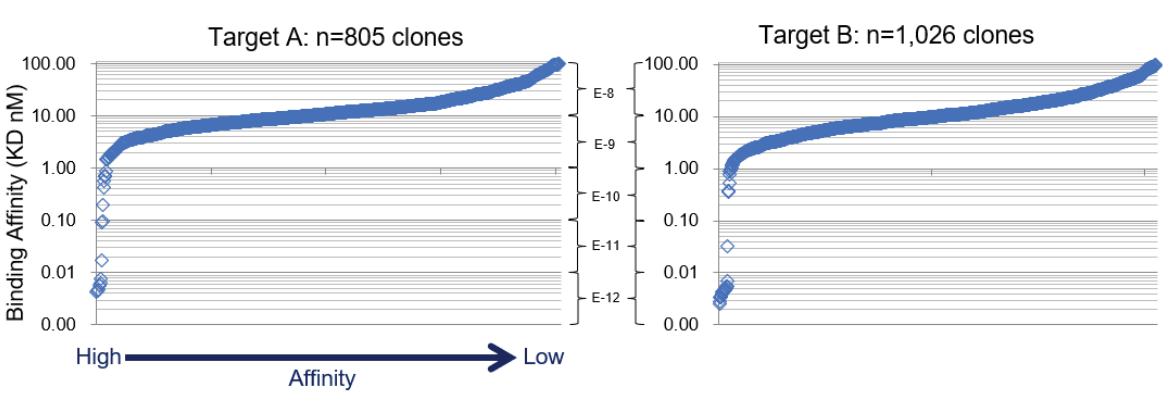
RenLite® Mouse Platform for Common Light Chain-KIH BsAbs

- Expression is limited to a common human kappa light chain to facilitate bispecific or multispecific antibody discovery.
- Diversified heavy chain repertoire similar to that of humans.
- Robust immune response comparable to wild type mice.
- High binding affinity in the subnanomolar range.

Generating Bispecific Antibodies Using RenLite® Mice

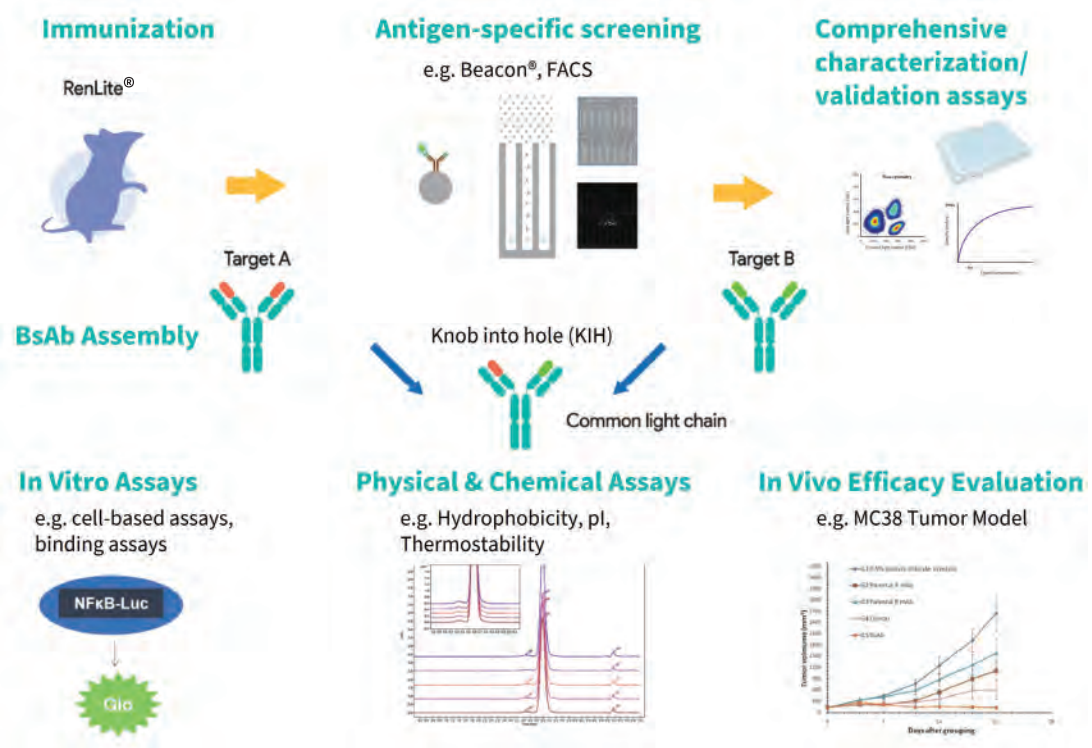


All antibodies derived from RenLite® mice share the same kappa light chain, which streamlines bispecific antibody assembly. When wild-type mice are used, the assembly of correct heavy/light chains is highly inefficient.



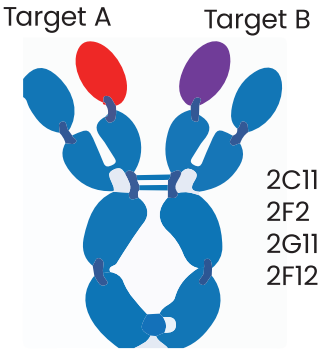
Affinity range of RenLite-derived antibodies for Targets A and B. Many antibodies fall in the subnanomolar range. The range varies by antigen, immunization scheme, adjuvant, and screening technology used.

Development of Common Light Chain BsAbs



Antibody hits with a common light chain are tested in multiple assays prior to assembly into bispecifics with multiple structural formats. To ensure that antibodies have desirable biologic activity and drug-like properties, multiple functional and developability assays are performed. Different target combinations may require different skeletons and binding epitopes to achieve their desired activity.

Common Light Chain BsAbs Exhibit Good Developabilities



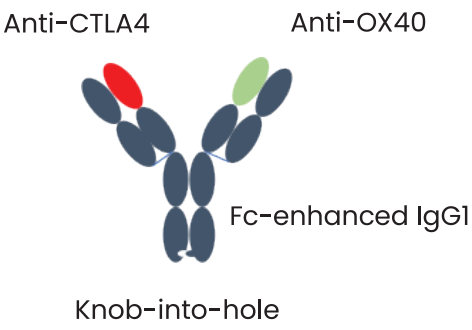
4 clones from campaign A and B yield up to 16 BsAb combinations, which were evaluated for purity by SEC-HPLC.

BsAb	SEC-HPLC (%)
5E3+2C11	95.2
5E3+2F12	94.3
5E3+2F2	94.9
5E3+2G11	96
5F9+2C11	97.8
5F9+2F12	98.3
5F9+2F2	96
5F9+2G11	98.5
3D2+2C11	90.6
3D2+2F12	98.9

BsAb	SEC-HPLC(%)
3D2+2F2	96
3D2+2G11	98.2
5E10+2C11	98.4
5E10+2F12	97.2
5E10+2F2	98
5E10+2G11	98.8
4E12+2C11	98.6
4E12+2F12	98.1
4E12+2F2	98.3
4E12+2G11	97

BsAb Development Case Study: **YH006**

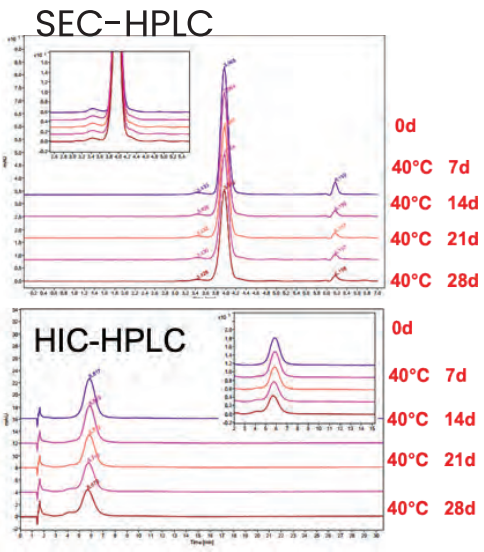
Format

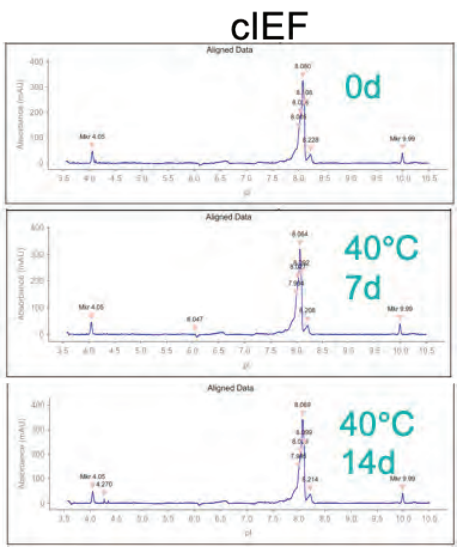


Highlights

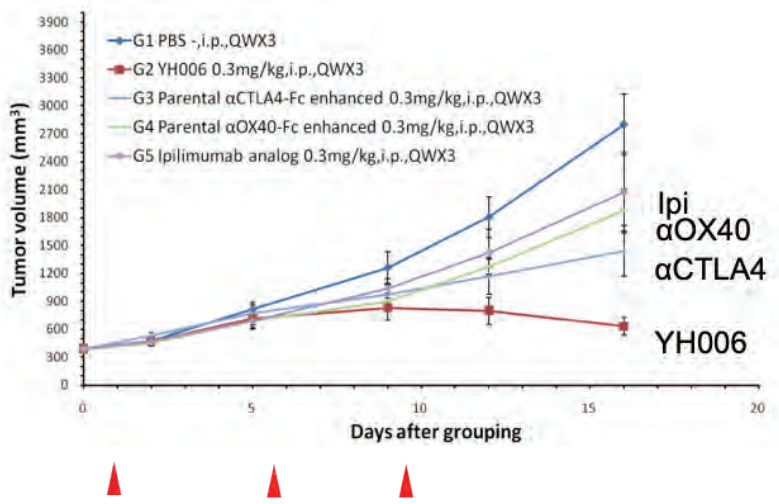
- Tumor-infiltrating Tregs exhibit co-expression of high levels of both CTLA4 and OX40
- Dual recognition allows increased Treg binding specificity and enhanced efficacy
- Fc-enhanced IgG1 isotype can potentially improve anti-tumor response in CD16-low affinity patients
- Designed to reduce CTLA-4 and OX40 blocking activity
- Fixed common light chain format ensures good manufacturability

High Purity and Stability of YH006





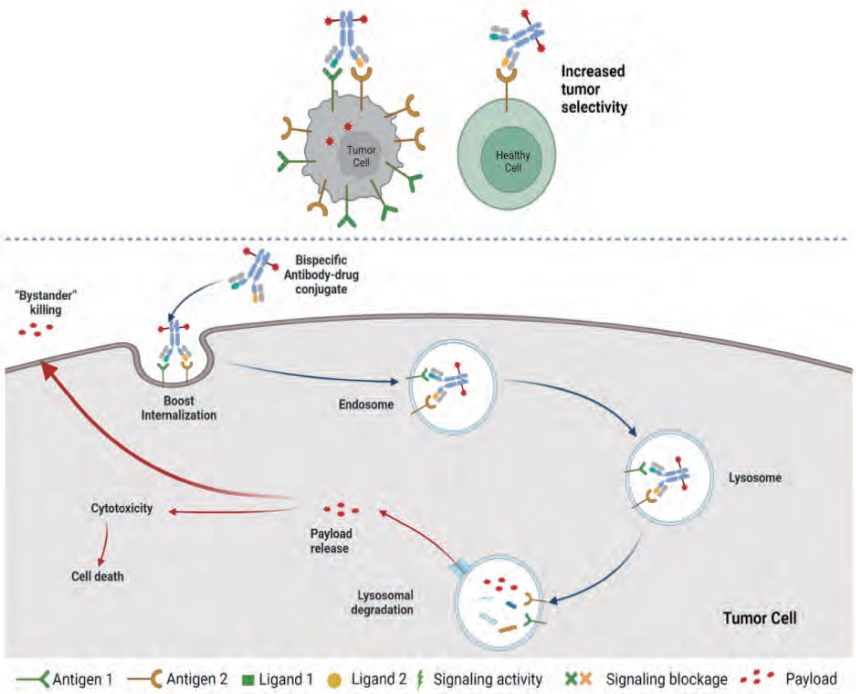
YH006 Inhibits Tumor Growth in a MC38 Syngeneic Model



B-hCTLA4/hOX40 humanized mice with established subcutaneous MC38 tumors were given 3 doses (red arrows) of the indicated antibody. Each group (n=6/group) was injected intraperitoneally with mAbs. The anti-tumor effect of YH006 was superior to Ipilimumab (Ipi) analog and the parental mAbs (Fc-enhanced IgG1).

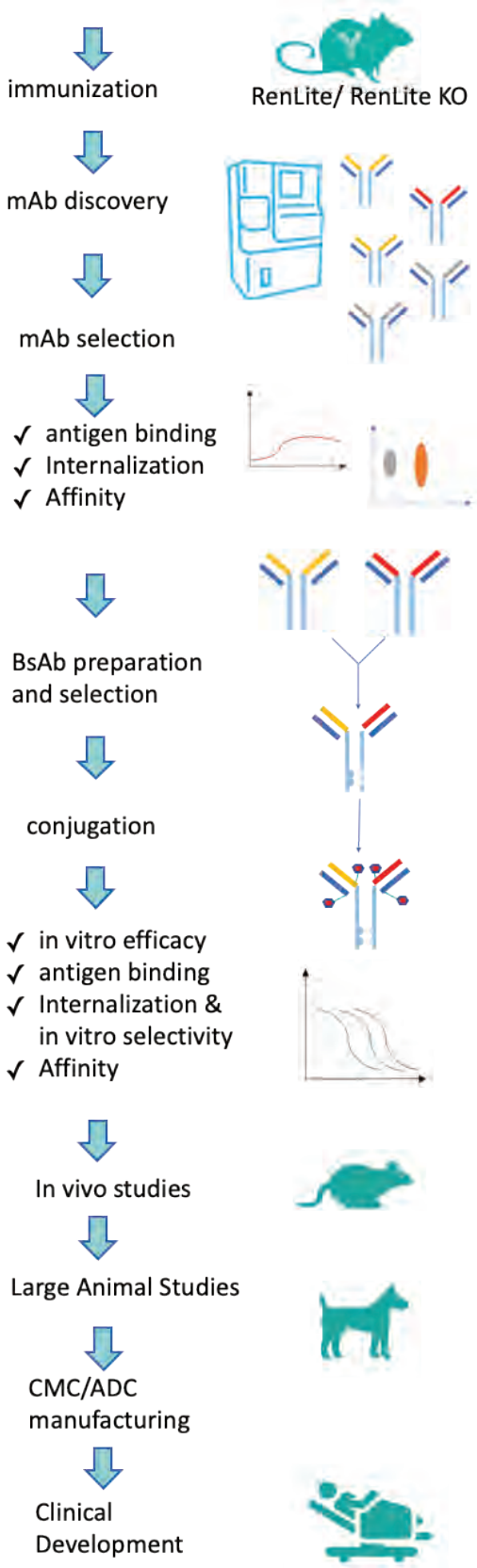
BISPECIFIC ADC PLATFORM

Mechanism of Action



- **Ideal for targeting two tumor-associated antigens (TAAs)**
- improved efficacy due to synergistic effects
- increased target cross-linking and internalization
- increased tumor cell specificity and minimal side effects in normal tissues

Development Process

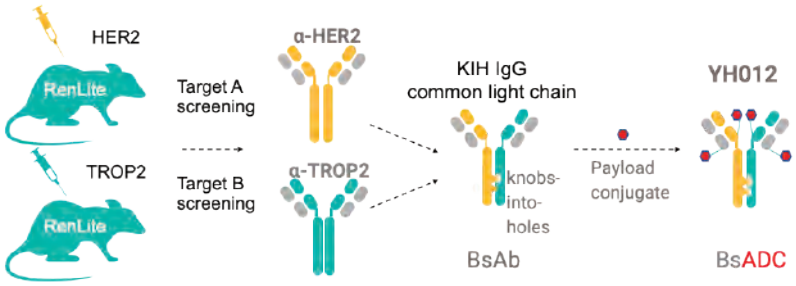


Platform Highlights

- High-throughput and rapid generation of BsADCs
- Huge potential for a large number of BsADCs targeting dual TAAs
- Improved translational efficiency through preclinical testing in large animals
- Target knock-out in RenLite mice increases the chance of obtaining novel binding epitopes and species cross-reactivity, resulting in more diverse products
- Conjugation of payload to naturally available amino acid side-chains (cysteine) is similar to mAbs.

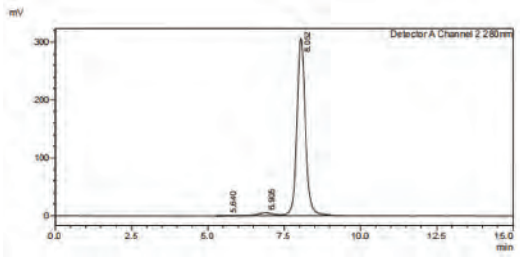
Case Study: **A Novel Bispecific HER2 and TROP2 Antibody-Drug Conjugate (YH012)**

Design of YH012

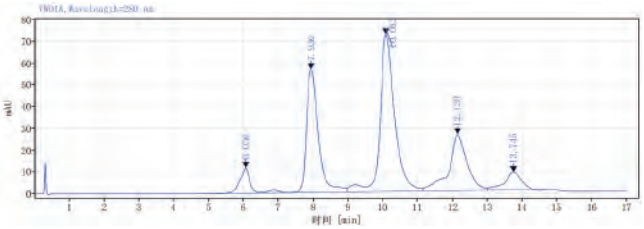


HER2 and TROP2 are co-expressed on multiple cancer types, so they are attractive candidates for a BsADC. Graphs denote the purity of the BsAb (top) and the conjugation ratio (DAR) of YH012.

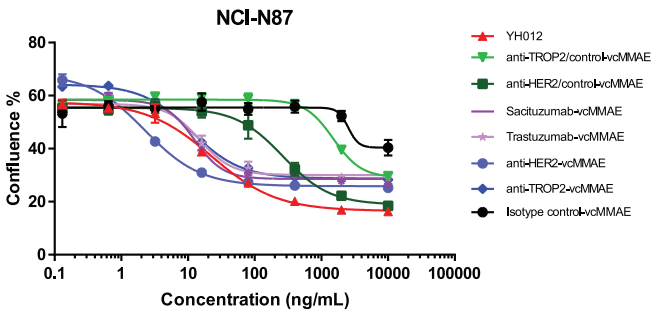
α-HER2/TROP2 BsAb SEC-HPLC

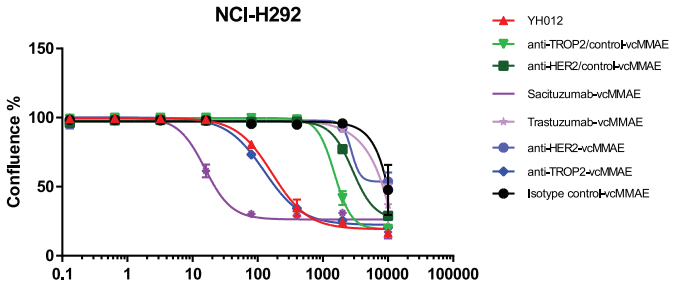


YH012 BsADC HIC-HPLC

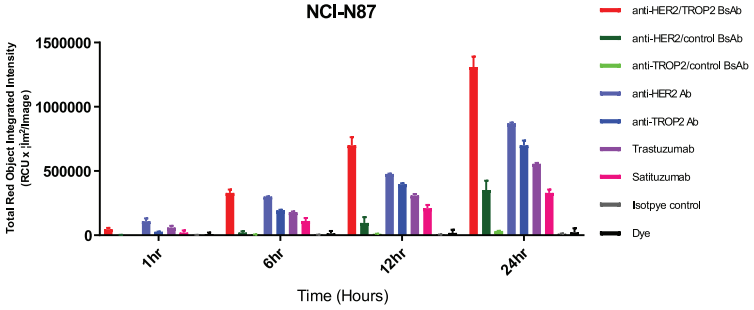


In Vitro Cell Growth Inhibitory Activity



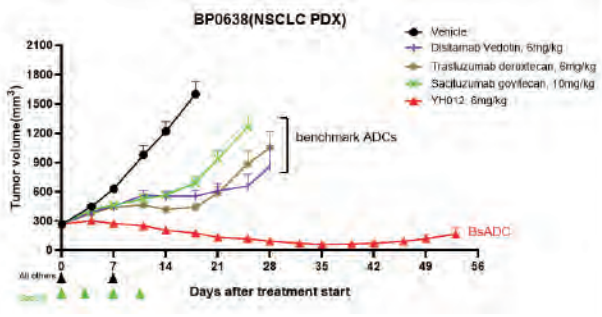


Endocytosis in NCI-N87 Cells



The anti-HER2/TROP2 BsAb showed increased endocytosis activity compared with its parental mAbs(anti-HER2 Ab or anti-TROP2 Ab) in tumor cells co-expressing HER2/TROP2(NCI-N87 cells), whereas the monovalent anti-TROP2/control or anti-HER2/control BsAb showed reduced internalization.

Anti-Tumor Activity of YH012



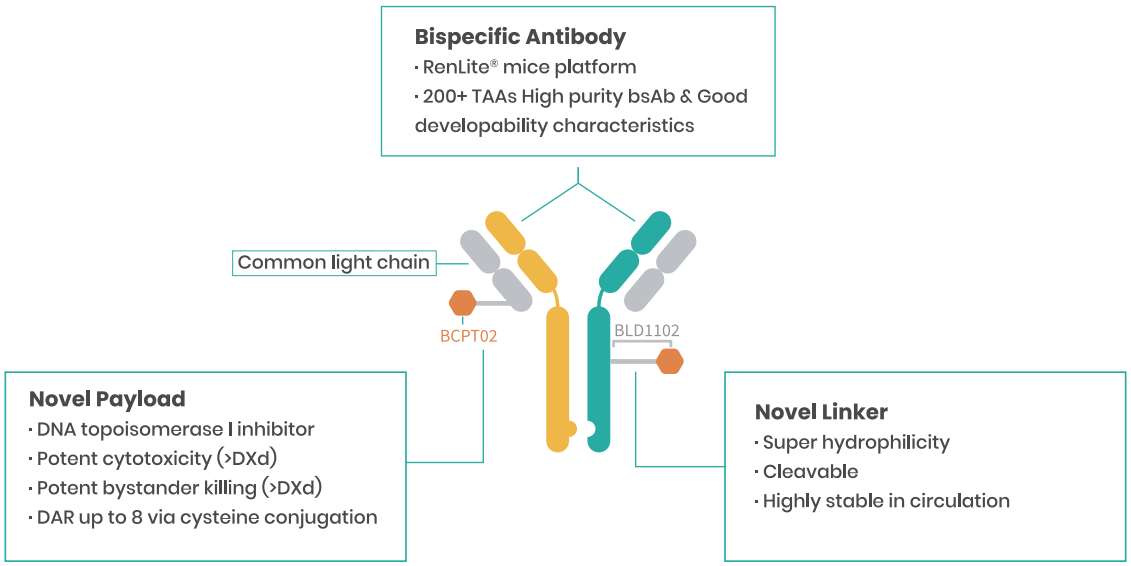
YH012 showed strong and durable antitumor activity in HER2-low NSCLC PDX model compared with benchmark ADCs, indicating that YH012 has strong therapeutic potential to overcome the drug resistance of single target ADCs caused by tumor heterogeneit.

TAA Targeting Antibody Backbones for Plug & Play from RenLite Platform

ADAM9	AFP	AMHR2	B7-H3	B7-H4	CAIX	CCR9	CD105	CD142	CD155
CD22	CD30	CD7	CD70	CDCP1	CDH11	CDH17	CDH3	CDH6	CEACAM5
CEACAM6	Claudin 18.2	CLDN3	CLDN6	CLEC12A	DDR1	DLK1	DR5	EGFR	EPCAM
EPHA2	EPHB2	FAP	FLT3	FOLR1	GPC-1	GUCY2C	Her2	HER3	HLA-G
HPN	IL3RA	ITGB6	KIT	KREMEN2	LGR5	LIV-1	LRRC15	LUNX	LY6G6D
LYPD3	MET	MSLN	MUC1	MUC16	MUC18	Nectin-4	PALP	PRLR	PSMA
PTK7	ROR1	SEZ6	SLC34A2	SSTR2	TIM1	TPBG	TROP2	and more	

Proprietary Bispecific ADC Platform

With Novel High Potency DNA Topoisomerase I Inhibitor Payload and Novel Hydrophilic Linker



Flexible business models

RenMice Platform Licensing

Antibody Licensing/Assignment and Co-Development

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About Biocytogen

Biocytogen (HKEX: 02315) is a global biotechnology company that drives the research and development of novel antibody-based drugs with innovative technologies. Founded on gene editing technology, Biocytogen leverages genetically engineered proprietary RenMice® (RenMab™/ RenLite®/ RenNano®/ RenTCR-mimic™) platforms for fully human monoclonal/bispecific/multispecific antibody discovery, bispecific antibody-drug conjugate discovery, nanobody discovery and TCR-mimic antibody discovery, and has established a sub-brand, RenBiologics™, to explore global partnerships for an off-the-shelf library of >400,000 fully human antibody sequences against approximately 1000 targets for worldwide collaboration. As of June 30, 2024, approximately 150 therapeutic antibody and multiple clinical asset co-development/out-licensing/transfer agreements and nearly 50 target-nominated RenMice® licensing projects have been established with over 60 global pharmaceutical and biotech companies, including several partnerships with multinational pharmaceutical companies (MNCs). Biocytogen pioneered the generation of drug target knock-in humanized models for preclinical research, and currently provides a few thousand off-the-shelf animal and cell models under the company's sub-brand, BioMice™, along with preclinical pharmacology and gene-editing services for clients worldwide. Headquartered in Beijing, Biocytogen has branches in China (Haimen Jiangsu, Shanghai), USA (Boston, San Francisco), and Germany (Heidelberg). For more information, please visit http://en.biocytogen.com.cn.

1,000+
Targets

200+
TAA Targets

~150
Ongoing Partnerships

Worked with all of the top **10** Pharmaceutical Companies

1,000+
Employees Worldwide