Henlius

创新致远 为众为先

INNOVATION REACHES FAR PIONEERING FOR PEOPLE

复宏汉霖全球研发开放日

股份代号：2696.HK

2020.06.13 中国 上海

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R&D and Clinical Strategy and Updates

Scott Liu

Co-founder & CEO

Major Updates

Major Updates – Product Development

Biosimilar drugs	• **Multiple progress achieved for further development of 汉利康®（HLX01）** Application for new indications CLL&FL received by NMPA (2020.05)；sNDA for 2000L and 500mg approved by NMPA (2020.04) • **First “Chinese” biosimilar received positive opinion from EMA CHMP** EU MAA of HLX02(trastuzumab) received positive opinion from EMA CHMP（2020.05） • **3 biosimilar INDs approved by NMPA** HLX11 (Pertuzumab) (2020.01); HLX13(Ipilimumab)(2020.04); HLX14(Denosumab)(2020.5) • **2 study results published on international journals** Phase 3 clinical study results of 汉利康® published on JHO (2020.04)；Similarity study results of HLX02 published on BioDrugs（2020.02）
Bio-innovative drugs	• **First patient dosed in 4 domestic/overseas clinical trials, 1 Phase 1 trial completed** Overseas first patient dosed in an international multicenter Phase 3 clinical trial of HLX10 (PD-1) for 1L sqNSCLC（2020.04） Overseas first patient dosed in an international multicenter Phase 3 clinical trial of HLX10 (PD-1) for 1L ES-SCLC （2020.04） First patient dosed in a Phase 2 clinical trial of HLX10 (PD-1) for Cervical Cancer (2020.03) First patient dosed in a Phase 1 clinical trial of HLX55 (innovative c-MET mAb)（2020.03） Phase 1 clinical trial of HLX07(innovative EGFR mAb) demonstrated good safety and tolerability（2020.03） • **1 bio-innovative drug IND approved** HLX56 (DR4 mAb) received IND approval in Taiwan（2020.05）
COVID-19 projects	• **HLX70(Anti-S1 neutralizing antibody) and HLX71(ACE2-Fc fusion protein)received special fund support from Ministry of Science and Technology’ s “National Key R&D Project” (2020.05)**

Period：2020.01.01-2020.06.12

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Major Updates – Platform Technologies

R&D platform technology	• Successfully built proprietary **tumor animal model platform** containing **>70** different mouse tumor models • Successfully constructed Humanized Llama VHH **Phage Display Library** with **super big library capacity (2 x 10^{12})** • Proactively advanced preclinical development of **~20 novel antibody/fusion protein projects based on VHH or scFv**，among which relevant China and international patent applications were filed on HLX301 and HLX35
Process development platform technology	• **Continuous process technology** completed **pilot (200L) concept test**, downstream time reduced to 1.5 days from 6 days with consistent product quality compared with batch production • **ATF perfusion culture process** applied to lab-level production with >20g/L titer • Already owned self-development capability for **high concentration preparation and prefilled syringe product**, high-dose subcutaneous injection in development
Innovation partnership	• Partnered with **Fosun Kite** to explore development and application of CAR-T and BiCAR-T cell therapy product in solid tumors（2020.04） • Partnered with **Sanyou Biopharmaceuticals Co., Ltd.** and **Shanghai ZJ Bio-Tech Co., Ltd.** to develop fully human antibody drug for COVID-19（2020.05） • Partnered with **MEDx Translational Medicine Co., Ltd.** in the relevant area of innovative tumor drug biomarker and companion diagnostics（2020.03） • Partnered with **AnchorDx** to develop companion diagnostic products for gastric cancer HER2 gene amplification liquid biopsy（2020.05）

Period：2020.01.01-2020.06.12

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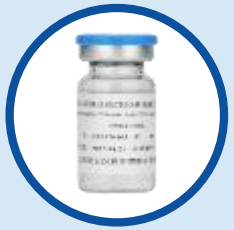
Innovation Track Record

Willing to Try – Successful Innovation Cases of Henlius since Inception



First
Biosimilar IND and NDA Filings

First
China-manufactured biosimilar entering global phase 3 trials

First
Biosimilar developed in China filing for EMA Approval

First
Adopter of single-use technologies

First
Multinational research operation

First
Developing continuous bioprocessing technologies

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汉利康®: China’ s First Biosimilar

2019.02 HLX01(汉利康®) NDA approved by NMPA
--China’ s first approved monoclonal antibody based on “Guiding Principles of Biosimilars”

2019.02 Research on HLX01 similarity published on journal of *mAbs*
--China’ s first published article to evaluate similarity of biosimilars

2019.05 The first prescription written of 汉利康®
--China’ s first commercially launched biosimilar

Source: EMA, FDA and NMPA websites

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First Global “Chinese” biosimilar - Henlius HLX02(汉曲优®；Zercepac ®)

- **China’s first** biosimilar with global multi-center Phase 3 clinical trial (2017-2019)
- **China’s first** trastuzumab developed based on “Guiding Principles of Biosimilars” with NDA accepted by NMPA（2019.04）
- **China’s first** domestic mAb biosimilar to file NDA (2019.06) in EU as well as the first “Chinese” trastuzumab to receive EU GMP certificate (2020.04)

2010 — Benchmarking EU standard from pre-IND development

2015 — Built Global standard manufacturing facility

2016 — Manufacturing facility and quality management system passing EU QP inspections

2017 — Commenced global multi-center Phase 3 Clinical Trial

Being China’s first biosimilar to start global clinical trials, obtained Phase 3 clinical trial approval in China, Ukraine, Poland and Philippines, enrolling 608 patients

2017-2018 — Executing oversea licensing agreement with well-known pharmaceutical companies

accord
Pan Europe & MENA

Jacobson Pharma Corporation
Hong Kong & Macau

Cipla
Australia, NZ, Malaysia, Columbia

mAbxience
Argentina, Uruguay, Paraguay (2020.03)

2019 — Filed NMPA NDA Filed EU MAA Negotiating more oversea collaborations

2020.02 — Research on HLX02 similarity published on international journal of *BioDrugs*

2020.04-05 — EU GMP certificate & EMA CHMP positive opinion received

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Innovation Capability, Innovative Products & Innovation Strategy

Efficient Core R&D Capabilities: Integrated Platform Through the Entire R&D Process

Abs Screening Platform

- **Fully human natural phage display library**(1.5×10^{10})
- Traditional Hybridoma technology
- Antibody Fc reconstruction and humanization technology
- **>70 self-developed animal models of tumor**
- **Humanized VHH sdAbs phage library**(2×10^{12})
- **Bi-specific antibody technology platform**
- Fast clone screening system
- Automatic high-throughput antibody screening technology

Abs Process Development Platform

- **Cell culture**: self-developed medium, construction & screening technology of high-expression cell line, high density continuous perfusion culture
- **Downstream purification**: development of continuous flow purification technology
- **Preparation technology**: freeze-drying, pre-filled needle formulation, development of high concentration preparation
- **Analysis method:** critical quality attribute (CQA) study, similarity and technology comparability evaluation, E&L and preparation analysis and evaluation, in-vitro efficacy evaluation, PAT online quality control, biomarker platform technology etc.

Multi-tech platforms for innovation

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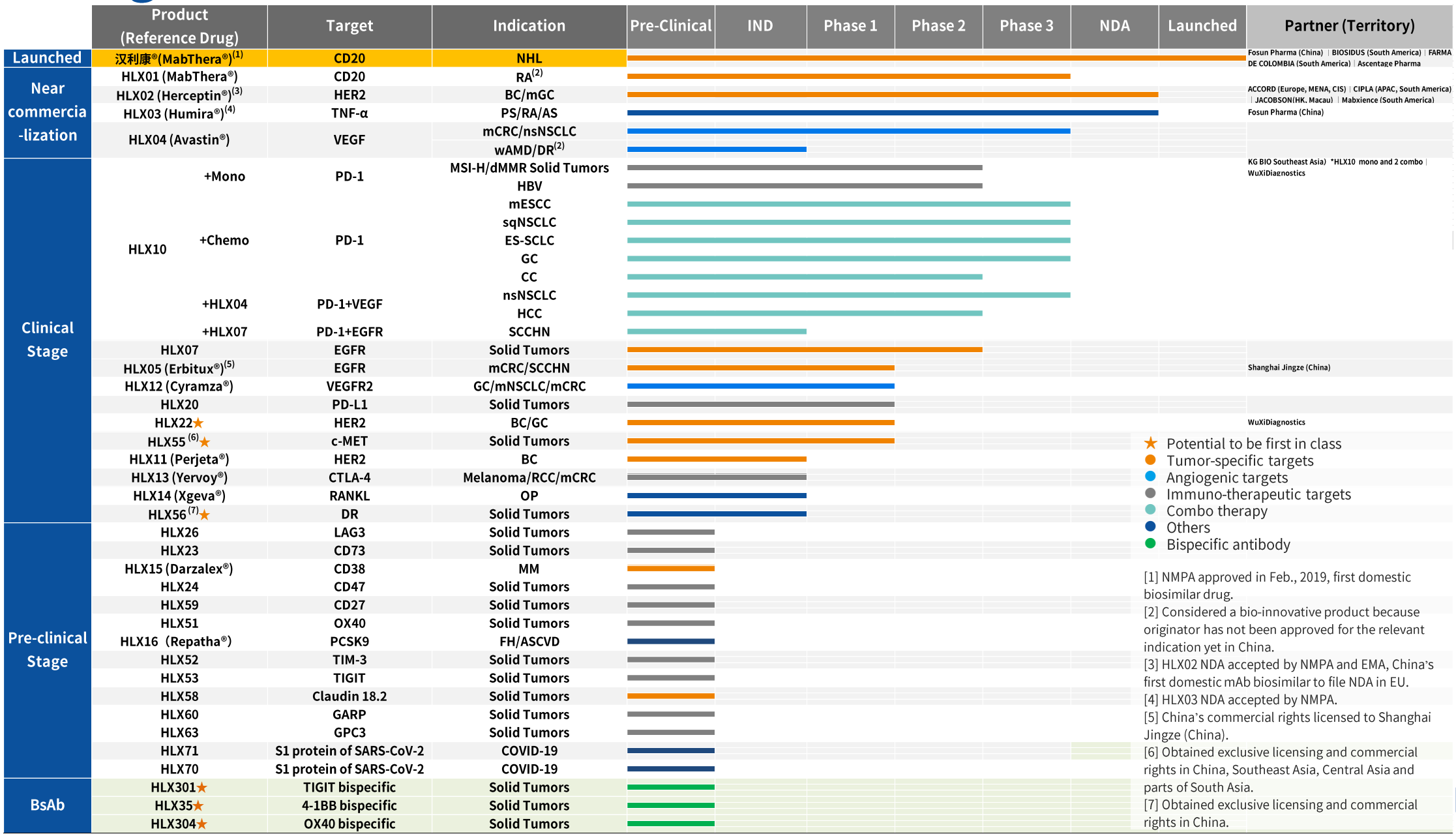
A Comprehensive & Diversified Antibody Pipeline Covers Major Targets

	Product (Reference Drug)	Target	Indication	Partner (Territory)
Launched	汉利康®(MabThera®)[1]	CD20	NHL	Fosun Pharma (China) | BIOSIDUS (South America) | FARMA DE COLOMBIA (South America) | Ascentage Pharma
Near commercia-lization	HLX01 (MabThera®)	CD20	RA[2]	
	HLX02 (Herceptin®)[3]	HER2	BC/mGC	ACCORD (Europe, MENA, CIS) | CIPLA (APAC, South America) | JACOBSON(HK. Macau) | Mabxience (South America)
	HLX03 (Humira®)[4]	TNF-α	PS/RA/AS	Fosun Pharma (China)
	HLX04 (Avastin®)	VEGF	mCRC/nsNSCLC	
			wAMD/DR[2]	
Clinical Stage	HLX10 +Mono	PD-1	MSI-H/dMMR Solid Tumors	KG BIO Southeast Asia) *HLX10 mono and 2 combo | WuXiDiagnostics
			HBV	
	HLX10 +Chemo	PD-1	mESCC	
			sqNSCLC	
			ES-SCLC	
			GC	
			CC	
	HLX10 +HLX04	PD-1+VEGF	nsNSCLC	
			HCC	
	HLX10 +HLX07	PD-1+EGFR	SCCHN	
	HLX07	EGFR	Solid Tumors	
	HLX05 (Erbitux®)[5]	EGFR	mCRC/SCCHN	Shanghai Jingze (China)
	HLX12 (Cyramza®)	VEGFR2	GC/mNSCLC/mCRC	
	HLX20	PD-L1	Solid Tumors	
	HLX22★	HER2	BC/GC	WuXiDiagnostics
	HLX55[6]★	c-MET	Solid Tumors	
	HLX11 (Perjeta®)	HER2	BC	
	HLX13 (Yervoy®)	CTLA-4	Melanoma/RCC/mCRC	
	HLX14 (Xgeva®)	RANKL	OP	
	HLX56[7]★	DR	Solid Tumors	
Pre-clinical Stage	HLX26	LAG3	Solid Tumors	
	HLX23	CD73	Solid Tumors	
	HLX15 (Darzalex®)	CD38	MM	
	HLX24	CD47	Solid Tumors	
	HLX59	CD27	Solid Tumors	
	HLX51	OX40	Solid Tumors	
	HLX16（Repatha®）	PCSK9	FH/ASCVD	
	HLX52	TIM-3	Solid Tumors	
	HLX53	TIGIT	Solid Tumors	
	HLX58	Claudin 18.2	Solid Tumors	
	HLX60	GARP	Solid Tumors	
	HLX63	GPC3	Solid Tumors	
	HLX71	S1 protein of SARS-CoV-2	COVID-19	
	HLX70	S1 protein of SARS-CoV-2	COVID-19	
BsAb	HLX301★	TIGIT bispecific	Solid Tumors	
	HLX35★	4-1BB bispecific	Solid Tumors	
	HLX304★	OX40 bispecific	Solid Tumors	



★ Potential to be first in class
● Tumor-specific targets
● Angiogenic targets
● Immuno-therapeutic targets
● Combo therapy
● Others
● Bispecific antibody

[1] NMPA approved in Feb., 2019, first domestic biosimilar drug.
[2] Considered a bio-innovative product because originator has not been approved for the relevant indication yet in China.
[3] HLX02 NDA accepted by NMPA and EMA, China's first domestic mAb biosimilar to file NDA in EU.
[4] HLX03 NDA accepted by NMPA.
[5] China's commercial rights licensed to Shanghai Jingze (China).
[6] Obtained exclusive licensing and commercial rights in China, Southeast Asia, Central Asia and parts of South Asia.
[7] Obtained exclusive licensing and commercial rights in China.

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Proprietary Pipeline Has Potential to Generate Multiple Innovative Combinations

A. Tumor-specific targets

CD20, HER-2, EGFR, cMET, …etc.

N = 9

B. Angiogenic targets

VEGF, PDGFR, VEGFR2, …etc.

N= 3

C. I/O targets

PD-1, PD-L1, CTLA-4, …etc.

N = 10

Potential combos

Potential combos of 2 mAbs:

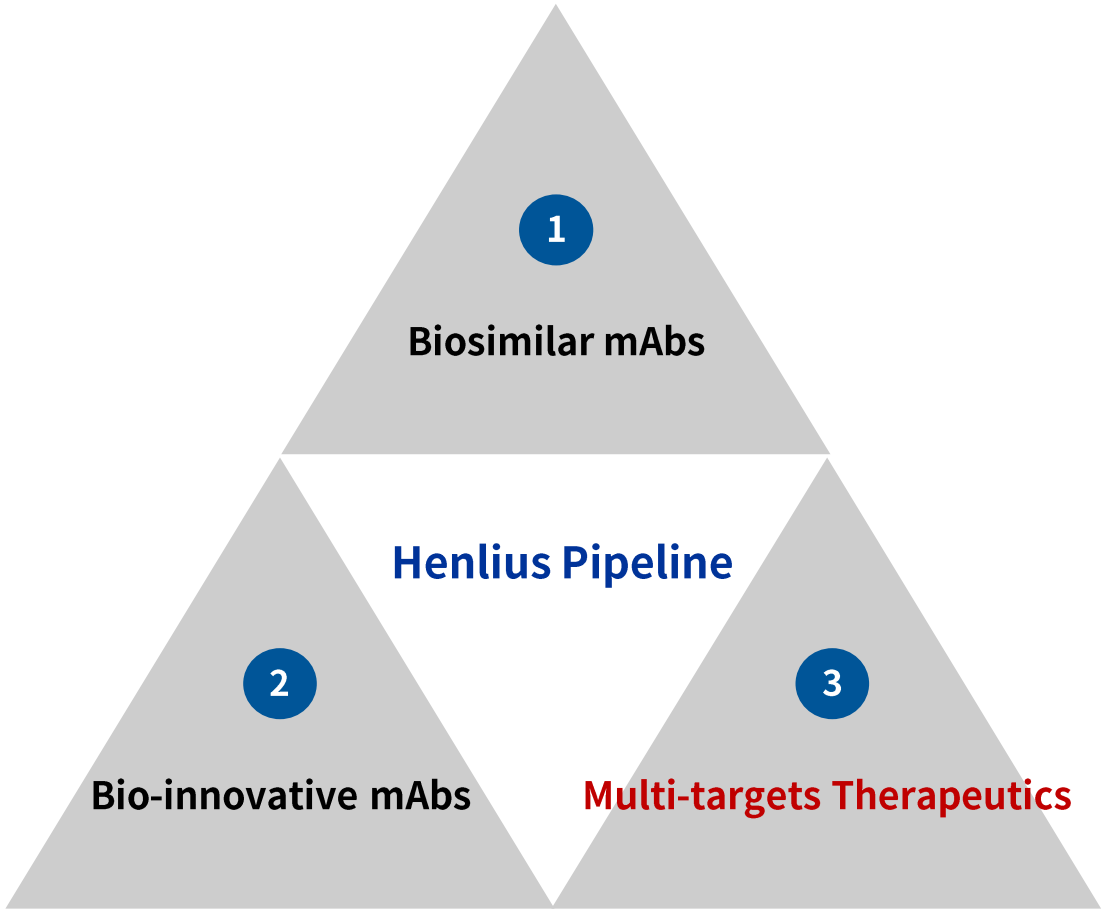
= 22 x 21 = 462

Screen combos to improve clinical efficacy

Proprietary pipeline has potential to generate multiple innovative combinations

- PD-(L)1 BsAb: >15
- EGFR BsAb: >10
- 4-1BB BsAb: >10
- Other I/O BsAb: >10

Next Strategic Focus – Multi-Targets Therapeutics



Multi-targets Therapeutics

a Bispecific/Multi-specific Therapies

- Ab + Ab
- Ab + cytokine fusion protein
- Ab + receptor protein
- …

* Based on different clinical demand, targets can be designed as tumor + I/O, I/O+I/O, tumor + tumor, I/O + inflammation, I/O + growth factor, etc

b Combo Therapies

- mAb + mAb HLX10+HLX04, HLX10+HLX07 etc.
- mAb + small molecule
- mAb + chemo

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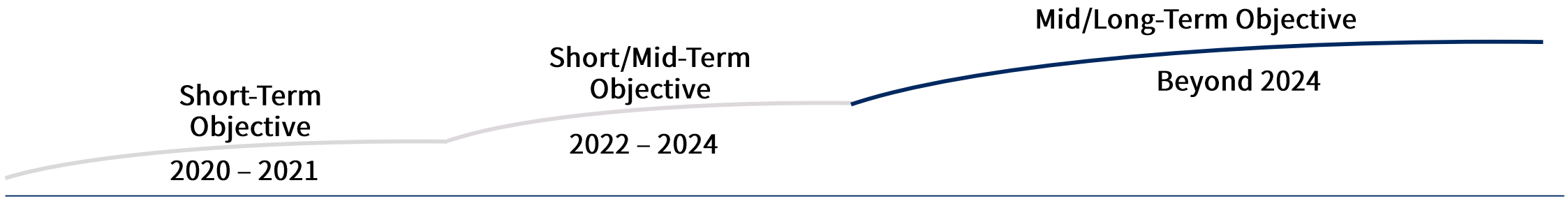
Strategic Planning for Pipeline Development: Three Steps of High-Efficiency Innovation



High quality biosimilars as continuous key products

- Maintain a leading position in domestic biosimilar industry
- Maximize return on biosimilar via development of high-potential and high-synergy portfolios
- Achieve risk control and stable return

Fast follower innovation

- Enhance innovative drug pipeline on selected tumors/targets
- Gradual R&D shift from biosimilar to bio-innovatives
- Build a preliminary long-term partnership with academic institutions

Fastest follower innovation

- Fully build innovative drug follow-on mechanism
- Achieve POC of fast R&D in 3-6 month in selected target/objective pipeline

First (wave)-in-class innovation

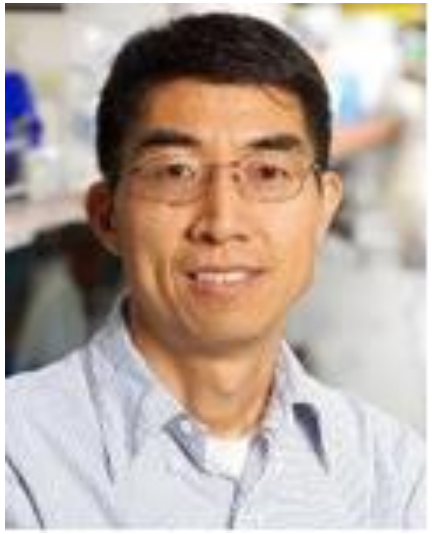
- Achieve successful development and POC of "first-in-class" drugs based on external partnership and long-term academic research
- Create high-return portfolios

Source: IQVIA & Company Analysis

Scientific Advisory Board Provides Strong R&D Support

Founded in May 2018, the Henlius Scientific Advisory Board is composed of distinguished scientists and physicians in the fields of tumor biology, immunology, and cancer therapy.

The SAB holds regular meetings to review research and development projects and priorities, and strongly supports the research and development of Henlius' innovative product line.



Kun-Liang Guan, Ph.D.

Chairman of Henlius SAB
Distinguished Professor of pharmacology, University of California San Diego

Published SCI 400+ papers，H-Index 144

Yiping Yang, M.D., Ph.D.

Professor of medicine and immunology, Duke University Medical Center
Associate director of hematologic malignancies and Cell Therapy at Duke University Cancer Institute and associate editor of the Journal of Clinical Research (JCI) and JCI Insight

Published SCI ~100 papers

Weiping Zou, Ph.D.

Charles B. DE Nancrede, Professor of surgery and director of the Center for Tumor Immunity and Immunotherapy, University of Michigan Medical School

Published SCI 150+ papers，H-Index 73

Zihai Li, M.D., Ph.D.

Professor emeritus in the Department of Microbiology and Immunology at the South Carolina School of Medicine and head of tumor immunology at the Hollings Cancer Center

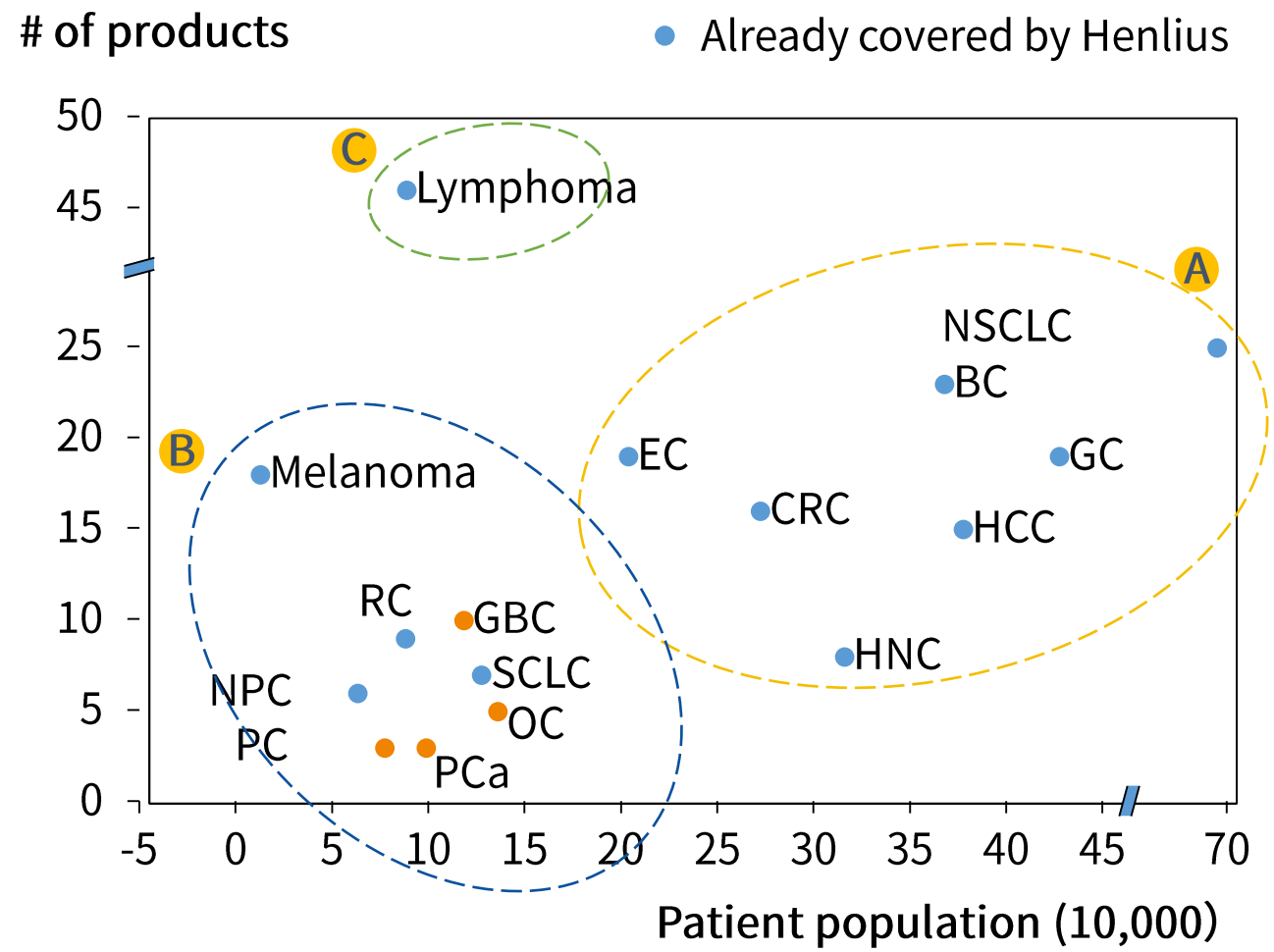
Published SCI 200+ papers，H-Index 49

Sources: Google Scholar Statistics; University websites

Clinical Overview & Updates

Focus on Unmet Clinical Needs, Henlius Pipeline Almost Covers All Domestic High-Incidence Cancers

Domestic cancer market size and competitive landscape



Key findings

A Core market

- Market features: high patient base, big market potential, highly competitive
- KSF
  - Sub-group of diseases subdivided to create differentiation among patient population
  - Higher prospective requirement on target selection
  - In class competition, launch speed becomes key factor

B Strategic market

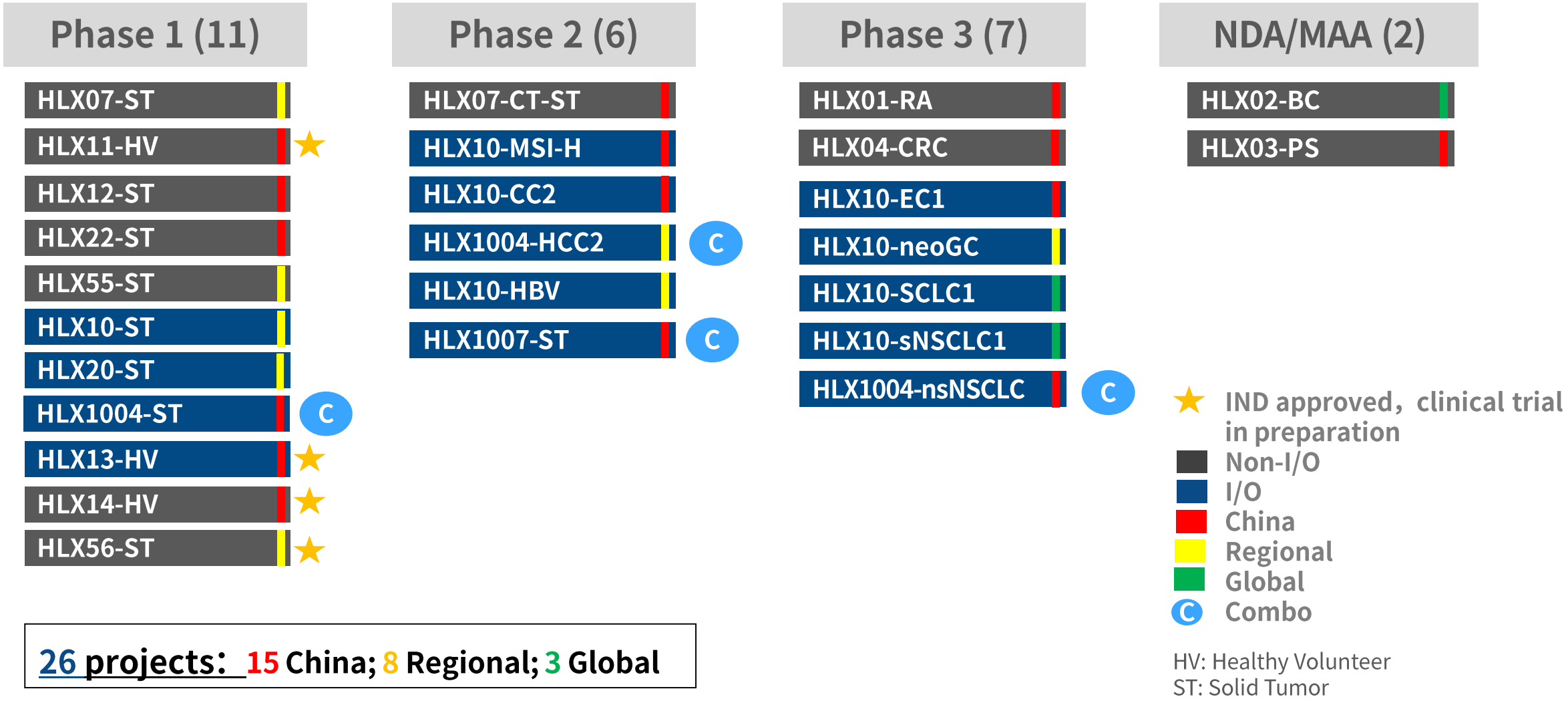
- Market features: low patient base, small market potential, less competitive
- KSF
  - Clear coverage purpose （Win the market/ fast launch)

C Strategic launch market

- Market features: low patient base, small market potential, highly competitive
- Many companies achieve fast launch to market through lymphoma

Sources: company annual reports; Chinese Cancer Registry Annual Report; Company Analysis

2020 Overview of Henlius Clinical Pipeline



26 projects：15 China; 8 Regional; 3 Global

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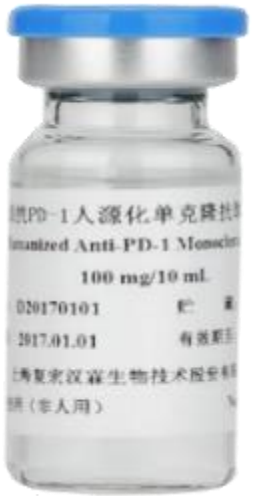
HLX10（PD-1）Differentiation Strategy – Combo + Global

Combo

- **Combo with current mAbs**
  - I/O targets
  - Anti-angiogenesis targets
  - Tumor-specific targets
- **Strong self-developed pipeline to create more combo therapies**
  - ✓ Flexible combo
  - ✓ Fast development
  - ✓ Cost advantage
- **Combo with chemo/radiation**



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HLX10 (PD-1)

Global

- Global multi-center clinical trials
- Enter major markets with global quality
- Enter emerging markets by leveraging FDA/EMA approvals
- Global BD partnership

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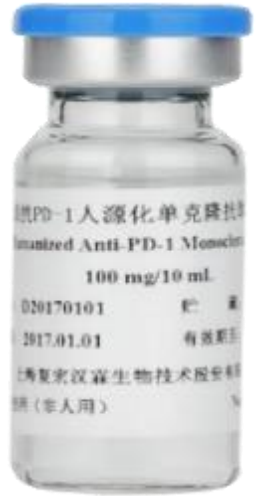
Achieved Major Progress in HLX10(PD-1) I/O Combo Therapy

	Product	Target	Indication	IND	Phase 1	Phase 2	Phase 3	NDA Filed	NDA Approved
Innovative mAb	HLX10	PD-1	HBV				2019.12 FPI		
			MSI-H/dMMR Solid Tumors				2019.08 FPI		
Combo Therapy	HLX04+HLX10	VEGF+PD-1	HCC				2019.09 FPI		
			nsNSCLC					2019.12 FPI	
	HLX07+HLX10	EGFR+PD-1	r/m HNSCC		2019.12 IND approved				
	HLX10+chemo	PD-1	mESCC					2019.06 FPI	
			ES-SCLC					2019.09 FPI	
			sqNSCLC					2019.08 FPI	
			GC					2019.12 FPI	
			CC				2020.03 FPI		



I/O target

Combo therapy

HBV=hepatitis B virus; MSI-H/dMMR=microsatellite instability-high/deficient mismatch repair;
nsNSCLC=non-squamous non-small cell lung cancer; HCC=hepatocellular carcinoma;
mESCC=locally advanced/metastatic esophageal squamous cell carcinoma;
ES-SCLC=extensive-stage small cell lung cancer;
sqNSCLC=squamous non-small cell lung cancer;
r/m HNSCC=relapsed/metastatic head and neck squamous cell carcinoma;
GC=gastric cancer; CC=cervical cancer

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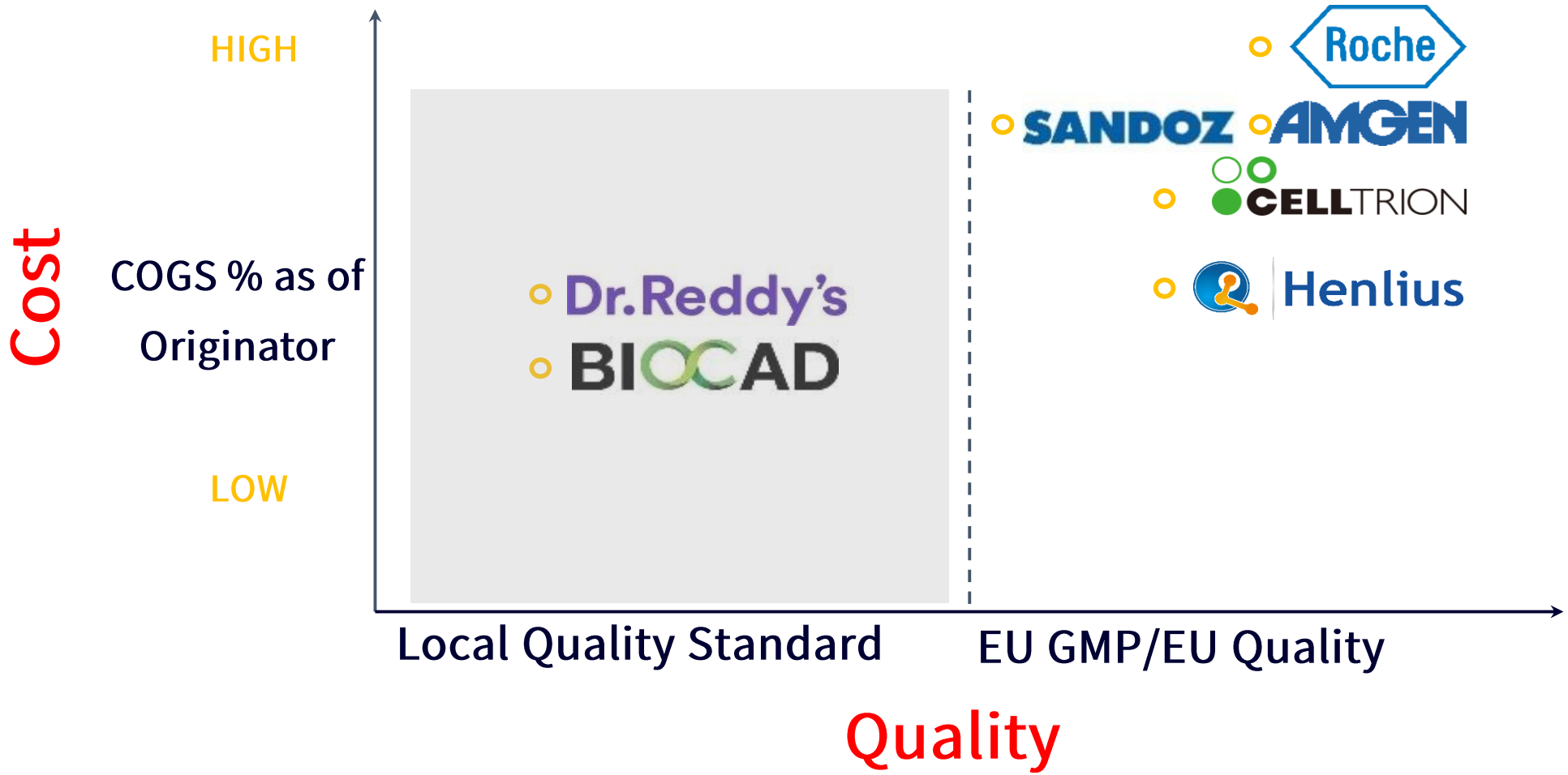
In China for Global: Global Innovation Strategy

Global Strategic Focus: High Quality and Affordable Price



Sources:

1. Price of Acellbia & Reditux in Vietnam compared with Mabthera.
2. Assume price of HLX01 in China compared with Mabthera.
3. Assumed pricing of Truxima, Rixathon, ABP 798 in EU market
4. Clinicaltiral.gov
5. Dr. Reddy's clinical trials registry in India

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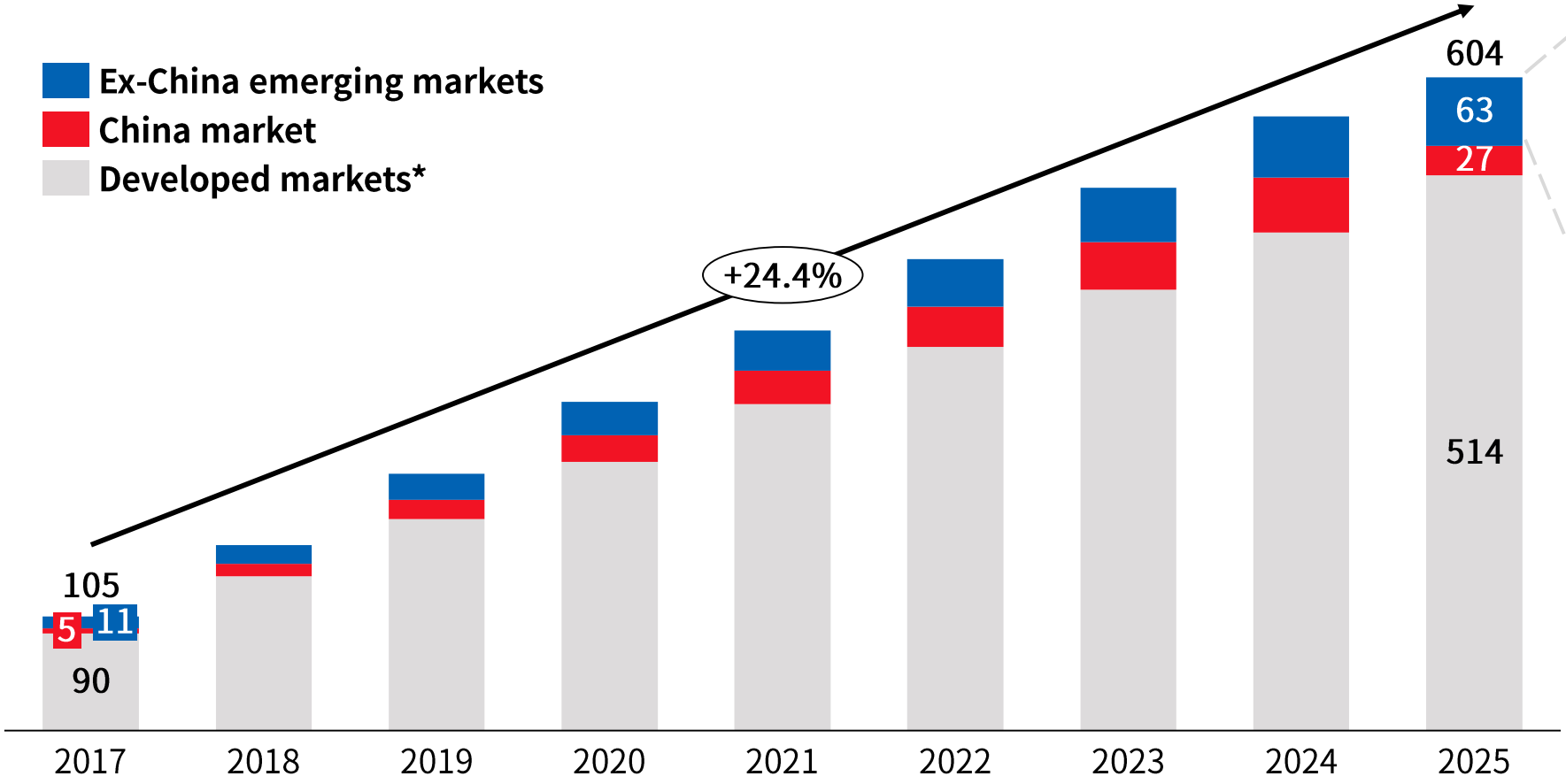
Overseas Emerging Markets Have Huge Potential and Less Competition for PD-(L)1

PD-(L)1 overseas emerging markets: noteworthy growth, MNCs currently dominate *($100M)*



Bristol-Myers Squibb
MSD
AstraZeneca
Roche
Henlius

Developed markets: including US, EU5, Japan, South Korea, Canada, Australia
Sources: Research And Markets; IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Dec 2019; compiled by Henlius SP

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Summary of Clinical Development Differentiation Strategy and Advantage

	Differentiation Strategy	Potential Competitive Advantage
Clinical Development	1. Wide indication coverage	• Help future medical insurance negotiation, hospital access, etc.
	2.Global development	• Emerging markets still have huge unmet clinical needs • Enhance domestic brand recognition with globally-certified high quality
	3. Proprietary pipeline combo therapy	• Generate multiple innovative combo therapies from proprietary pipeline • Economy of scale on R&D, manufacturing and sales
	4. Cautious indication selection + Timely strategy adjustment	• Maintain competitive advantage with risk control
Quality	5. Recognition from multiple top PIs	• Ensure high-quality clinical trial design and completion of trials • Basis for smooth market access after approval
	6. Global quality certification; global brand	• Product recognition from more doctors and patients • Serve Chinese and global patients

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Henlius R&D Platform and Pipeline

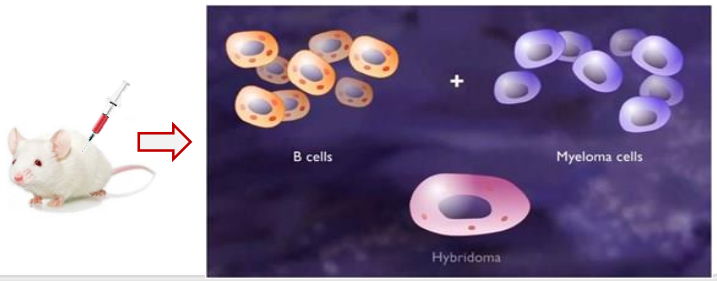
Weidong Jiang
Co-founder & CSO

Henlius R&D Platform

Antibody Discovery and Screening Platform

➢ Animal immunization and antibody cloning

- Hybridoma (HLX10/PD-1)
- Phage display library VHH (4-1BB)

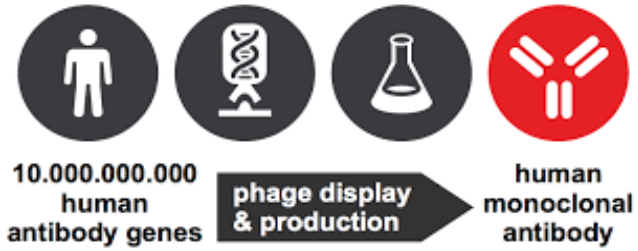


http://www.adaltis.net/services/hybridomas-cell-lines-monoclonal-antibody-production/

➢ Fully human naive phage display library

(HLX20/PD-L1)

capacity: 1.5 x 10^{10}

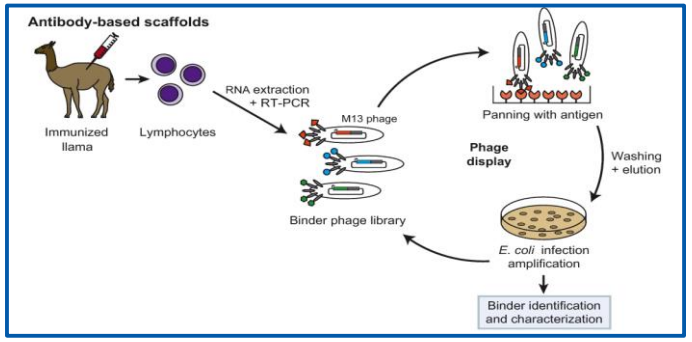


http://yumab.com/in-vitro-antibody-selection/

➢ Synthetic humanized Llama sdAb phage display library

(PD-L1, TIGIT, OX40, B7H3, TIM3, GPC3 , etc.)

capacity: 2 x 10^{12}



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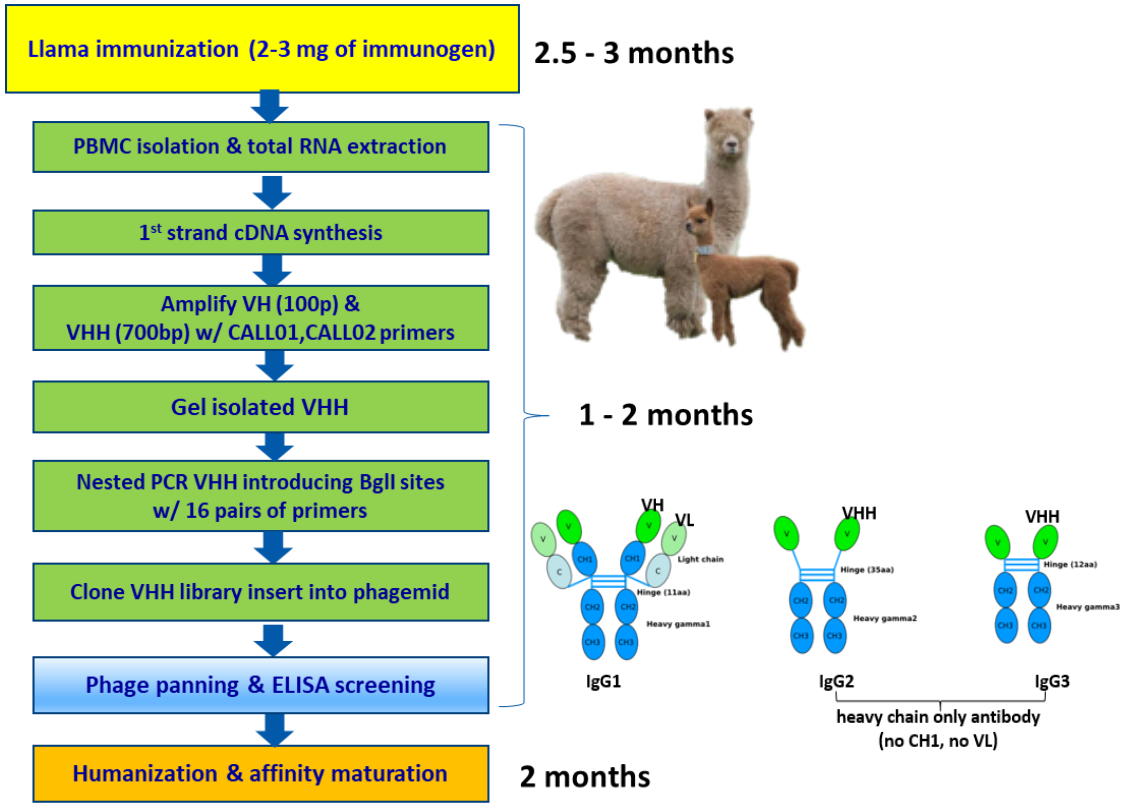
Synthetic humanized VHH single domain antibody phage library

Single domain antibody platform +
Humanized phage library Llama sdAb Platform



• Advantage

Synthetic sdAb phage library

Quality

- Final library size: $2x10^{12}$
- Productive clone rate: 74~82%
- CDR3 length from 15~21aa
- Removal of problematic AA (e.g. Met, Cys)

Speed

- Typical Llama immunization (3 months), VHH library construction and screening (1-2 months), and humanization and affinity maturation (2 months)
- Synthetic sdAb library screening: 2-4 weeks

Innovation

- Novel VHH for multiple targets:
  - Immune target A (13 FACS binders, cyno & mu)
  - Tumor target A (14 FACS binders)
  - Immune target B (48 ELISA binders)
  - Tumor target B (20+ ELSIA binders)
  - Tumor target C (8 ELISA binders)
- Building blocks for different bispecific formats

✓ Llama VHH antibodies for more than 8 different projects have been successfully obtained（PDL1, TIGIT, OX40, B7H3, TIM3, GPC3, etc)

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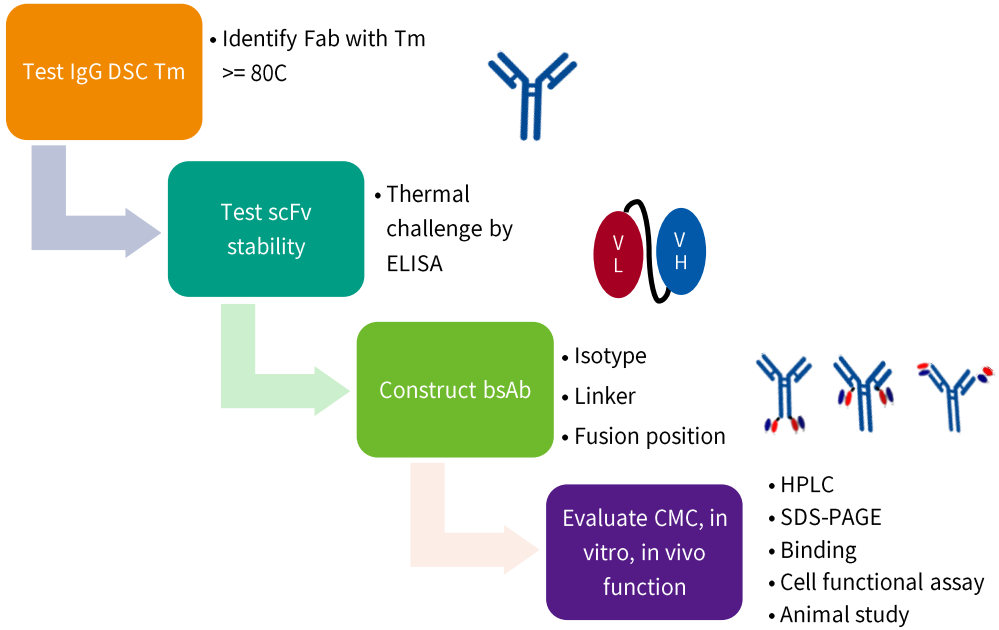
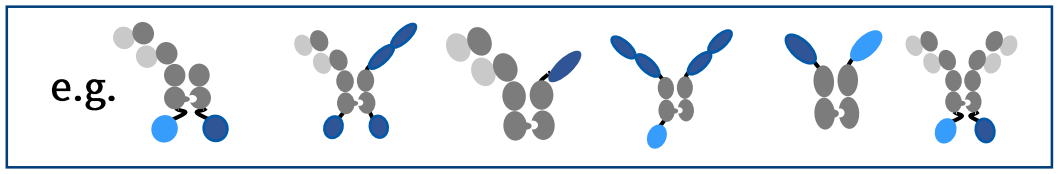
Multi-Functional Antibody Platform

• Bispecific Platform

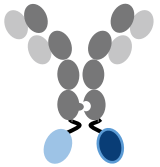


✓ More than 12 different items of bifunctional antibodies have been successfully obtained



Bispecific antibody platform optimization

- **Asymmetric:**
  - ✓ Establish a consistent allodimer transfection/purification process
  - ✓ Engineered Fc mutations assist in the purification of heterodimers



- **Multivalent:**
  - ✓ Multiple VHH domains were used to realize the binding of polyvalent variants to receptors

- **Affinity enhancement （Avidity based bispecific）:**
  - ✓ High selectivity is achieved by binding two low affinity antibodies to the same cellular target
  - ✓ Reduce the toxicity (anti-HER2, anti-EGFR, anti-c-MET)

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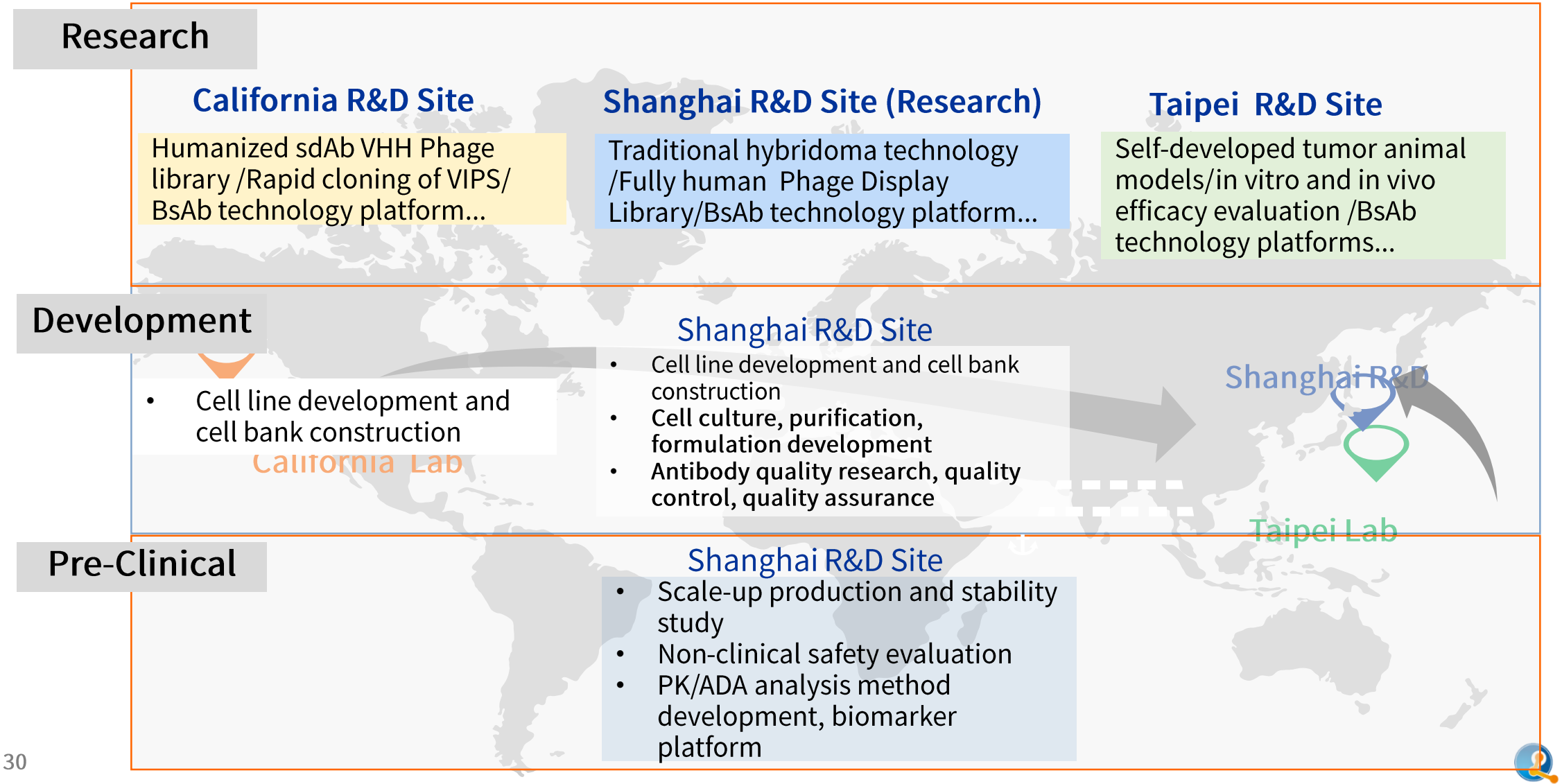
Synergy of Three Research Sites

- 3 Research sites have synergistic effect in managing multiple projects and building up technology platforms



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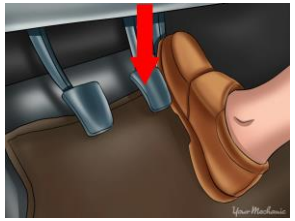
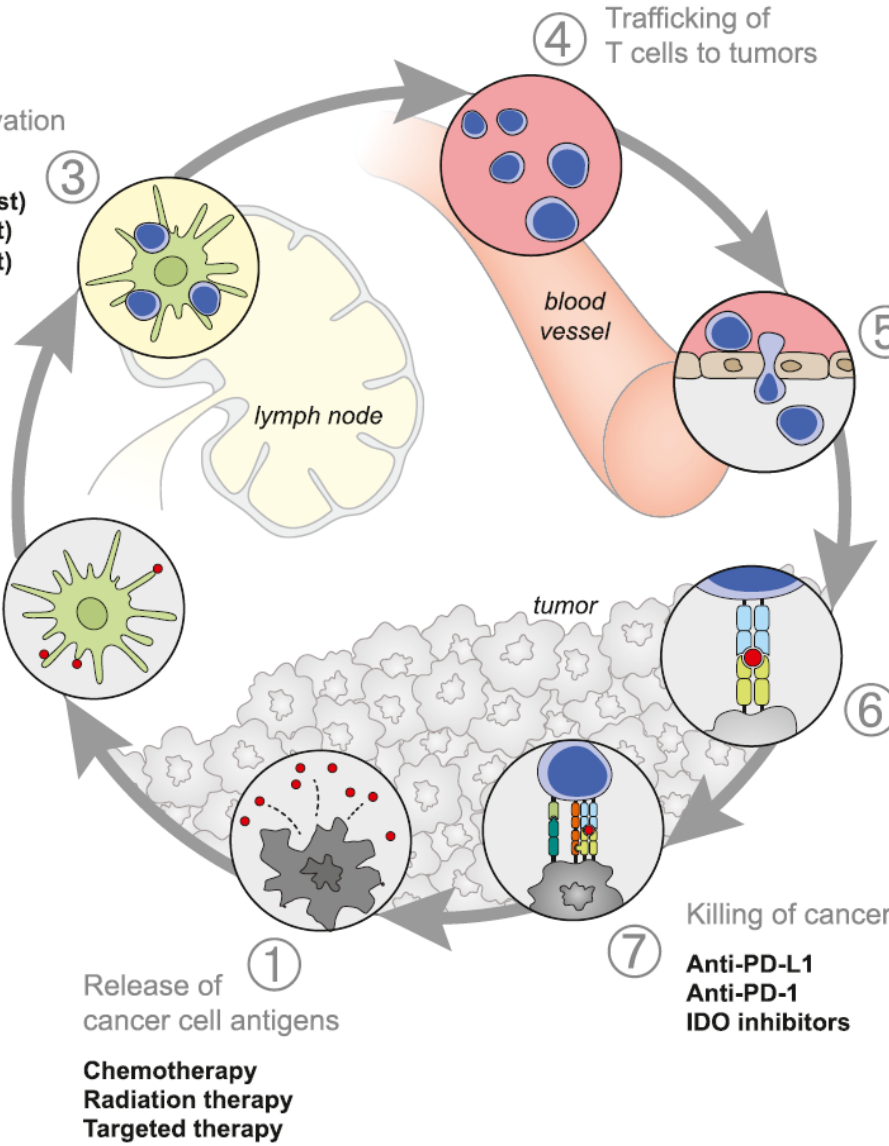
Innovative Research Pipeline: Single-Target Drugs

Henlius Pipeline Covers Multiple MOAs



HLX09 (CTLA4)
HLX51 (OX40)
HLX59 (CD27)



HLX04 (VEGF)
HLX06 (VEFGR2)

HLX01 (CD20)
HLX02 (Her2)
HLX07 (EGFR)
HLX58 (Claudin18.2)
HLX63 (GPC3)
HLX55 (c-MET)
HLX56 (DR4)

HLX09 (CTLA-4) HLX51 (OX40)
HLX10 (PD-1) HLX52 (TIM-3)
HLX20 (PD-L1) HLX53 (TIGIT)
HLX23 (CD73) HLX56 (DR4)
HLX24 (CD47) HLX59 (CD27)
HLX26 (LAG-3) HLX63 (GPC3)

Source: Chen and Mellman, *Immunity* 2013

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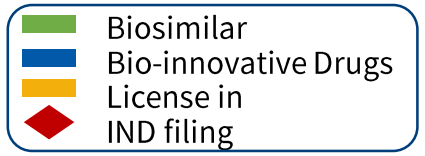
2020 IND Project Pipeline Under Development

➢ More than 90% projects are independently developed by Henlius

Cell line construction 25%	Process and method development 55%	Non-GMP production 65%	GMP production 70%	Non-clinical study 98%	Pre-IND communication 99%	IND submit 100%

Product	Target	Target Indications	Research	Candidate Selection/Cell line	Process/Method development	Preclinical/ IND	IND % achievement
HLX13	CTLA-4	ST					100%
HLX14	RANKL	OP					100%
HLX56	DR4	ST					100%
HLX71	S1 protein	COVID-19					75%
HLX70	S1 protein	COVID-19					60%
HLX15	CD38	MM					70%
HLX26	LAG-3	ST					65%
HLX23	CD73	ST					60%
HLX301	TIGIT x XXXX	ST					40%
HLX35	4-1BB x XXXX	ST					20%
HLX36	PD-1 x XXXX	ST					30%
HLX17	PD-1	ST					35%
HLX16	PCSK9	FH/ASCVD					30%
HLX18	PD-1	ST					20%
Others	Claudin 18.2, CD27, and undisclosed innovative mAbs and multi-target drugs						



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Overview of Anti-Coronavirus Projects

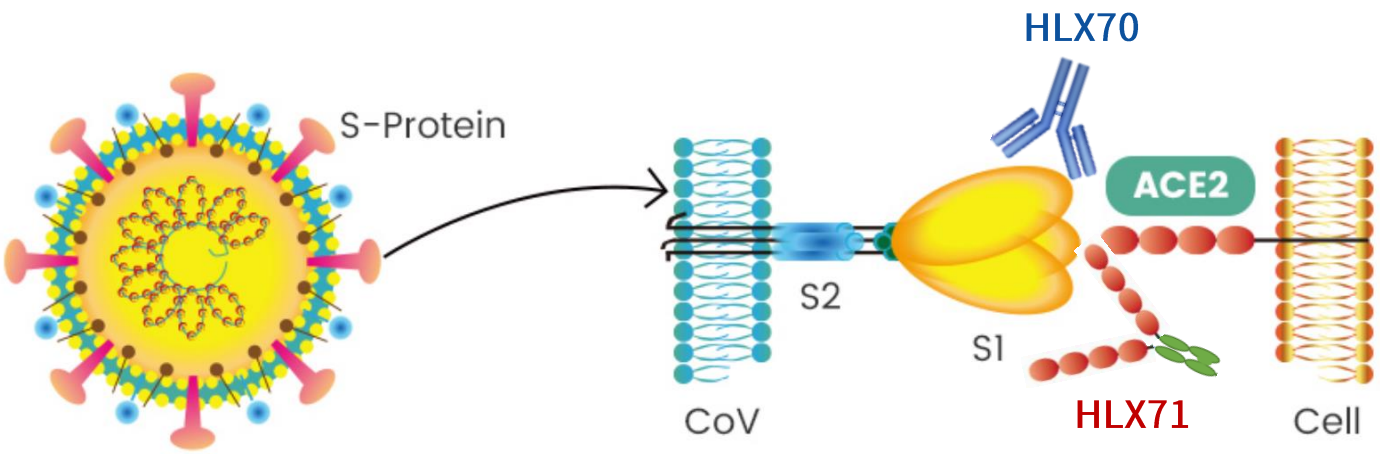
汉霖快讯｜复宏汉霖与三优生物、之江生物达成合作，共同研发针对新冠病毒全人源抗体药物

Henlius 复宏汉霖 5月6日

可负担的创新 值得信赖的品质

2020年5月6日，复宏汉霖（香港联交所代码：2696）今日宣布与三优生物医药（上海）有限公司（“三优生物”）、上海之江生物科技股份有限公司（“之江生物”）达成项目合作协议，三方将合作研发针对新型冠状病毒肺炎（COVID-19）的全人源抗体药物。

Combo



HLX70	HLX71
Monoclonal antibody that targets the Spike protein on the surface of the COVID-19 virus ● IgG1 kappa immunoglobulin ✓ Proved neutralization activity in vitro and preventing and treating virus efficacy in vivo in virus infection transgenic mouse models ✓ GMP lot production on-going	Human ACE2-FC recombinant protein competitively binds to the Spike protein on the surface of the COVID-19 virus ● Glycosylated fusion protein with molecular weight of about 218 kDa ● C terminal fusion with Fc: extended serum half-life ✓ Proved neutralization activity in vitro ✓ Non-clinical safety study on-going ✓ GMP lot production on-going

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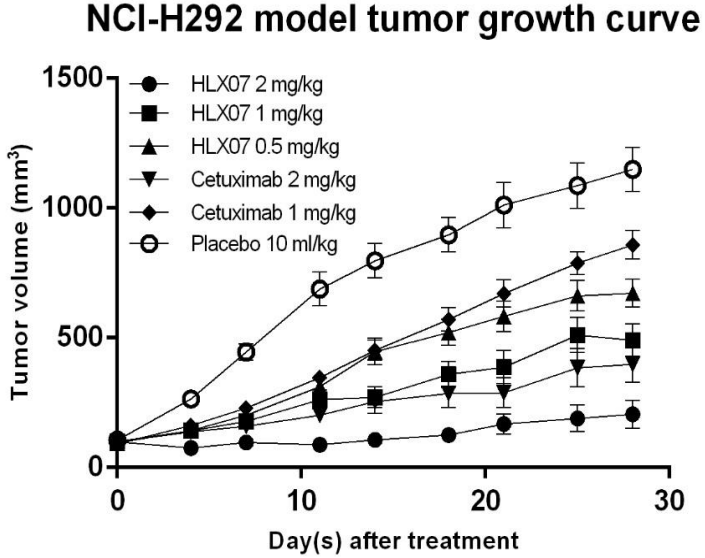
Biobetter: Anti-EGFR mAb, HLX07

Progress:

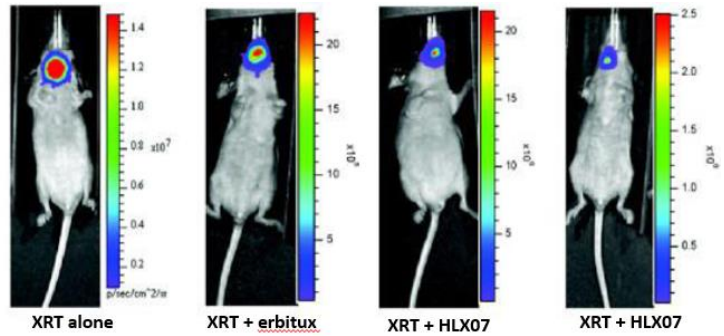
- ✓ HLX07 is in the phase Ib/2 clinical study, and its preliminary clinical data show that in the highest dose group (800mg), dose limiting toxicity (DLT) was not observed, and the maximum tolerated dose (MTD) was not achieved.
- ✓ HLX07+HLX10 combo is also in clinical stage

The Reference drug	Biobetter (HLX07)	
Human and mouse chimerism	Humanized	Reduced immunogenicity
Heavy chain CDR2 has excess Glycan chains	Glycosylation	Reduced immunogenicity
Lower affinity	Affinity maturation	Better efficacy
SP2 cell line (mouse origin)	CHO cell lines	Fc glycan chains are closer to human
Low titer （<1 g/L)	Higher titer	Nearly 6 g/L, reducing costs

Human lung mucoepithelioid carcinoma (NCI-H292 cell) model



Combo with radiotherapy



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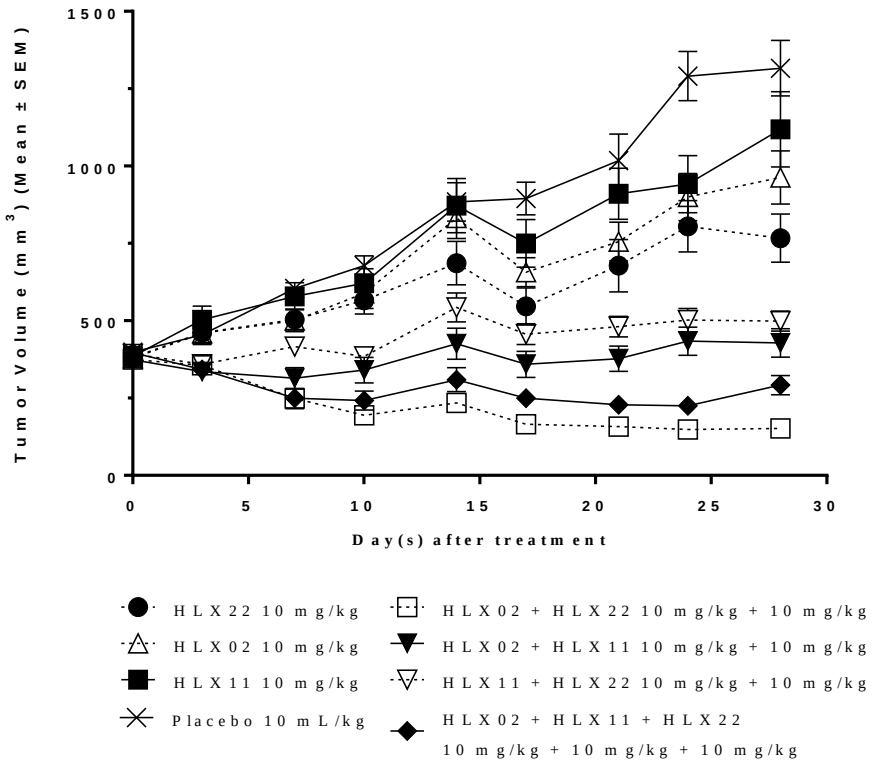
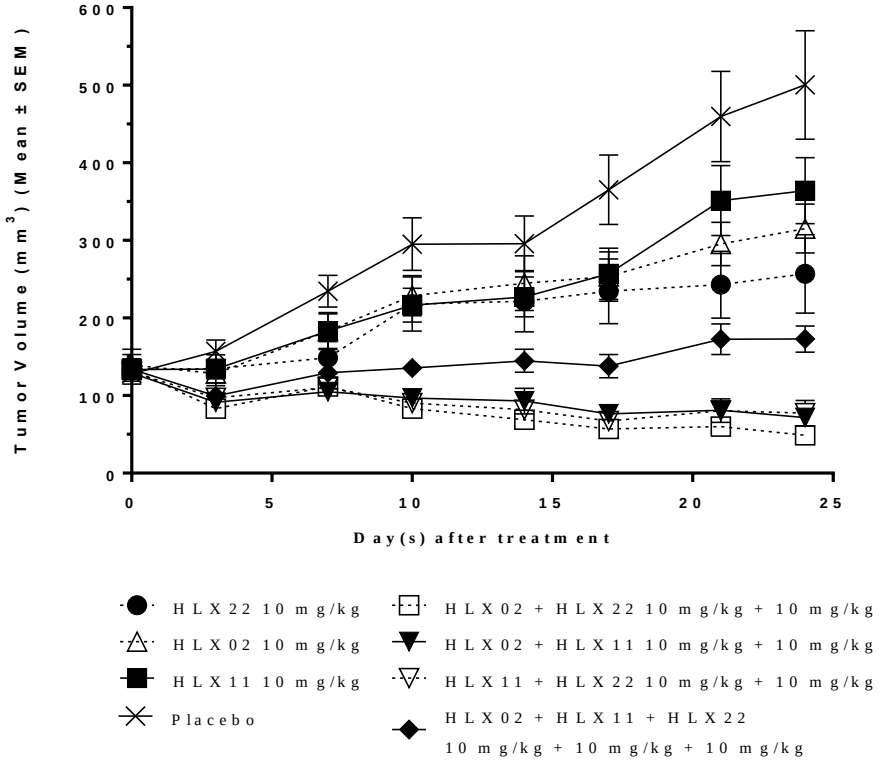
Innovative: Anti-HER2 mAb，HLX22

- New binding epitope
- Combo with other HER2 antibodies

Progress: Phase I clinical



Tumor growth curve of NCI-N87 xenograft tumor model
Gastric Cancer



Tumor growth curve of HCC1954 xenograft tumor model
Breast Cancer

✓ HLX22 has anti-tumor activity, and the combination of HLX22 and HLX02 (trastuzumab) has a synergistic effect in tumor inhibition.

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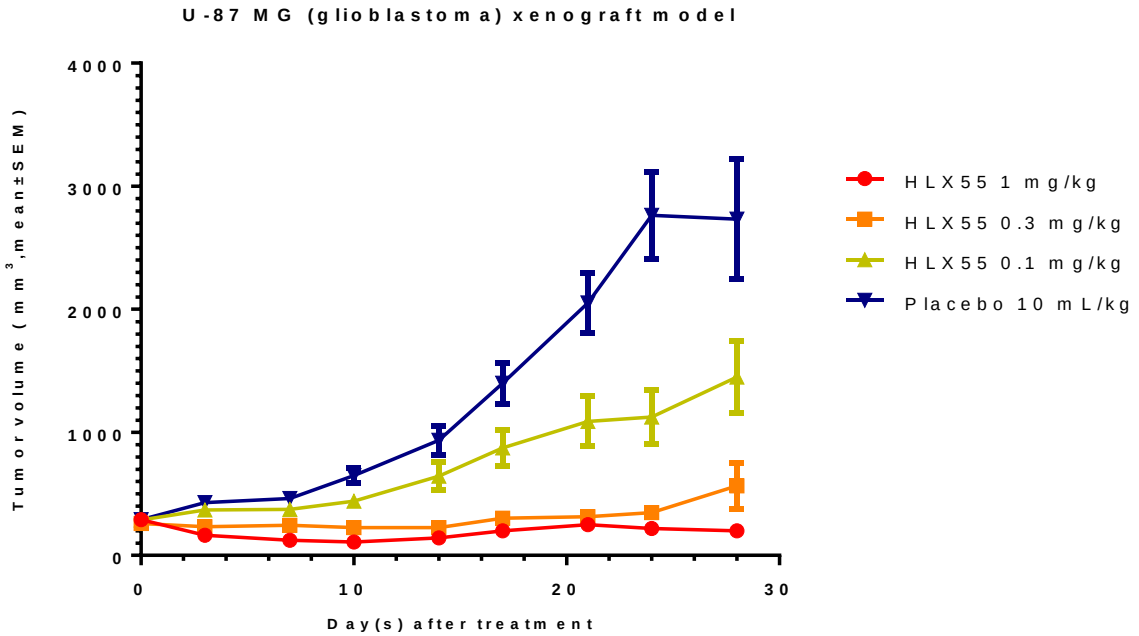
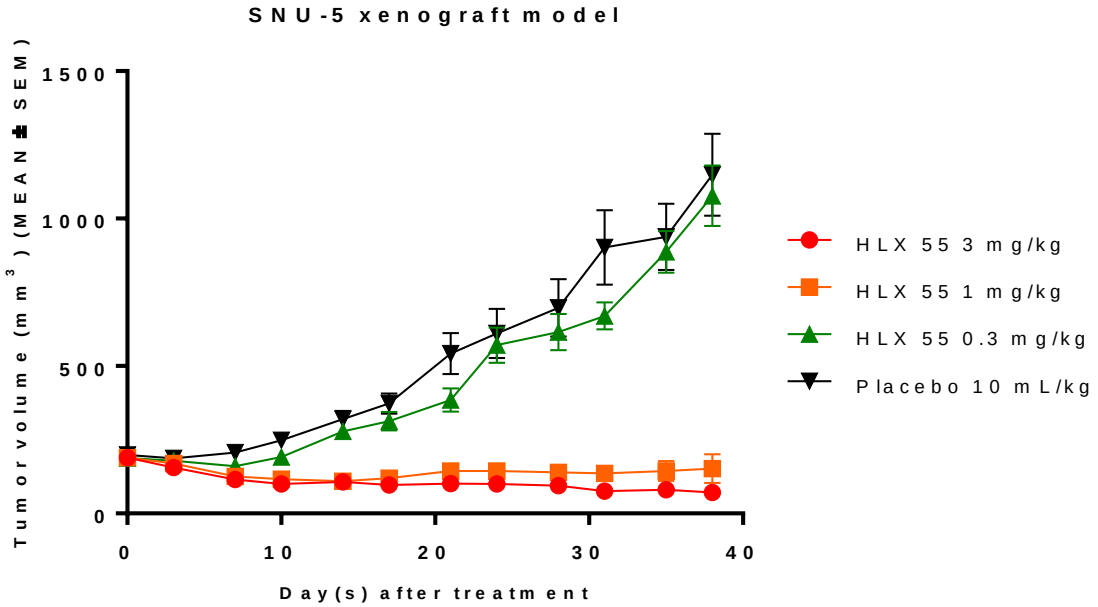
Innovative: Anti-c-MET mAb，HLX55

Progress: Phase I clinical

❖ IgG2, significantly enhanced efficacy



U-87MG xenograft tumor model
glioblastoma cell (Autocrine HGF)



SNU-5 xenograft tumor model
SNU-5 human Gastric cancer cells (C-MET amplification)

✓ HLX55 has significant anti-tumor activities in a dose-dependent manner

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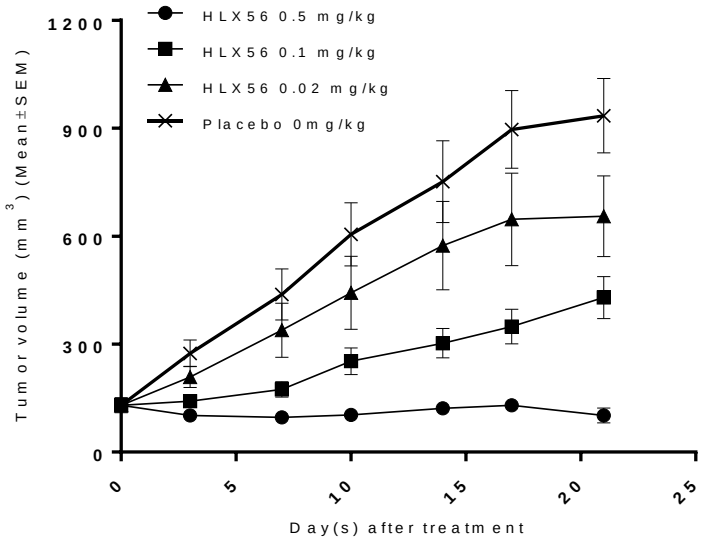
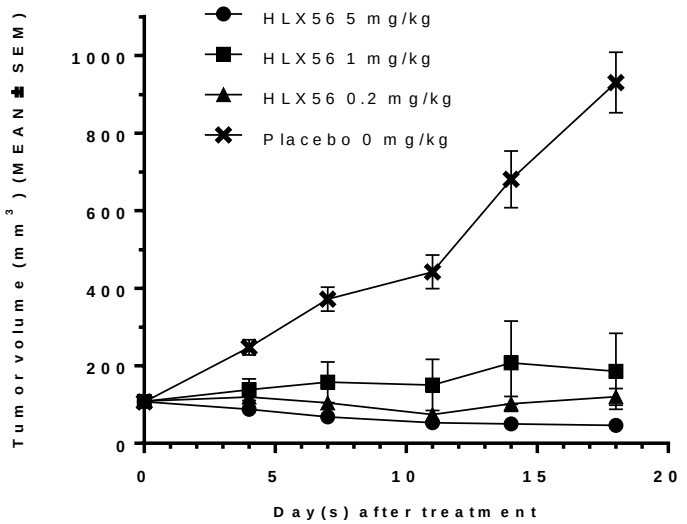
Innovative: Anti-DR4 mAb，HLX56

Progress: NMPA and TFDA have been approved and phase I is on-going

- ❖ Antitumor agonist
- ❖ Fc double mutations to enhance the anti-tumor activity



COLO205 xenograft mouse tumor
Colon cancer cells



OE19 xenograft mouse tumor
Human esophageal carcinoma cells

✓ HLX56 has a significant anti-tumor activity in a dose-dependent manner with good safety data in monkey

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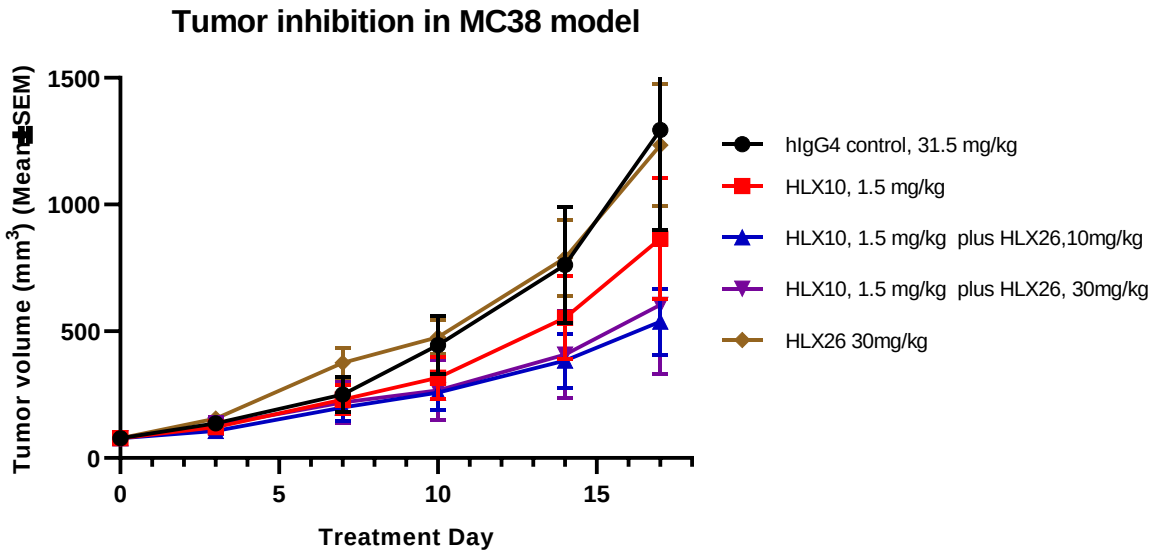
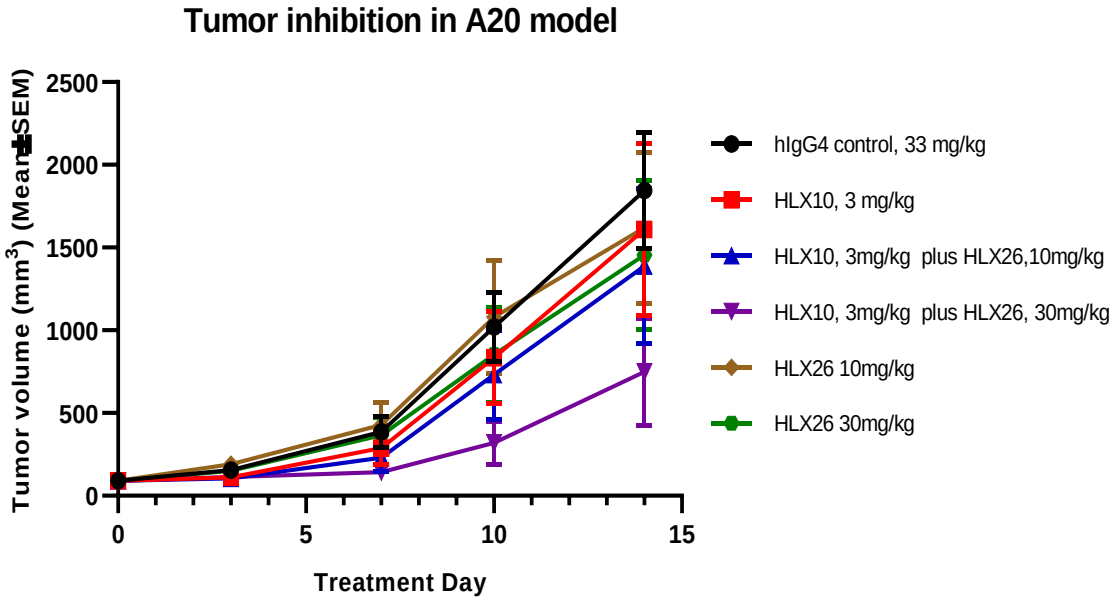
Innovative: Anti-LAG-3 mAb，HLX26

Progress: Will submit IND at 2020 Q4

❖ LAG-3 mAb blocks for all ligands binding tested





Dual KI(hPD-1 and hLAG-3)/MC38 model

- ✓ HLX10 and HLX26 showed synergistic effect in MC38 model;
- ✓ 10 mg/kg of HLX26 reached LAG-3 saturation in this model

Dual KI(hPD-1 and hLAG-3)/A20 model

- ✓ HLX26 combined with HLX10 has better tumor inhibition activity than monotherapy group;
- ✓ The combination efficacy of HLX26 and HLX10 was dose-dependent;
- ✓ HLX26 (30mg/kg) monotherapy group also showed tumor inhibition activity

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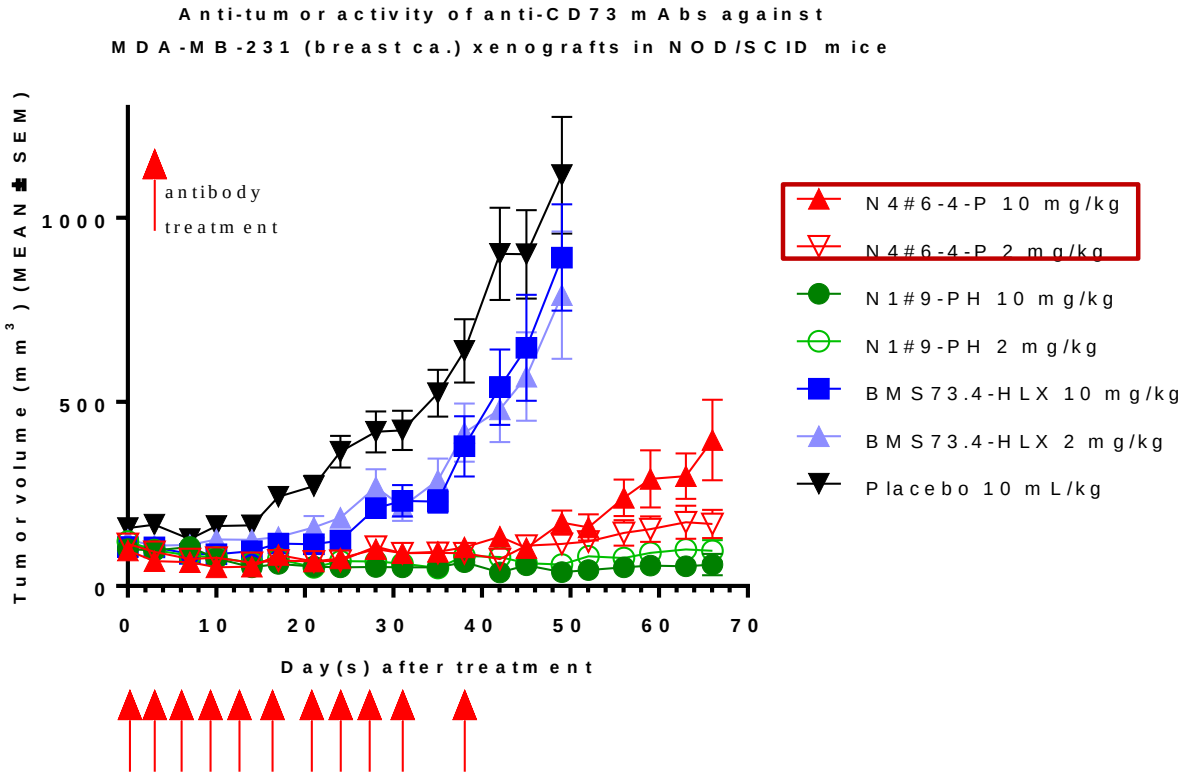
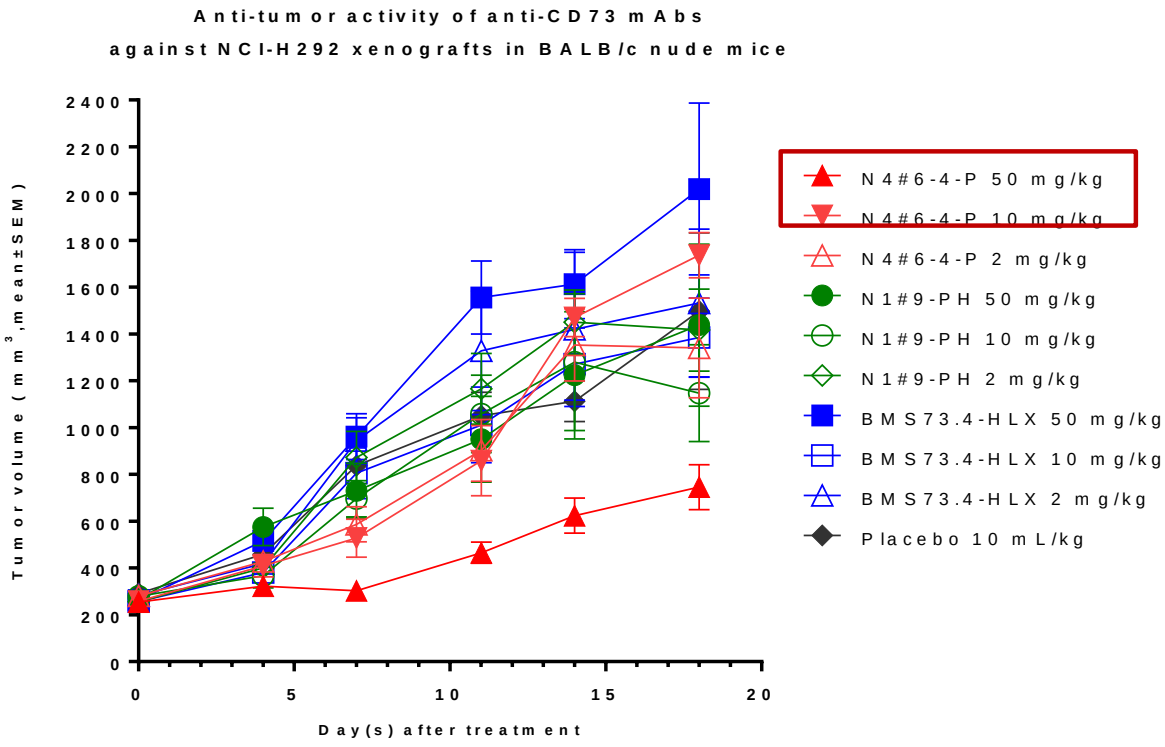
Innovative: Anti- CD73 mAb，HLX23

Progress: Will submit IND in 2020 Q4 or 2021 Q1

Efficacy of HLX23 (anti-CD73) in human breast cancer xenograft mouse model



Efficacy of HLX23(anti-CD73) in human NSCLC xenograft mouse model



✓ Anti-CD73 mAb has a significant anti-tumor activity

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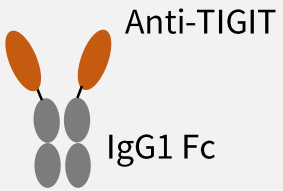
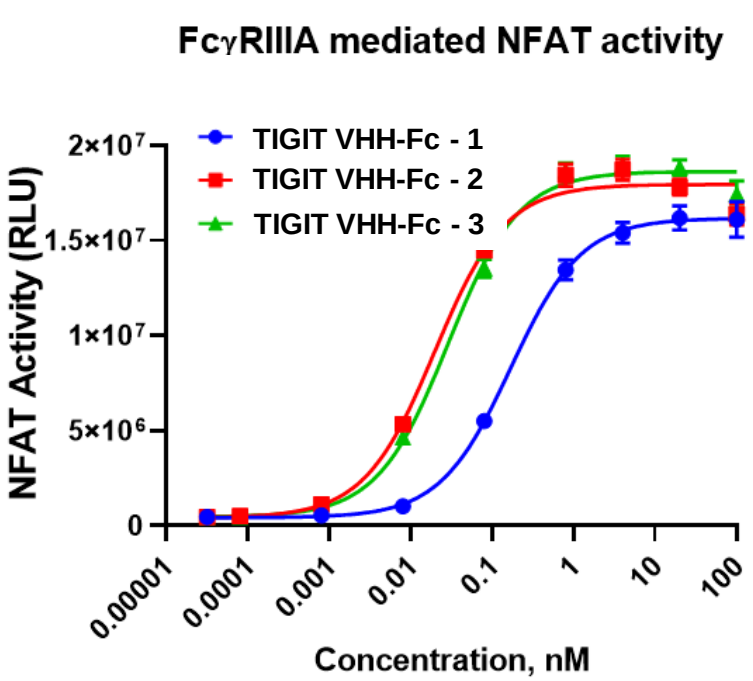
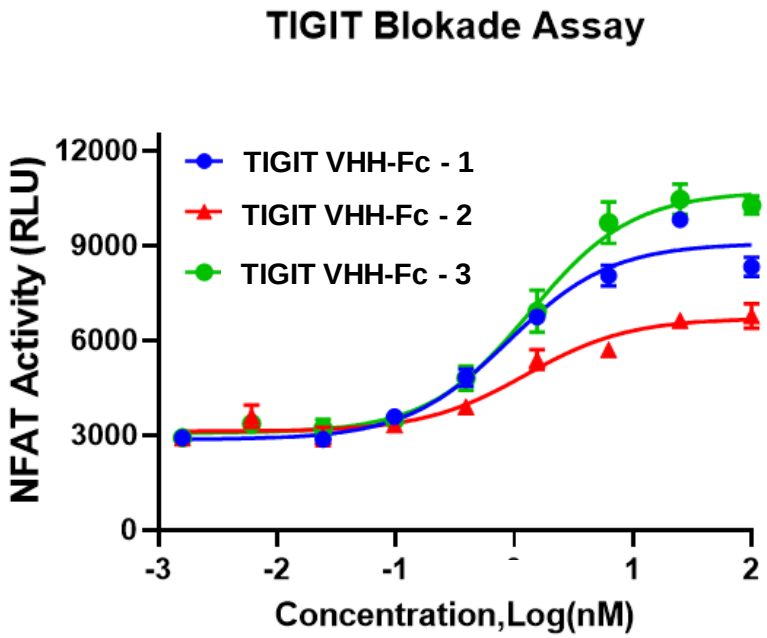
Innovative: Anti-TIGIT mAb，HLX53

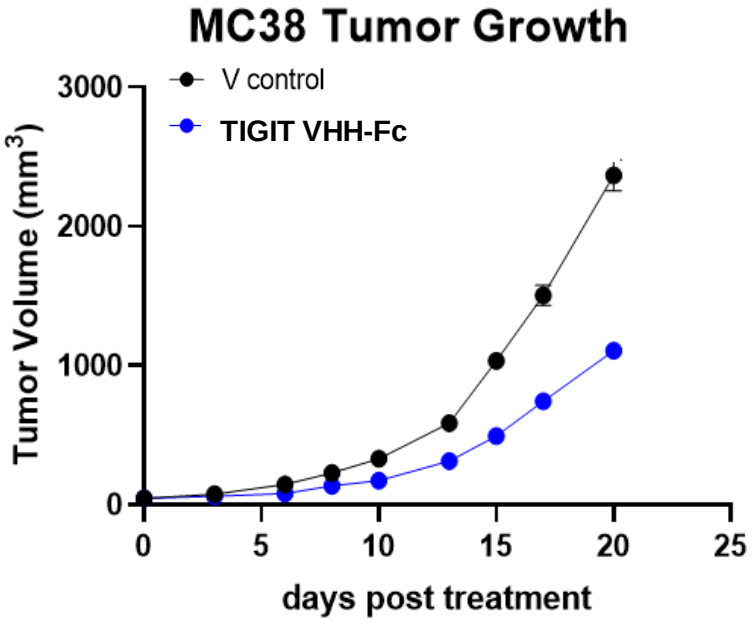
HLX53：anti-TIGIT VHH-Fc

In vitro efficacy: with Fc mutations, TIGIT VHH antibody showed higher FcgRIIIA activity and better TIGIT blocking activity



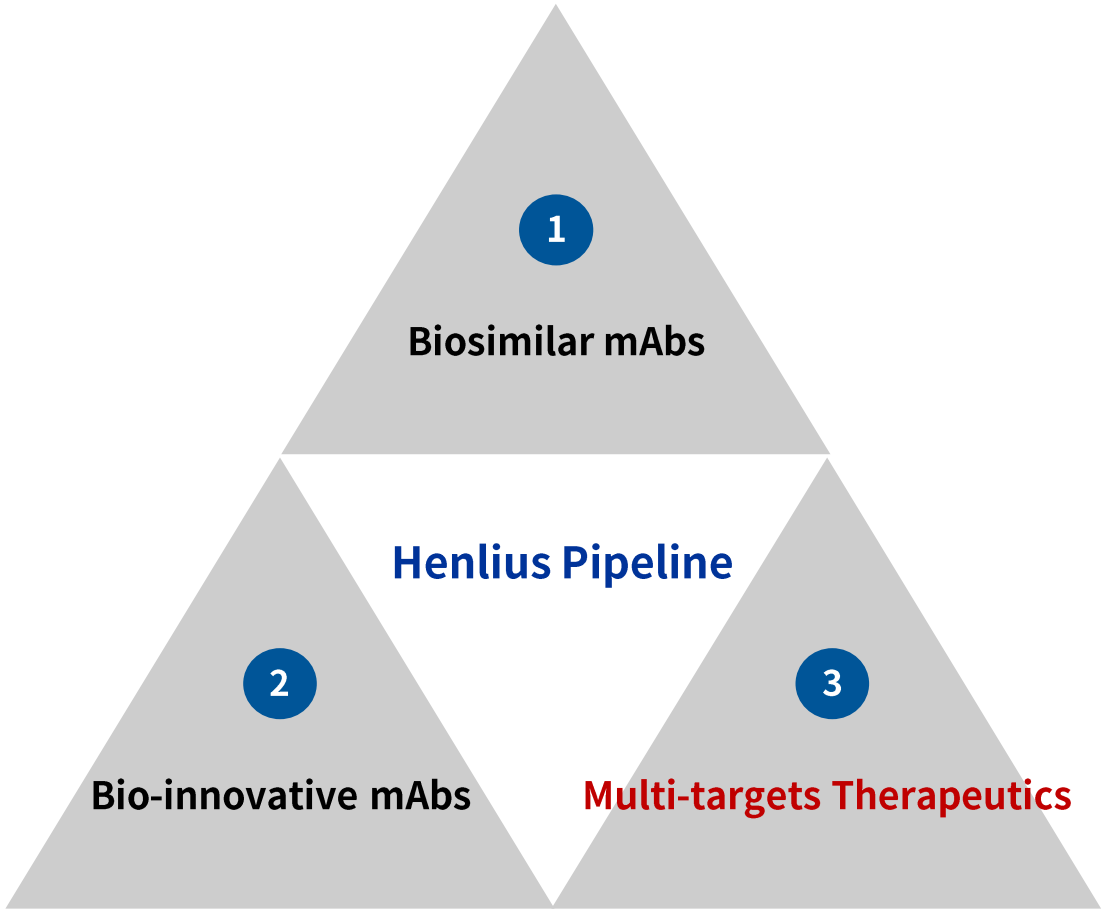






Innovative Research Pipeline: Multi-Target Drugs

Next Strategic Focus – Multi-Targets Therapeutics



Multi-targets Therapeutics

a Bispecific/Multi-specific Therapies

- Ab + Ab
- Ab + cytokine fusion protein
- Ab + receptor protein
- …

* Based on different clinical demand, targets can be designed as tumor+I/O, I/O+I/O, tumor+tumor, I/O+inflammation, I/O+growth factor, etc

b Combo Therapies

- mAb + mAb HLX10+HLX04, HLX10+HLX07 etc.
- mAb + small molecule
- mAb + chemo

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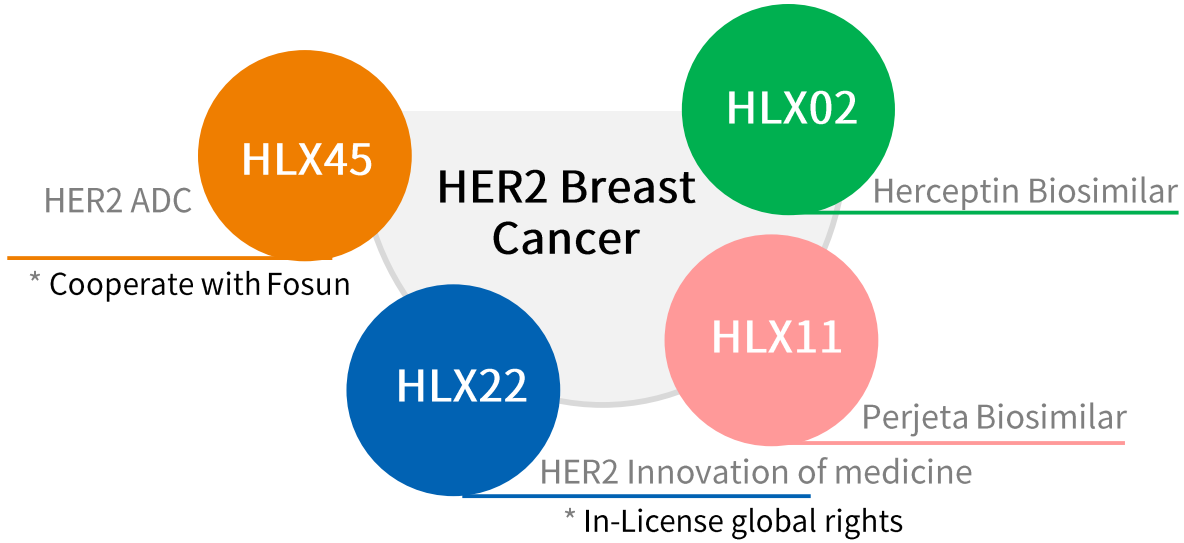
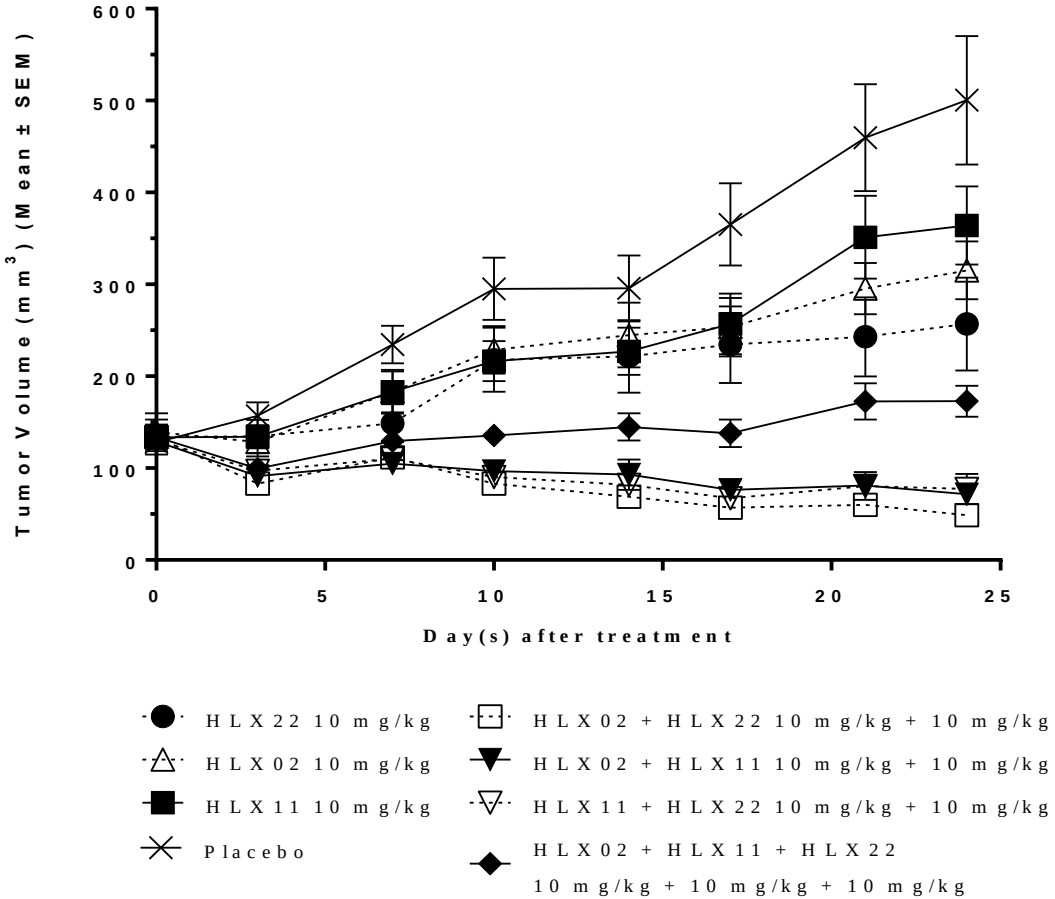
Combo: Her2-Based Combination therapy

➢ HER2



e.g.
HLX02+HLX22



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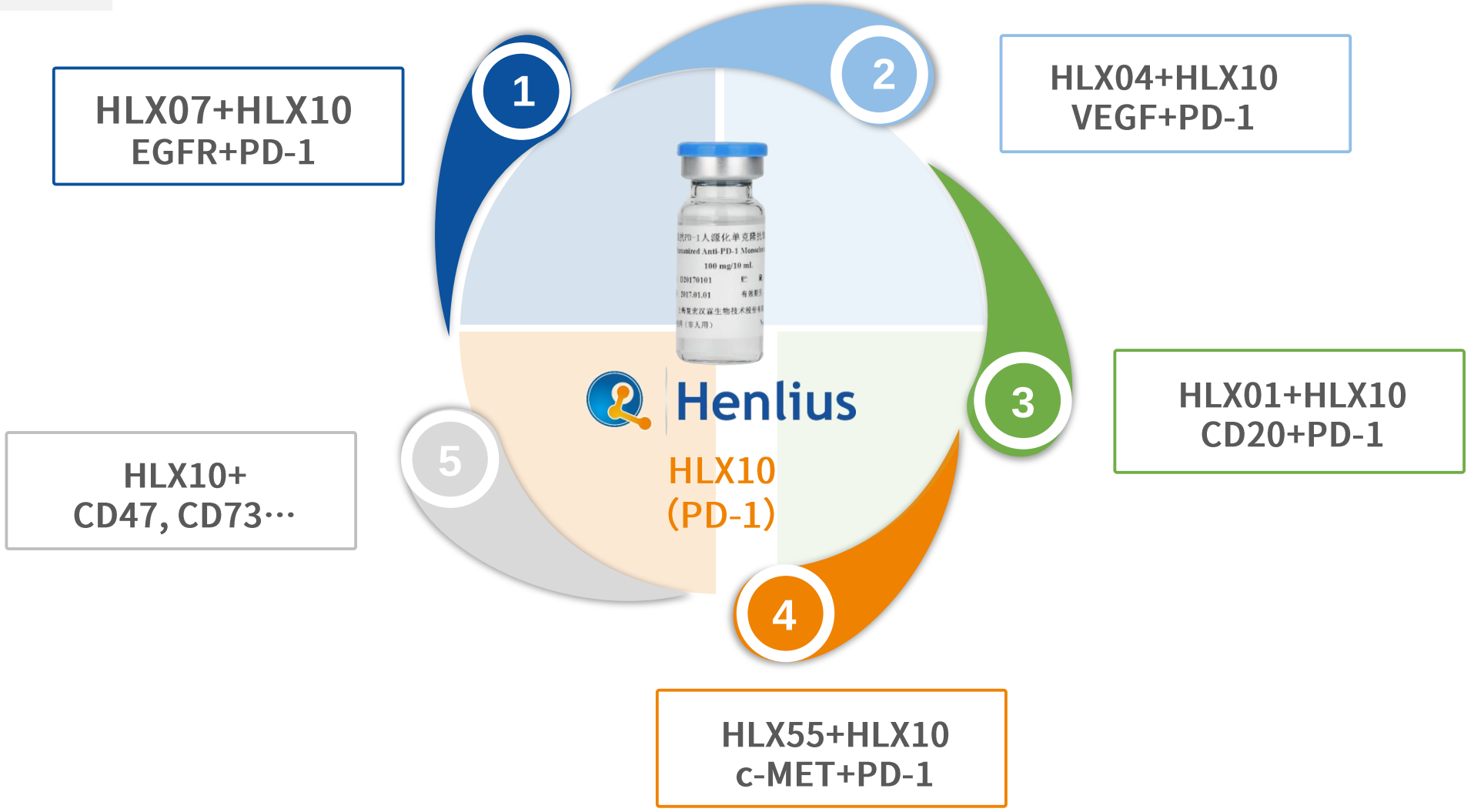
Combo: PD1 /PD-L1 Combination Therapy

➢ **PD1/PD-L1**



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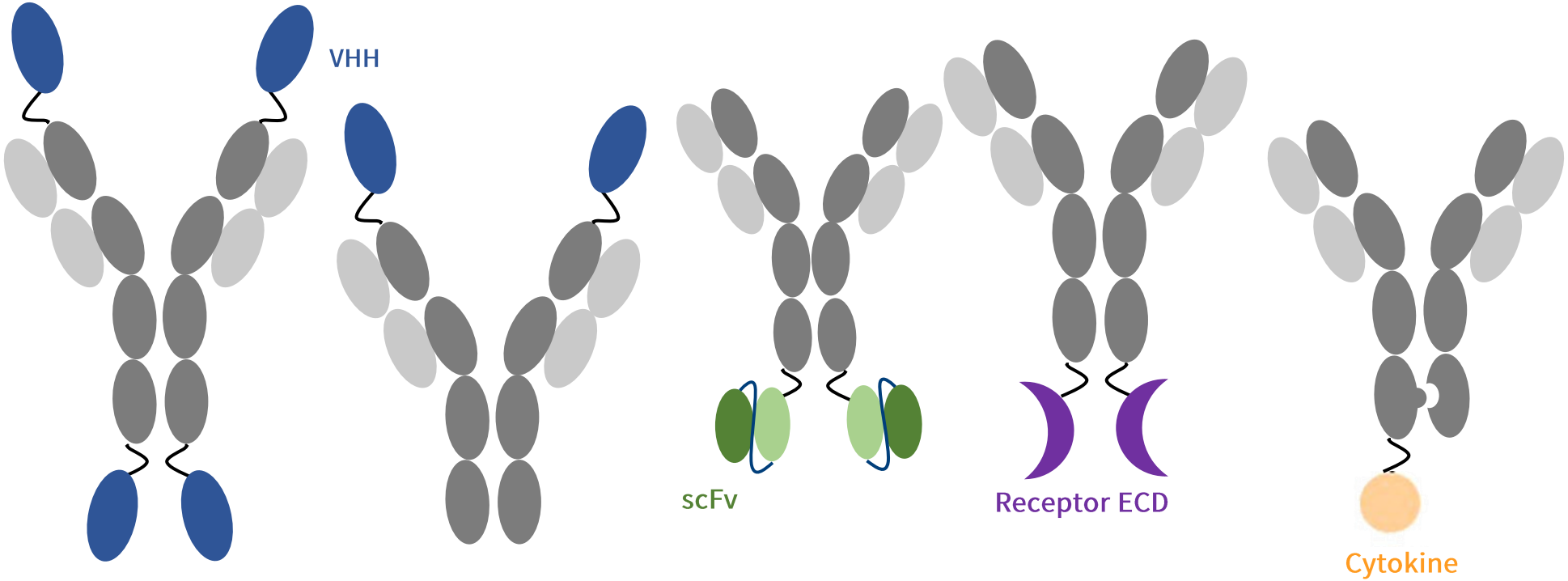
Henlius Bispecific Platforms

- Fit-for-purpose design
  - Serves MoA and biology
  - Balance safety and efficacy
- Streamlined lead generation
  - Epitope, affinity, valency
  - Modular, activity, developability

—— No “One Single Platform Fits for All”



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HLX301: TIGIT x XXX Bispecific Antibody - Tumor Enriched Dual T/NK Cell Checkpoint Blockade

Target selection	• Both TIGIT and XXXX are expressed on T and NK cells. It belongs to different tumor immune escape pathways.
Mode of Action	• Simultaneous blockade of 2 checkpoint molecules. Dual mechanisms limit tumor immune escape • Reactivation of exhausted T cells • Resistance is expected to be overcome
Clinical prospects	• Solid tumors • It is expected to develop effective biomarkers: T cells and tumor cells
Competition & Differentiation	• combo Ph2/3 trials ongoing (Genentech, Merck, BMS) • First-in Class
Preclinical study	• HLX301 has better efficacy than mAb • HLX301 has better survival benefits than combo

HLX35：4-1BB x TAA Bispecific

Target selection	• Tumor site 4-1BB co-stimulation enhances efficacy and reduce AE
Mode of Action	• TAA induces clustering of 4-1BB on T/NK cells for co-stimulation, and enhance co-stimulation signals
Clinical prospects	• Solid tumors (head and neck, colorectal cancer) • Patients with monoclonal antibody resistance
Competition & Differentiation	• Several 4-1BB mAb trials and other 4-1BB x TAA molecules reported • First-to-IND potential: no report of 4-1BB x TAA by other companies
Preclinical study	• HLX35 is more efficacious than anti-4-1BB and anti-TAA mAb alone or combination in a colon cancer (LoVo) xenograft model

Henlius Advantages in Developing Innovative Drugs

- Multi-target products + Single-target Combination，Pipeline advantage
- Multiple Platforms

  No “one single platform fits for all”
- 3-sites Synergy: US/California/Taiwan locations
  - ✓ California: Relying on Silicon Valley, academic and industrial resources and international talents
  - ✓ Shanghai: An international center, biomedicine companies intensive , attracts talents
  - ✓ Taipei: Solid academic atmosphere, Consolidate technology, stable personnel
- The R&D Scientists and SAB team with decades of international experience

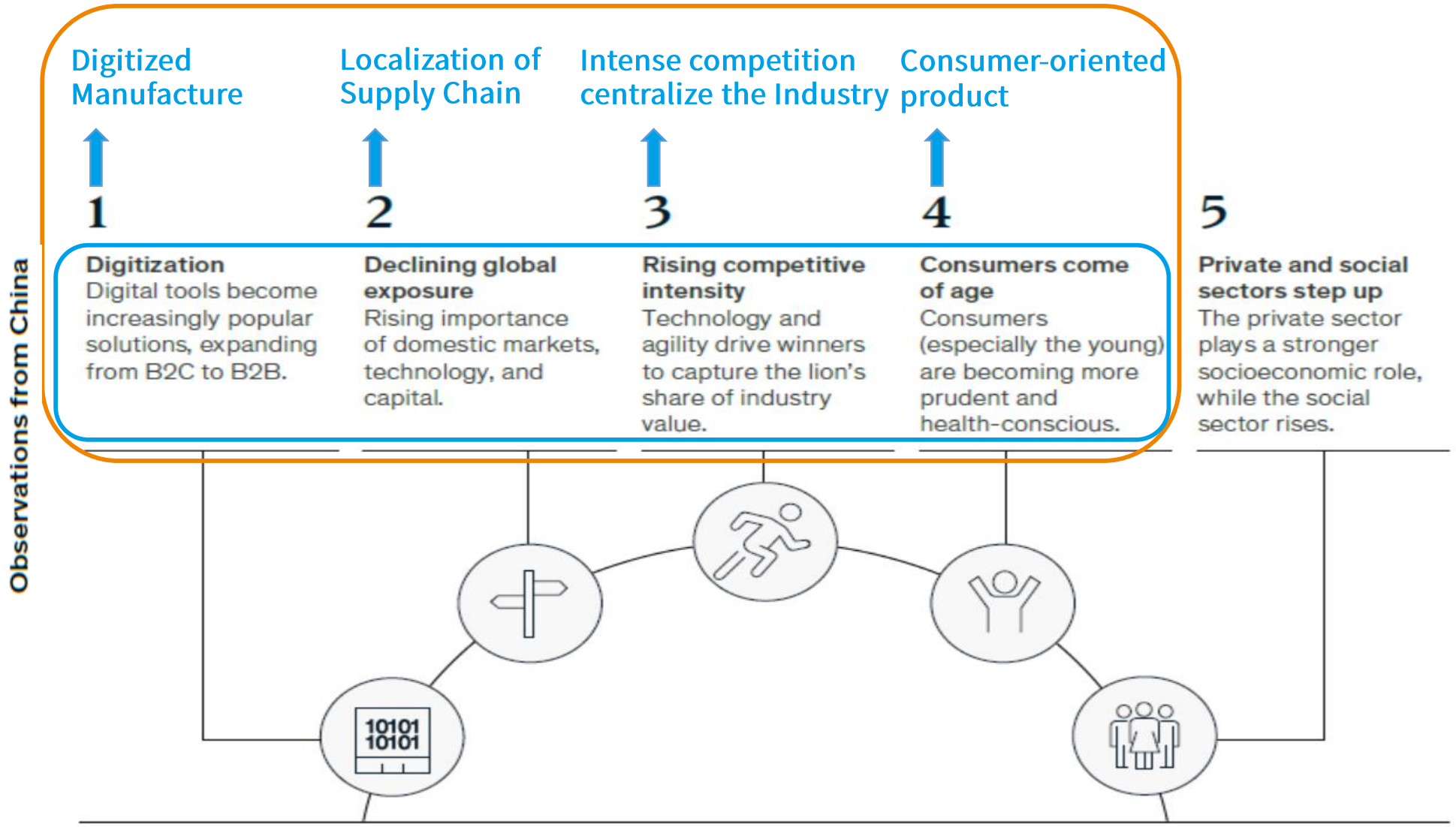
Henlius

Innovative Process Technology: Status and Advantages

Simon Hsu

SVP, Tech Operations

Five Accelerating Trends in China since COVID-19



Source: McKinsey analysis

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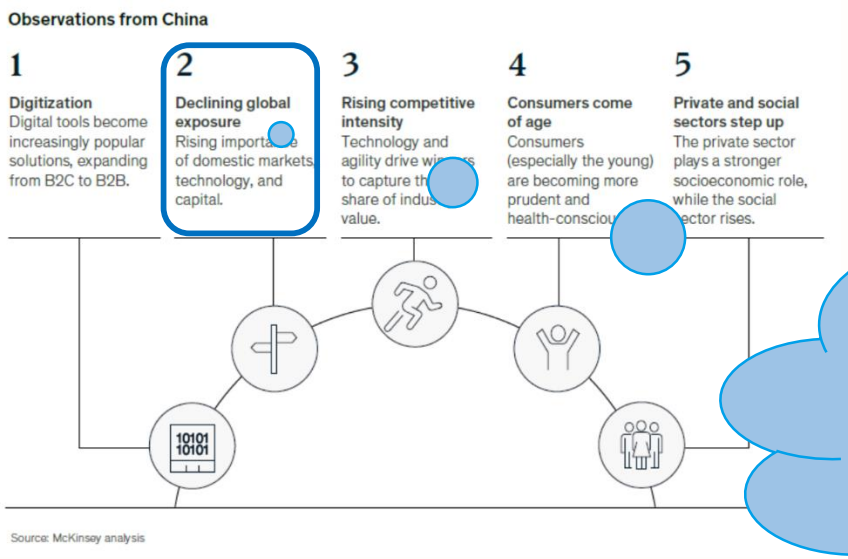
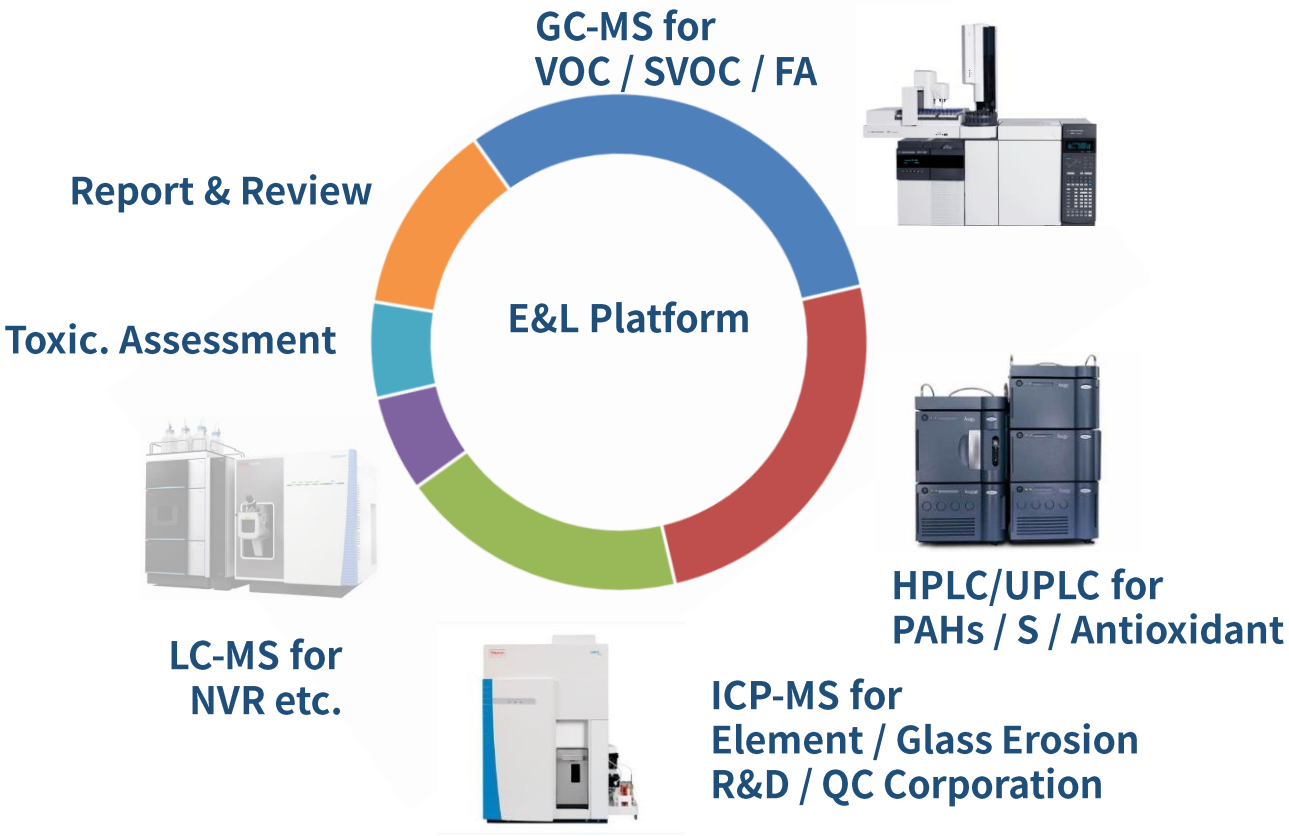


Localization of Supply Chain

Henlius E&L Platform – Significant Cost and Time Reduction

E&L Work Arrangement



- Henlius' E&L Team is founded in 2019, as a fast-growing platform in Henlius
- For an innovative drug going from 500L bag to 2000L bag we saved ~60% vs a quote from CRO
- The same project was completed within 1M vs 16M by the vendor

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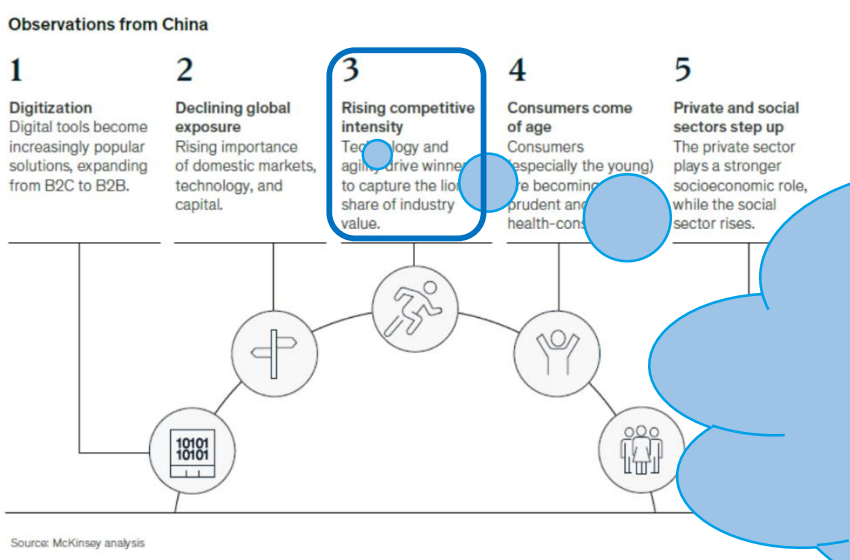
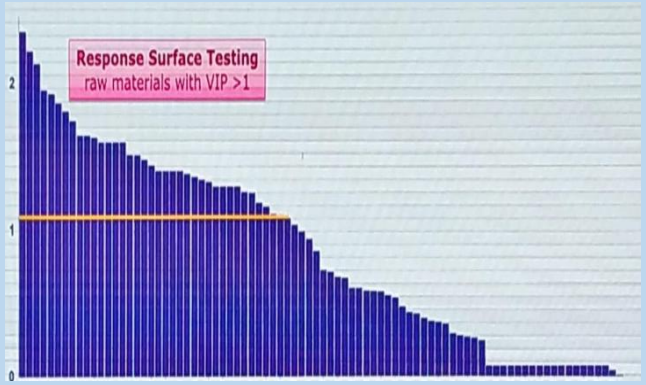
2



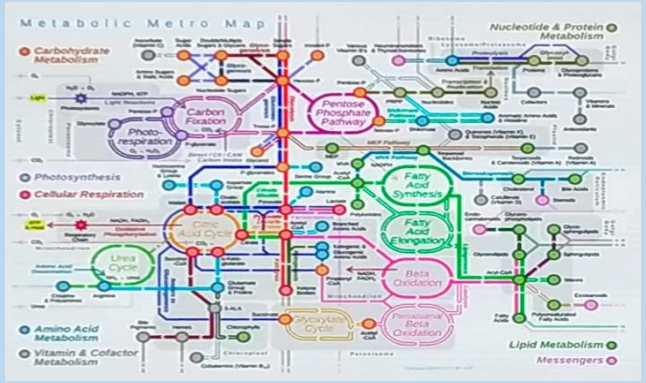
Commercialization of In-House Media and Higher Titer Process

Culture Media Development Platform – Tool Sets

Medium Component Analysis

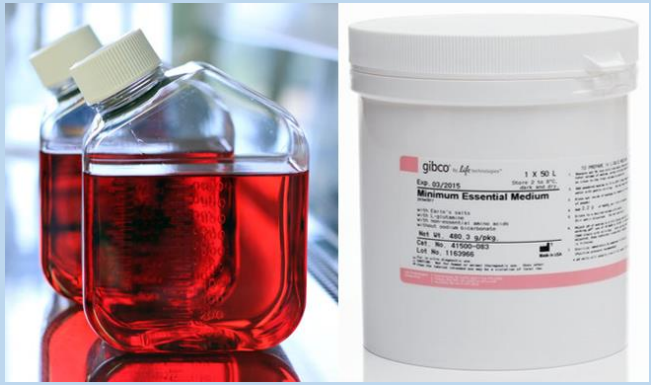


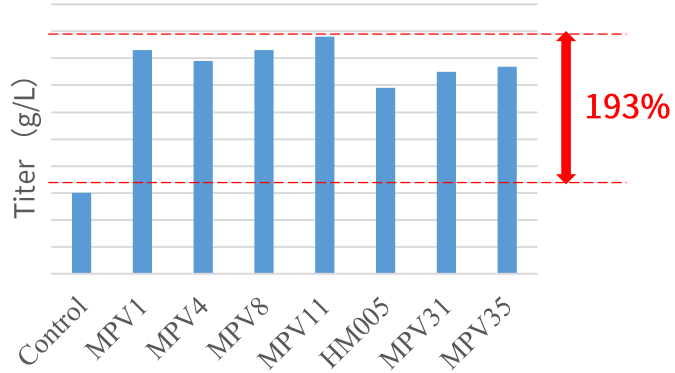
Metabolic Analysis



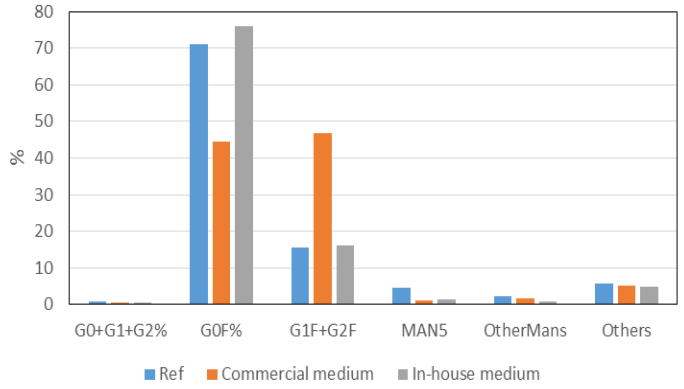
High Throughput

In-house Medium





Higher Titer & Better Quality



Design of Experiment	Statistical Analysis	Nutrient and Metabolic Analysis	High Throughput Screening

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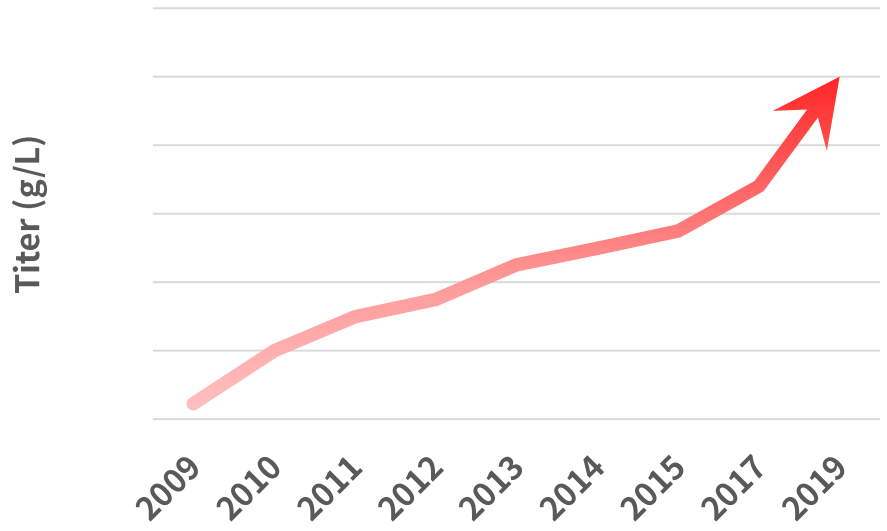
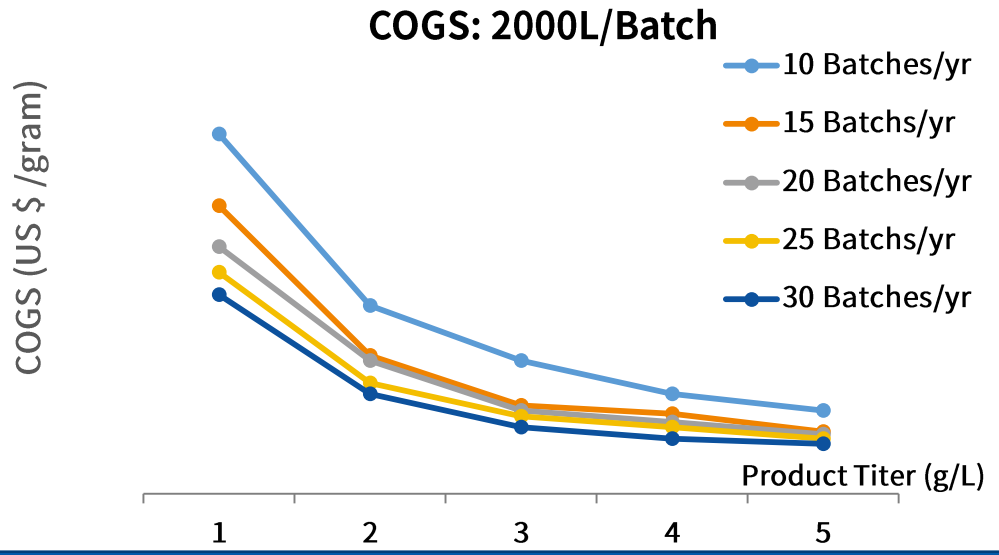
Culture Media Development Platform – 80% Cost Reduction

Continuously enhanced productivity



Titer is one of the most important factors to reduce cost



Type		Unit Price ($/L)
Basal Medium	Commercial	20
	In-house	5
Feed Medium	Commercial	50
	In-house	12

- ✓ The development and application of in-house media is the key to enhance productivities and reduce cost
- ✓ Henlius' in-house medium is about 80% cost saving as compare to commercial media

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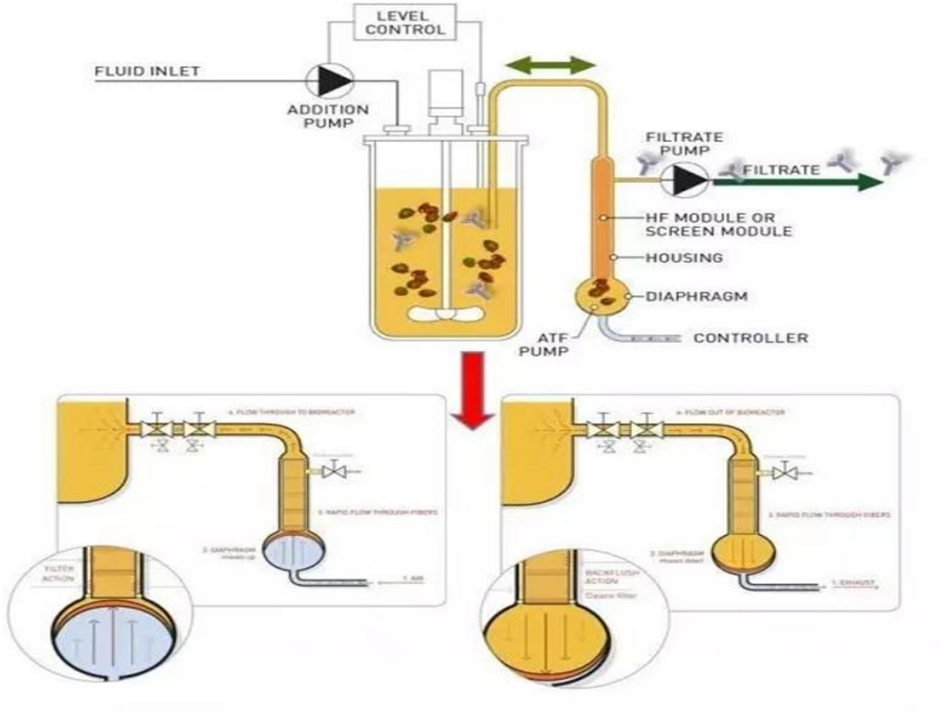
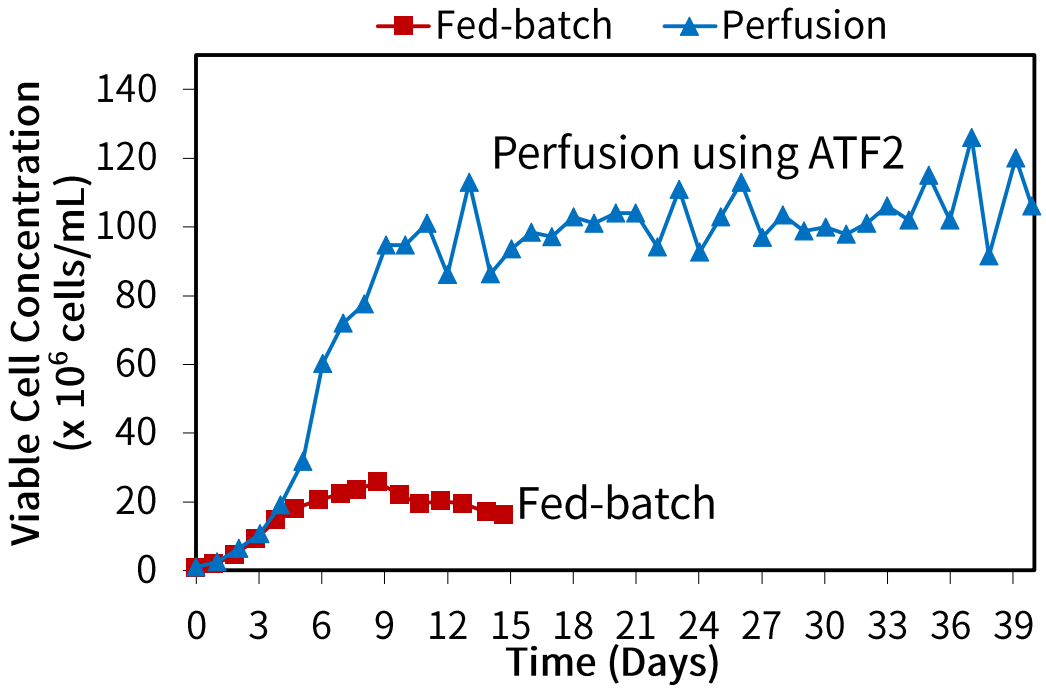
Perfusion Culture Technology

- **Perfusion cell culture technology:** The process of running a bioreactor at a fixed volume with a constant flow of media, combined with a cell retention device to keep cell in a constant growth state.
- The employment of most recent retention devices (such as TFF and ATF) enables reduced filter fouling and higher cell densities (100-200E6 cells/mL) and hence productivities compared to fed-batch process.





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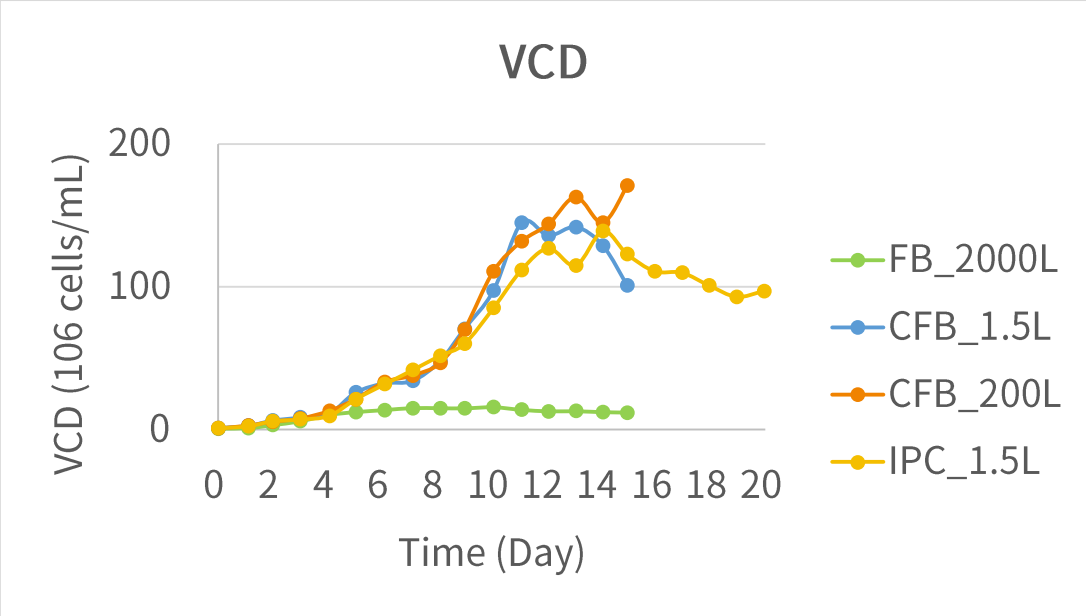
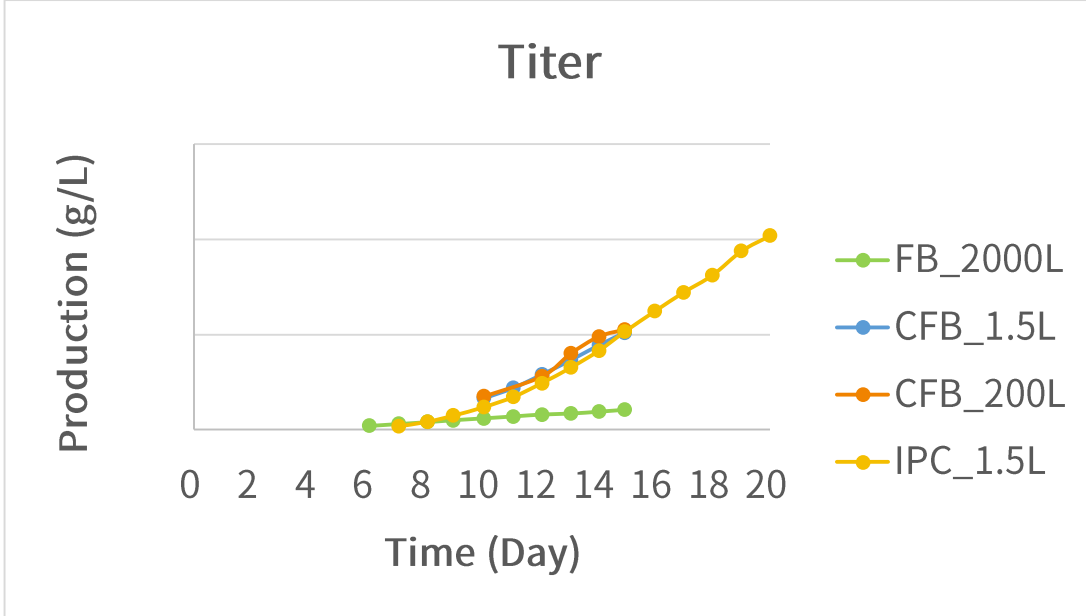
Case Study of Perfusion Technology





Ultra-high VCD (100-200E6) within 20 days

Cumulative titer ~ 10 fold of fed-batch process

Perfusion technology can increase productivity and reduce cost

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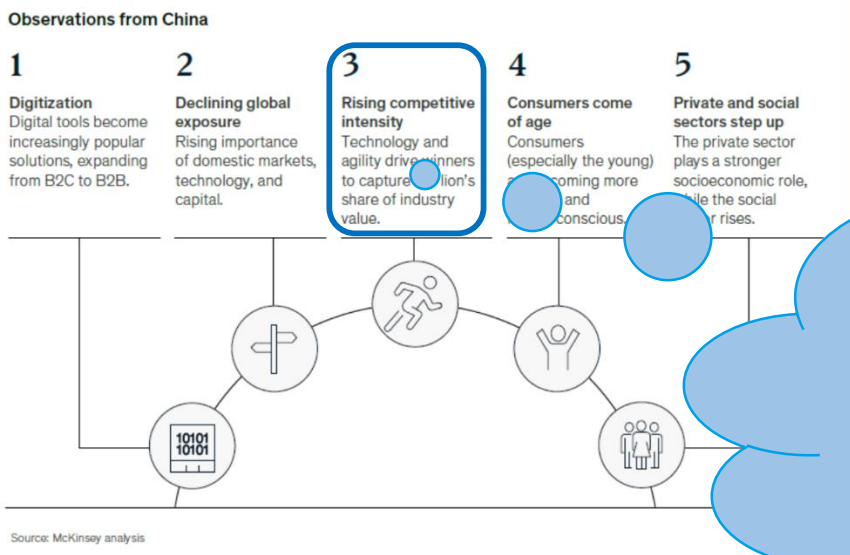
3



Continuous Manufacturing

Advantages of Continuous Manufacturing

Better Quality

- ✓ steady state;
- ✓ Reduced residence time;
- ✓ Lower lot variability

Lower Cost

- ✓ Decrease material/ labor cost;
- ✓ small footprint
- ✓ Increase productivity

More Efficiency

- ✓ Streamline;
- ✓ Remove hold-up step;
- ✓ Process integration

Easier to Adjust

- ✓ Short change over time;
- ✓ Flexible scale

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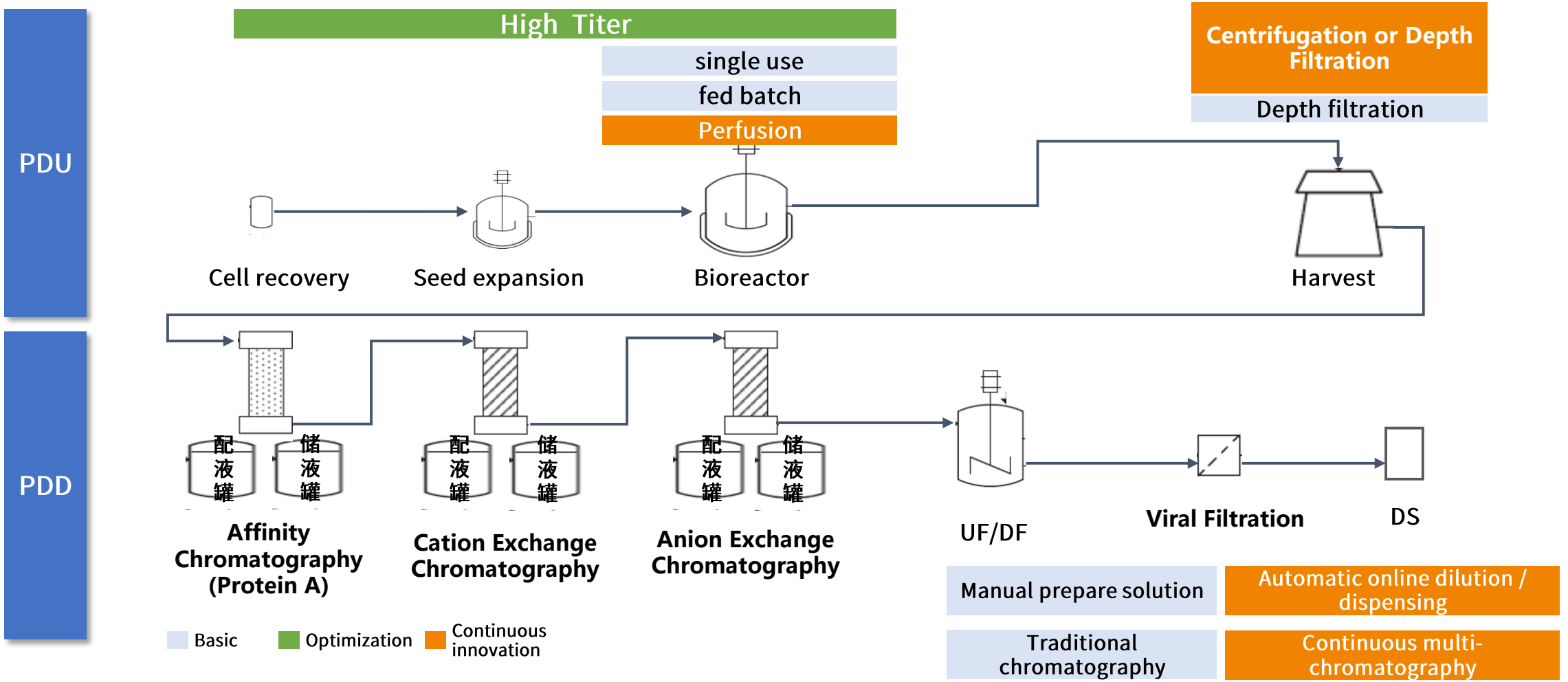
Continuous Technology Innovation, Our Visions for High Value Cost Ratio

Continue the innovation and research of international advanced production process, promote process update and reduce cost.

- Perfusion technology combined with ATF
- Downstream continuous combined with large column, automation and PAT



Source: Internal documents; PWC Manufacturing Strategy Project & Company Analysis

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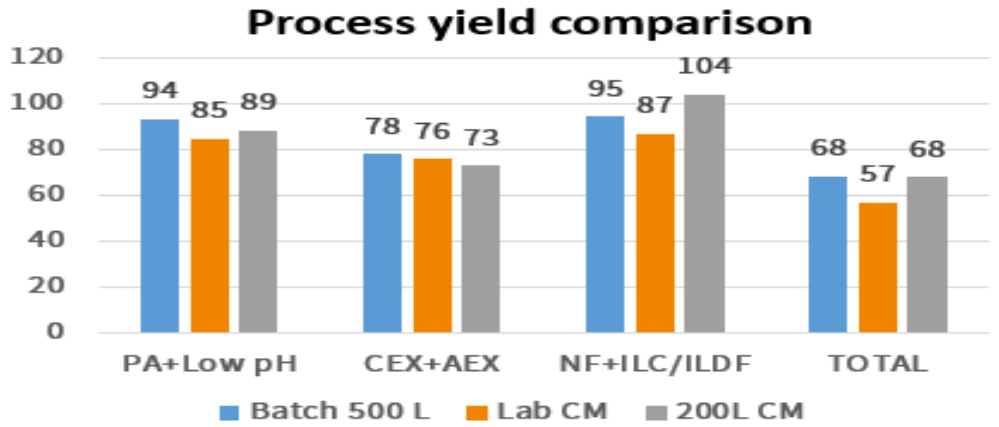
Henlius Continuous Manufacturing Platform: Lab Scale and Pilot Scale

Bioprocess system — Automatic control system

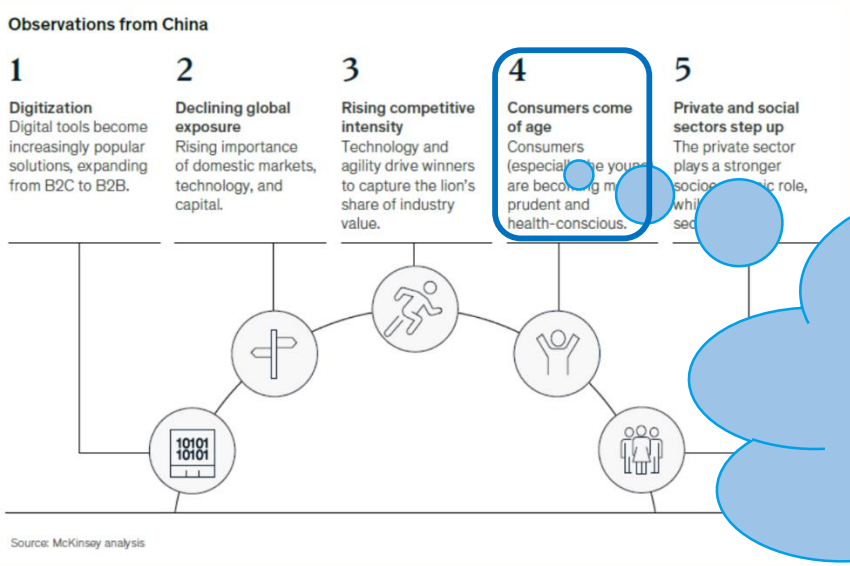
- Process development
- Viral clearance study
- Process characterization
- PAT

Bioprocess system — Automatic control system



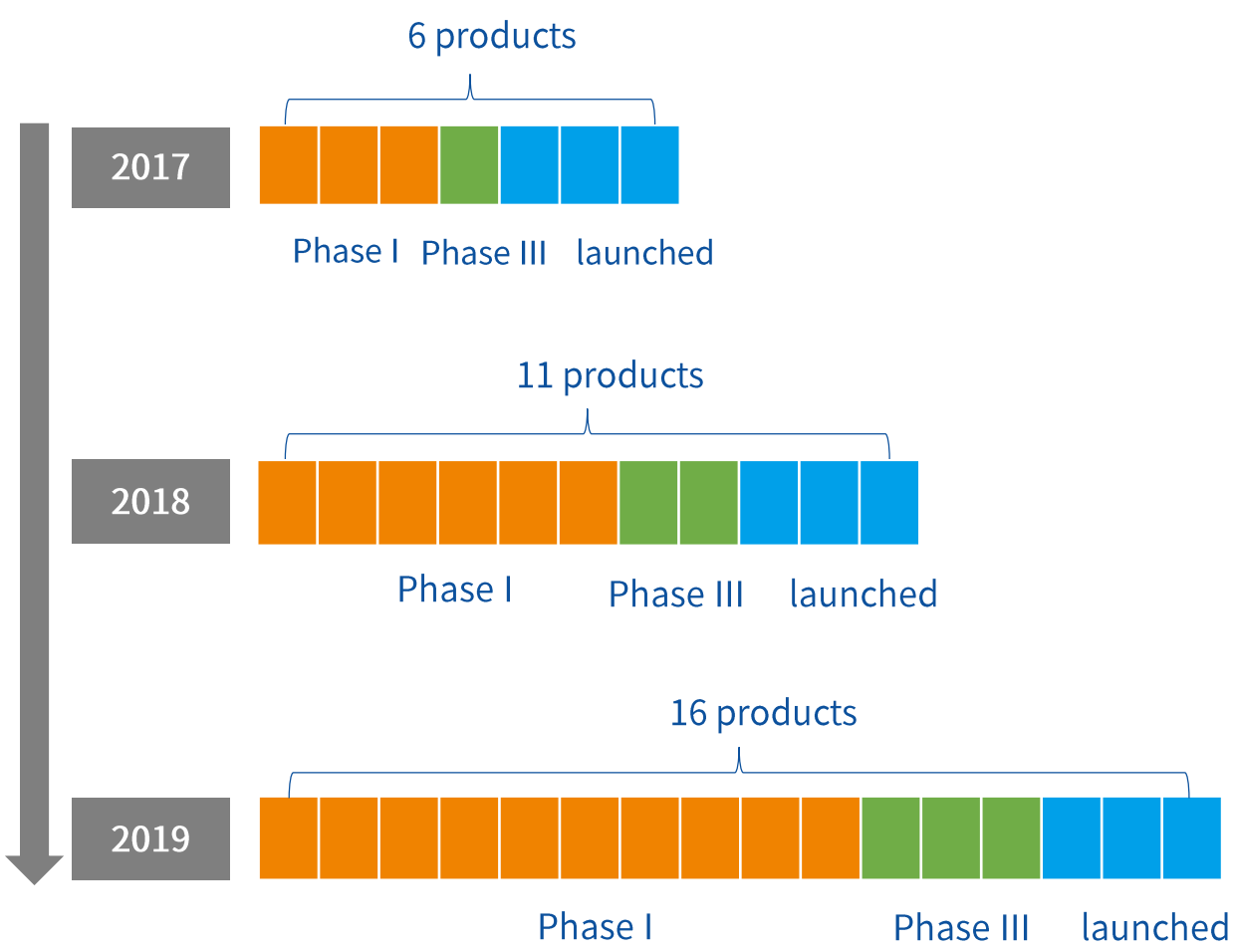
- 42 m^2 Non GMP facility to carry out 200-500 L scale production
- Estimated turn-over time 1.5-2 days，280g/day (PD-1, 200L scale)
- Comparable yield and quality to 500L batch production

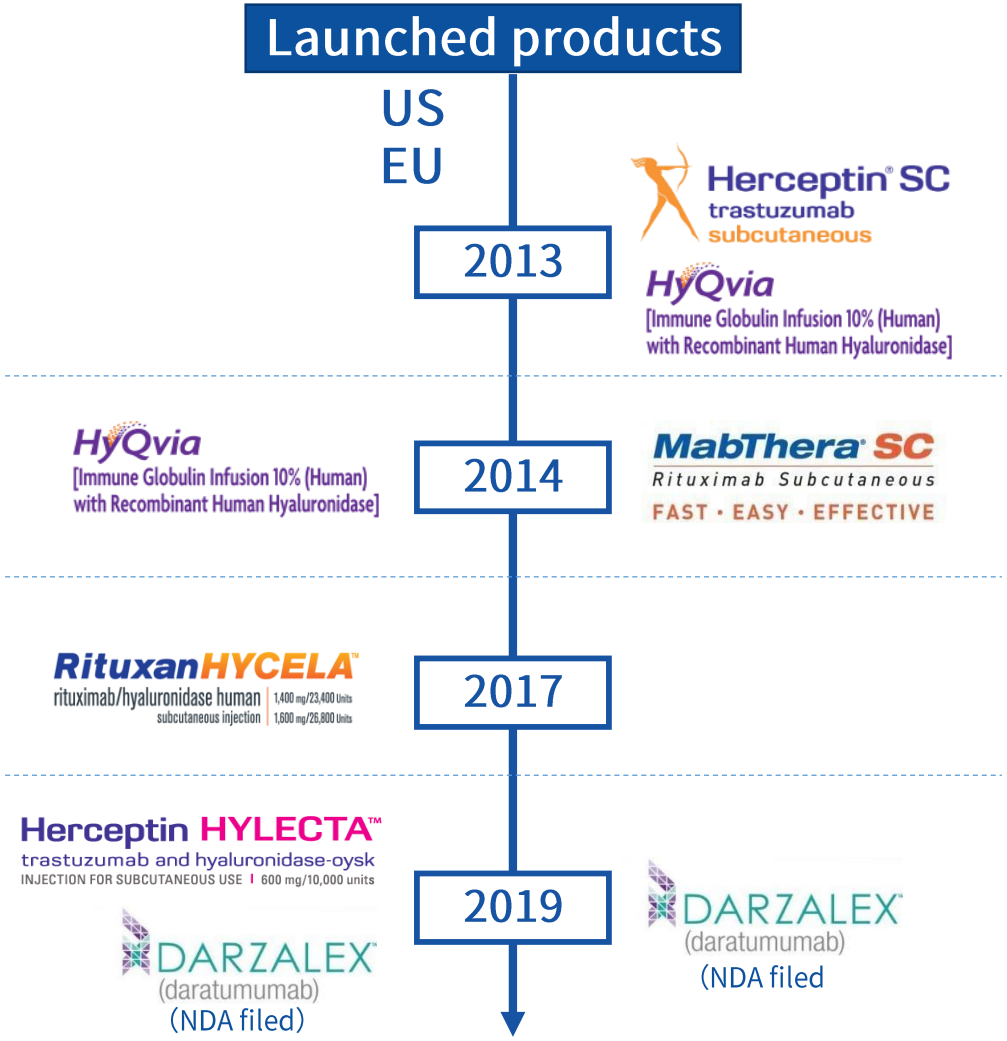
4



New Dosage Forms

New Dosage Form Development in US/EU - IV to SC





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Henlius Products Life Cycle Strategy - Competitive New Dosage Form

High concentration formulation for subcutaneous

- Henlius has both high concentration SC and PFS drug product platforms
- **HLXxx SC** project can continue
- **HLXxx PFS** finished development, Henlius is evaluating the establishment of PFS production line

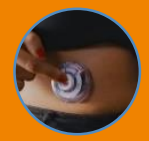
Pre-filled syringe (PFS)

Large dosage for subcutaneous

- Such products is being carried out through cooperation with key vendor and in-house development
- Henlius is working with key supplier and self developed enzyme for this development
- Currently **HLXxx SC** and large-dosage **HLXxx SC** in progress

Auto-Injector Products

- Such products require cooperation with device vendor
- Devices have high R&D cost, long development cycle (at least 2-3 years), high risk, and rapid changes in regulatory requirements in recent years.
- The demand for Device products are quite different at domestic and foreign markets. Henlius is currently in talk with new technology suppliers in order to determine best time to introduce into China.



Wearable products

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Manufacturing Overview and Updates

Wei Huang

SVP, Manufacturing & Engineering

Three Milestones Reached As Expected

Xuhui Facility

- 2020.04.14 HLX01 2,000L approved （previously expected end of April/early May)
- 2020.04.17-20 HLX02 received EU GMP certificates（previously expected 2Q20）
- Capacity increased from 12,000L to **20,000L**
- Support 汉利康® Commercial manufacturing

Songjiang Plant 1

- 2020.04.05 development run started(previously expected 2Q20)
- Planned capacity of 24,000L
- Single-Use System
- Fill & finish lines for lyophilized powder and liquid injection products
- Support commercial production needs

Songjiang Plant 2

- Site area is approximately 33 acres
- Single-use & stainless steel hybrid systems
- Fill & finish lines to support lyophilized powder/liquid injection & pre-filled syringe products
- Construction started in June 2019
- Starting engineering run and process validation in 2021

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Henlius Receives EU GMP Certificate for HLX02 in April, 2020

GMP Certificate	■ Certified product：HLX02 (trastuzumab for injection) (lyophilized powder for injection) ■ Certification organization：Chief Pharmaceutical Inspector (a health regulatory organization in Poland) ■ Certification scope：drug substance, cell banking, warehouse and management, lyophilized filling line in Xuhui facility ■ Valid period: 3 years
Applicable Regions	■ According to the GMP mutual recognition system of EU member states, the Company’ s Xuhui Facility has met the EU GMP standards ■ EU GMP certification is mutually recognized and shared among nearly 30 member states ■ Inspection results can be shared with nations such as U.S. and Canada which signed Mutual Recognition Agreement (MRA)
Global Impact	■ “EU Guidelines for Biosimilars” (CHMP/47/04) took effect in 2005, which is the world’ s first guiding principle for biosimilar research and evaluation ■ EU GMP certification is one of the world’ s most authoritative and stringent certifications, it has a significant global influence and is considered as a “PASS” for drugs to access global markets

Xuhui Facility

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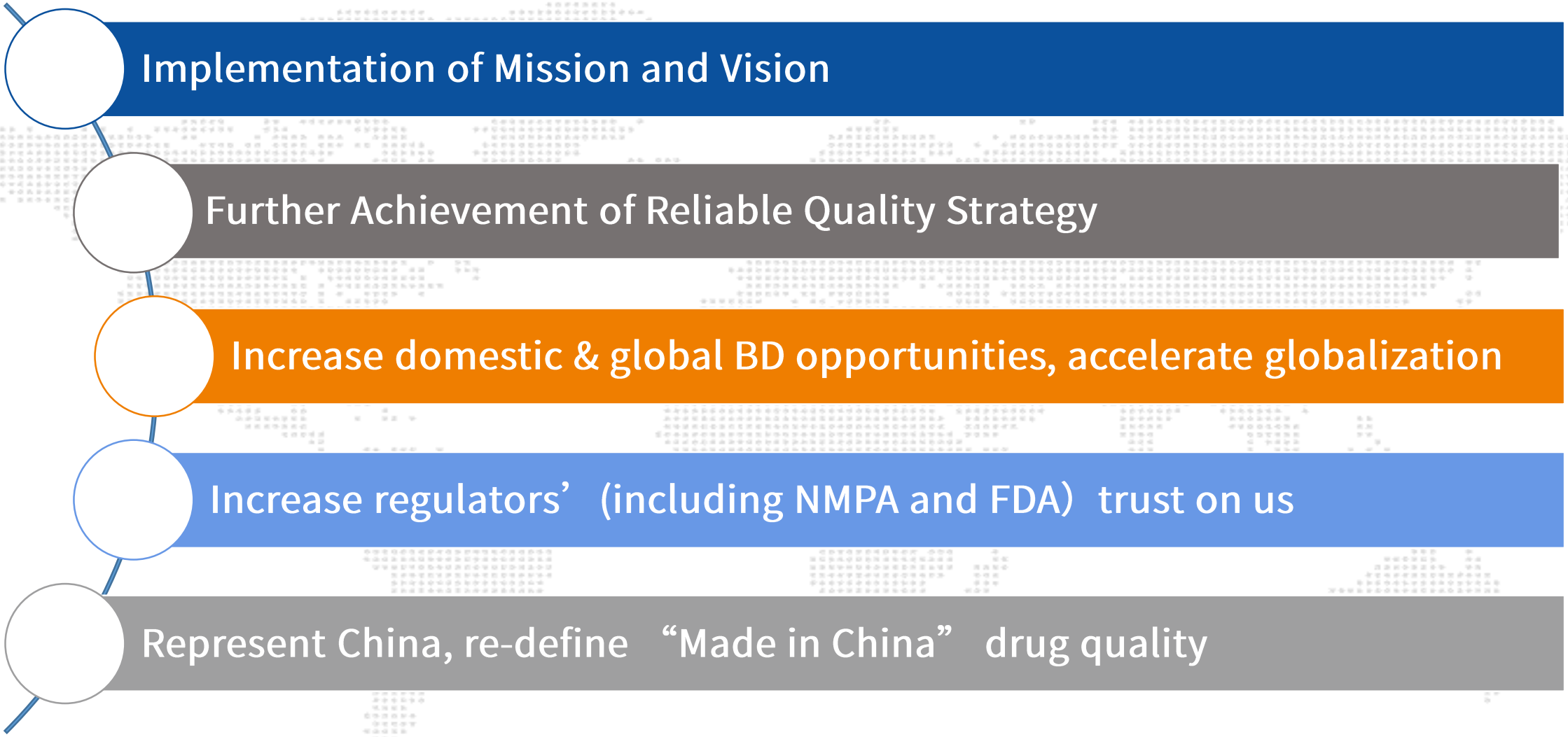
Significance of Receiving EU GMP Certificate for HLX02



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Advanced Manufacturing Equipments at Xuhui Facility


2000 L Bioreactor


Chromatography System


Buffer Preparation System


200 L Bioreactor


Ultrafiltration System


Buffer Preparation System

Upstream

Downstream

Aseptic Filling

Henlius has become the largest company using single-use bioreactor among domestic biopharmaceutical companies

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Master Plan for Henlius Songjiang Plant 1

3F	• R&D Lab & Office Area • QC Lab • Continuous Manufacturing Pilot Plant (in construction)
2F	• Warehouse • Manufacturing Support Lab • Engineering Command Center for Songjiang Plant Construction
1F	• DS Manufacturing Plant • Manufacturing Utilities Area • DP Manufacturing Plant (in construction)

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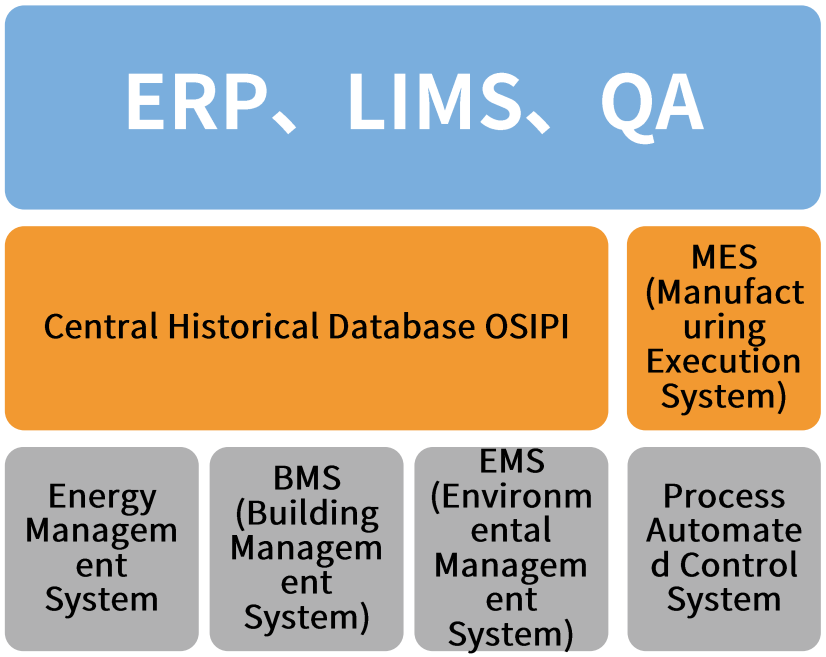
Songjiang Plant 2

Henlius signed an official agreement with the People’ s Government of Songjiang, Shanghai, to locate a 33 acre biopharmaceutical manufacturing facility in Dec., 2017 in order to meet the capacity demand for >20 future innovative products. Its capacity is expected to become No. 1 in China and top 3 in Asia.

- Designed and constructed with **global GMP standards**
- Fully use international new technology (**continuous process**) to ensure quality and reduce cost
- Global standards on biopharmaceutical **automation, digitization and intelligence** (Pharma 4.0)
- **Low-carbon, energy-efficient and environment-friendly** modern smart biopharmaceutical plant
- When construction is completed, total capacity is expected to serve **~3 million** patients

Smart Facility Construction of Songjiang Plant 2 Phase 1



Intensive production platform

Application of automation, informatinization and smart technology

Flexible process layout

Purpose

- ✓ Ensure drug quality
- ✓ Reduce labor cost
- ✓ Reduce human error
- ✓ Improve data integrity and traceability
- ✓ Increase global competitiveness

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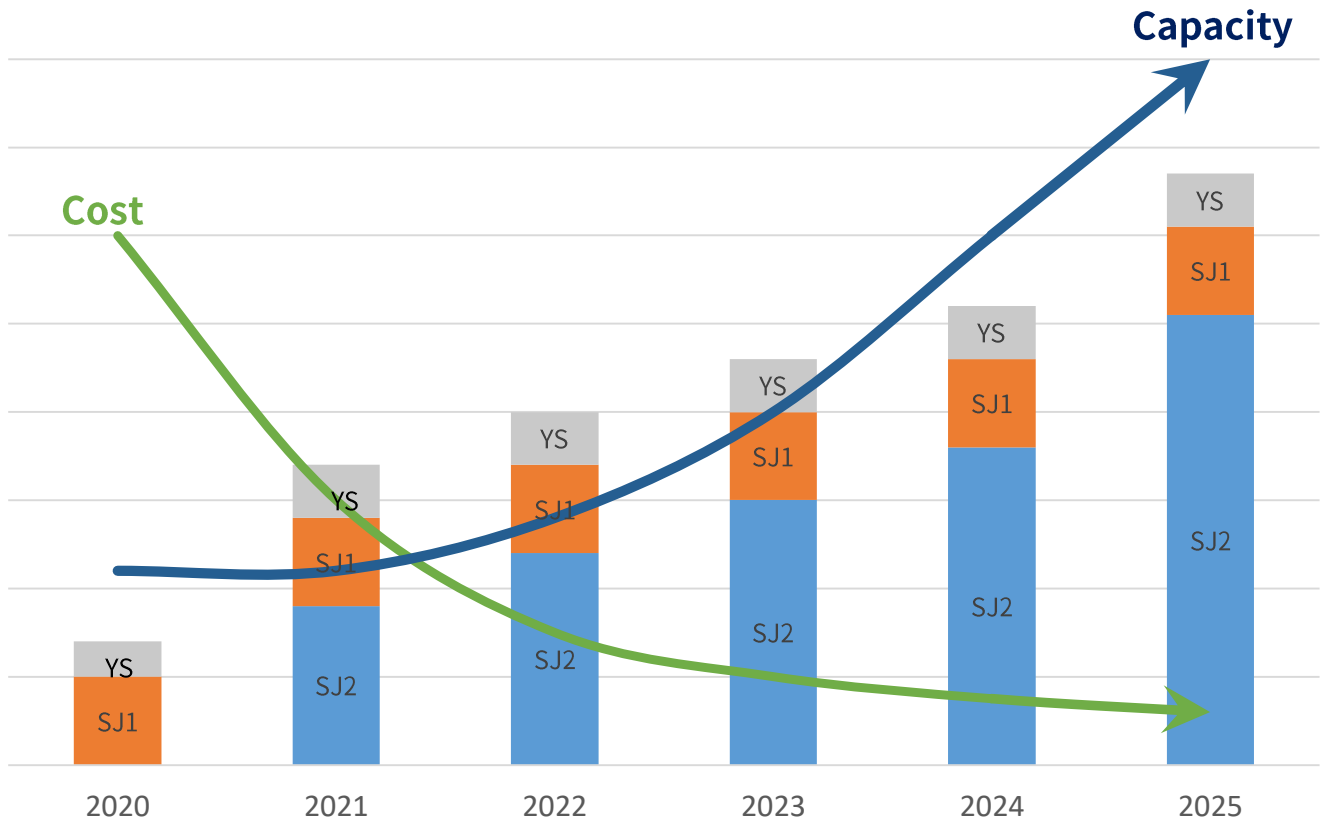
Commercial Manufacturing Capacity Achievement and Plan

FAST 2020	TO 2021 - 2023	WIN 2024+
• **Win 20/20：** fast achievement of "maximization and optimization" on capacity	• **Capacity expansion：** accelerate construction of Songjiang Plant 2, capacity to meet commercial demand	• **2024+ outlook：lead bimosimilar market in China**
• **Focus on quality：uncompromised** quality management to make high-quality biologics meeting EU and China standards	• **2nd-generation process：** submit application, significant yield cost advantage	• **Continuous process innovation, achieve affordable high quality:** ATF+ Continuous manufacturing
• **Process innovation：** 2nd-generation process enter late stage development, enable commercial production expansion	• **Focus on quality:** Receive PIC/S, WHO, FDA and other international quality standards certification, become top tier quality system	• **Operation of Songjiang Plant, rapid expansion of manufacturing capacity:** main products is could meet 70% of the Chinese market demand

Capacity cost analysis & production layout

Rapid Expansion of Capacity and Continue COGS Reduction

Large increase in capacity, significant decrease in cost



Achieve significant cost-efficient commercial manufacturing capacity via economy of scale and technology innovation

Songjiang Plant construction & process optimization will significantly increase capacity and lower cost

Comprehensive strategic mid-to-long term capacity planning to meet rapid market growth and deliver high-quality product

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Manufacturing High-Quality Biologics with US, EU and China Standards

Implement full scale quality management with highest standards: after receiving CFDA certification in 2018 and EU GMP certification, Henlius targets passing international highest quality certifications such as PIC/S, WHO, USFDA, etc. to become sector’ s best management system

2018

- In compliance with CFDA GMP
- Passed 2-in-1 inspection
- Passed all client inspection

国家药品监督管理局 国家市场监督管理总局

2019

- In compliance with CFDA and EMA GMP
- Passed EMA on site inspection
- Passed PIC/S member state inspection

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
An Agency of the European Union

2020

- In compliance with GMP requirements (CFDA, EMA, PIC/S , WHO, etc.)
- Passed global one site inspection

PIC/S World Health Organization

2021

- In compliance with global GMP requirements (CFDA, EMA, PIC/S, WHO, USFDA, etc.)
- Ready to receive global GMP on-site inspections (including FDA)

2023

- In compliance with global GMP requirements (CFDA, EMA, PIC/S, WHO, FDA,TGA, ANVISA, etc.)
- Ready to receive global GMP on-site inspection (including FDA) at any time
- Sector’ s best quality management system

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Henlius 复宏汉霖

Reliable Quality | **Affordable** Innovation