

# Unlock the Optimal Pairings of Bispecific Antibodies and Efficient Scale-Up Strategies

Protein Sciences



**WuXi Biologics**  
Global Solution Provider



# Leading Global Biologics CRDMO



**Vision:** “Every drug can be made and every disease can be treated” by building an open-access platform with the most comprehensive capabilities and technologies in the global biologics industry

**Mission:** To accelerate and transform the discovery, development and manufacturing of biologics through a comprehensive open-access platform, enabling our global healthcare partners and benefiting patients worldwide

**Business Model:** Dedicated CRDMO with “Follow and Win the Molecule” strategy to discover, develop, and manufacture biologics FOR CLIENTS ONLY

**Commercial Manufacturing Strategy:** Global Dual Sourcing within WuXi Biologics

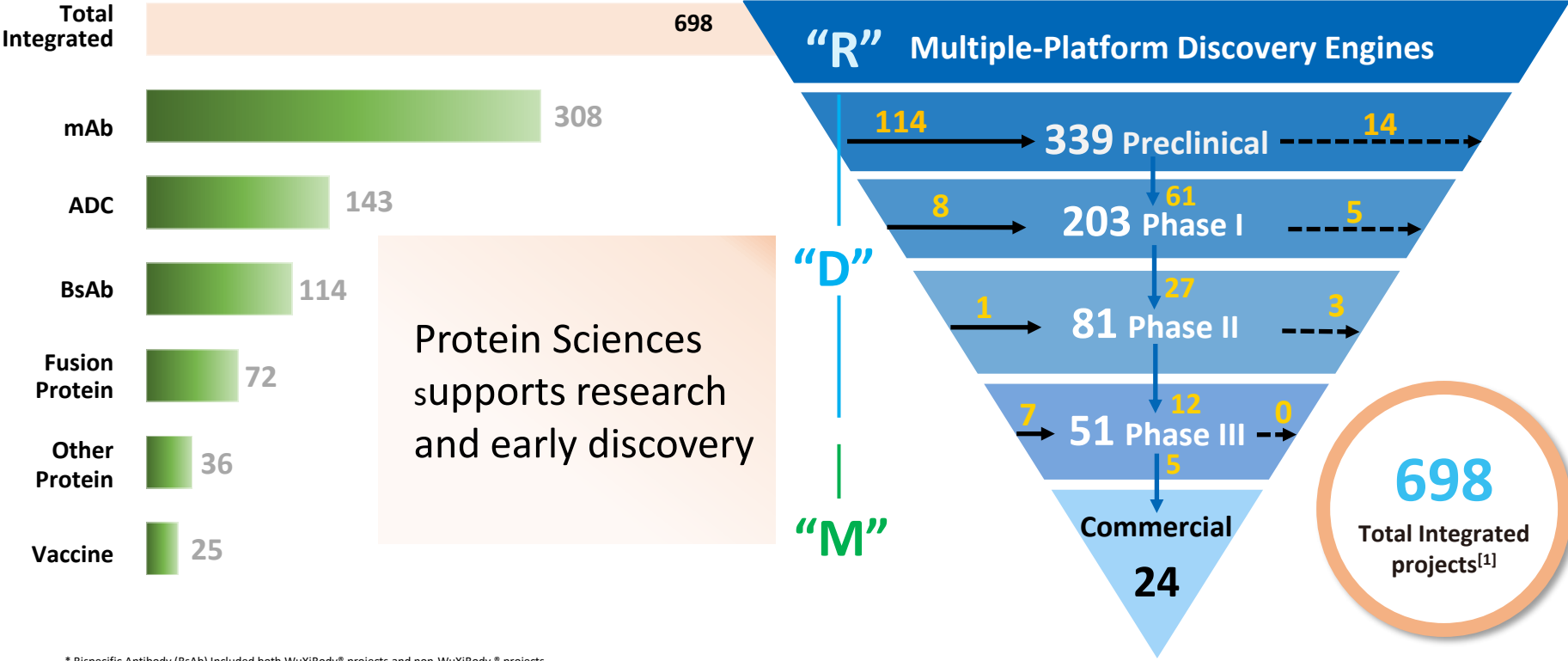
**World-class Quality System** certified by 13 regulatory agencies (e.g. U.S. FDA, EMA, China NMPA, Japan PMDA)  
**Robust and premier-quality global supply chain network** in China, Ireland, the U.S., Germany, and Singapore



[1] As of December 31<sup>st</sup> 2023

[2] As of June 30<sup>th</sup> 2023

# Rich Pipeline across Diverse Biologics Modalities



\* Bispecific Antibody (BsAb) Included both WuXiBody® projects and non-WuXiBody® projects  
 [1] As of December 31, 2023. [2] The commercial manufacturing projects refer to the projects approved by regulatory authorities and signed CMO contracts with the Group

# Drug Development Expertise, Protein Generation Excellence



Gene Synthesis

Cloning DNA Prep

Expression

Purification

Protein Characterization

As fast as **3 weeks**



Monoclonal  
Antibody



Bispecific  
Antibody



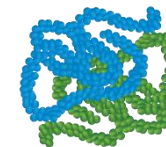
Antibody Drug  
Conjugate



Fc-fusion  
Protein

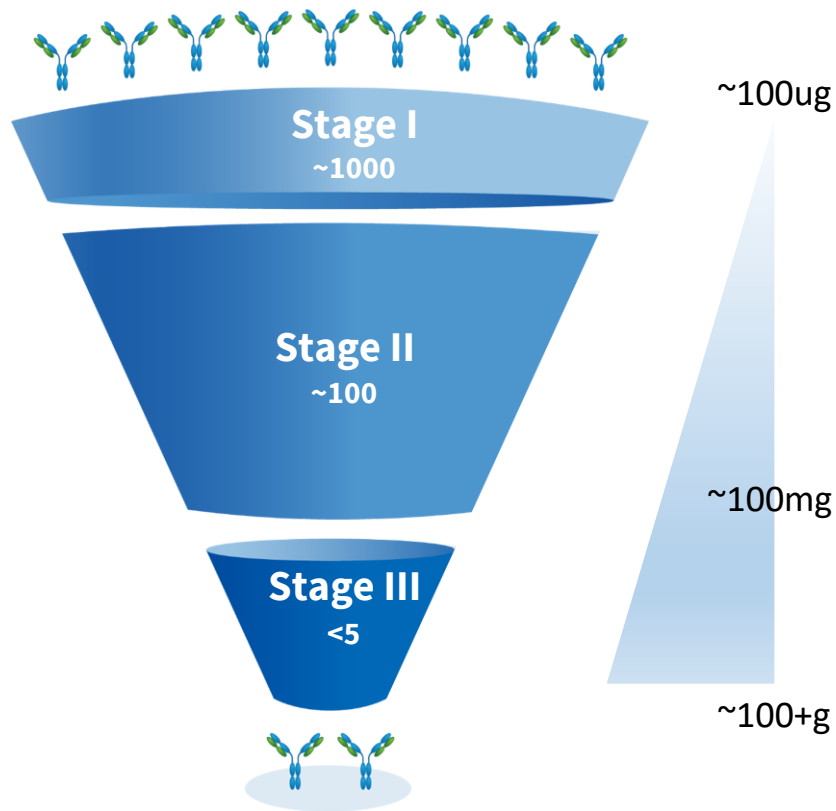


Antibody  
Fragment



Recombinant  
Protein

# Comprehensive Services for Antibody Drug Development



**Development**

**WuXian Transient**

**Ultra 96 +**

**777**

**Quick 'n' Clean**

**Micro Developability**

**Premium BsAb**

**GramExpress**

**Developability**

**WuXian Express**

- 96 DWP based production
- 100-500ug antibody
- For *in vitro* binding, etc

- 20+ ml
- 1-100mg antibody
- HTP mAb and BsAb
- For *In vitro*, *in vivo* studies

- Large scale production
- mAb
- Premium BsAb
- For *in vitro*, *in vivo* studies

# CONTENTS

01

## **Premium BsAb Production**

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- Optimization of Chain Ratio
- Optimization of Purification

02

## **Quick 'n' Clean: HTP BsAb Production for Screening at the Early Stage**

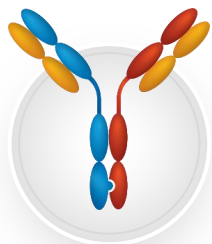
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- Introduction to Quick 'n' Clean
- Case studies

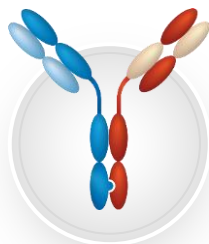


**Premium <sup>♦</sup>BsAb 01**

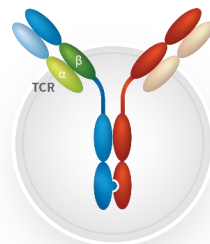
# Premium BsAb - LC-MS Assisted BsAb Production



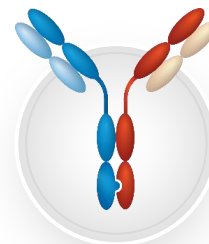
Common LC



Cross mAb



WuXiBody



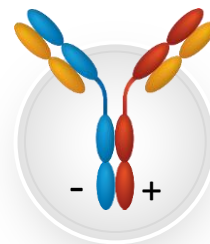
Different LC



Fc Fusion



ScFv Fab



Charged pairing



Others

- 10mg to grams BsAb in 4-6 weeks
- All premium BsAbs are verified by intact mass
- 3000+ premium BsAb delivered successfully



# Case Study 1: Chain Ratio Optimization

## Challenges

**Low** titer

**Low** SEC-HPLC purity

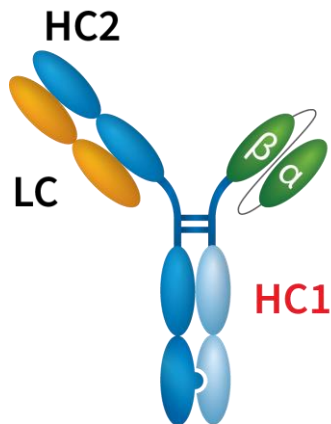
## Improving Strategy

**Optimize chain ratio**

## Better Product Quality

**Higher yield**

**Better purity**



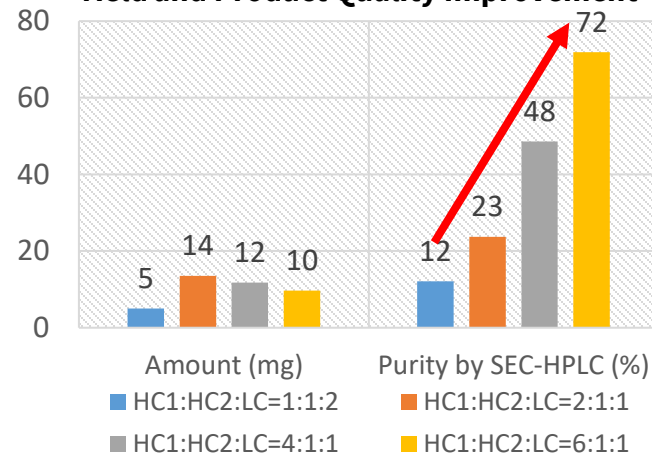
**HC1 was limiting**

**HC1** : HC2: LC = **2**:1: 1

**HC1** : HC2: LC = **4**:1: 1

**HC1** : HC2: LC = **6**:1: 1

## Yield and Product Quality Improvement



# Common Formats and Byproducts of Knob into Hole (KiH) BsAb

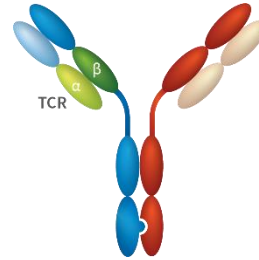
## Common KiH formats



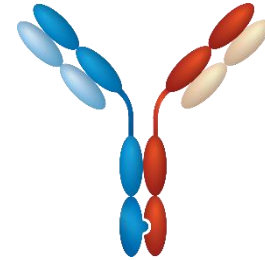
Common LC



CrossMab

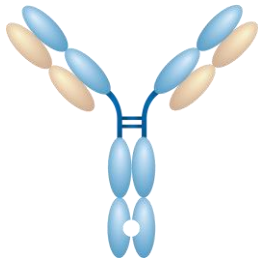


WuXiBody

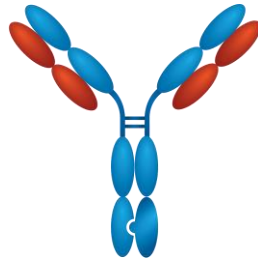


Hetero LC

## Main byproducts of KiH formats:



Homodimer



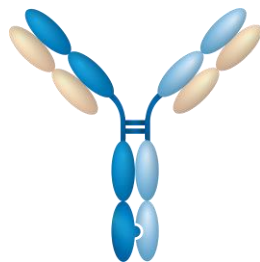
Mispaired LC



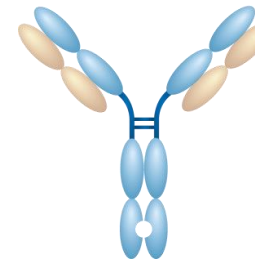
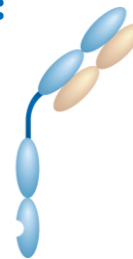
Half Antibody

# Case Study 1: Common LC BsAb

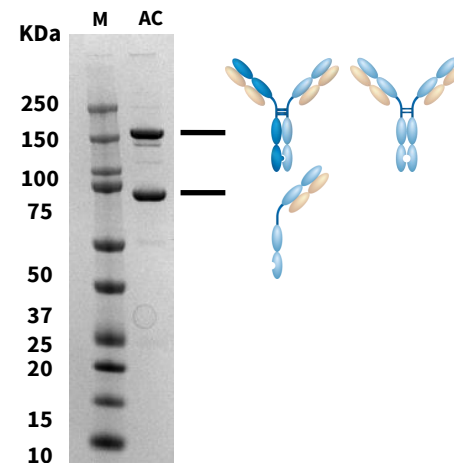
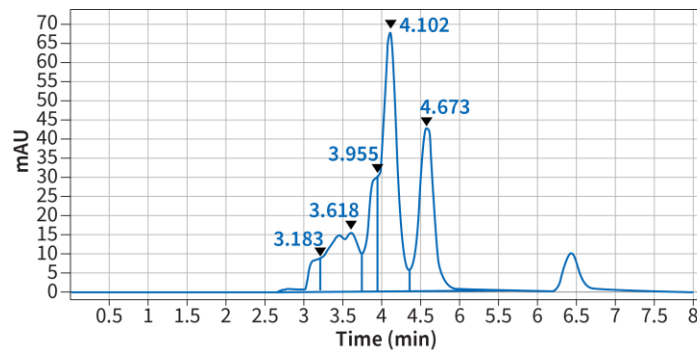
Target:



Main Byproducts:



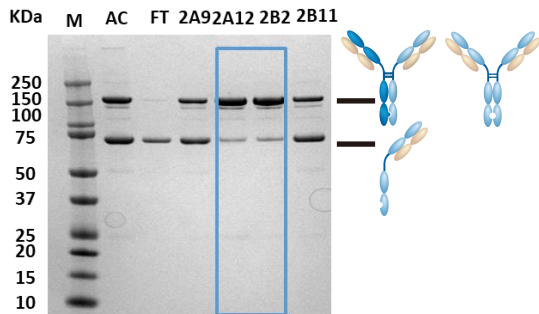
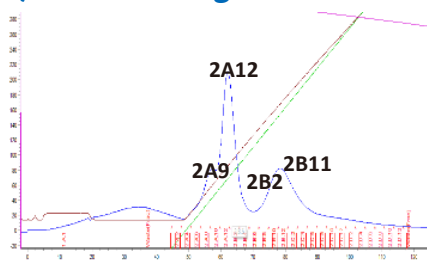
Post ProA Quality:



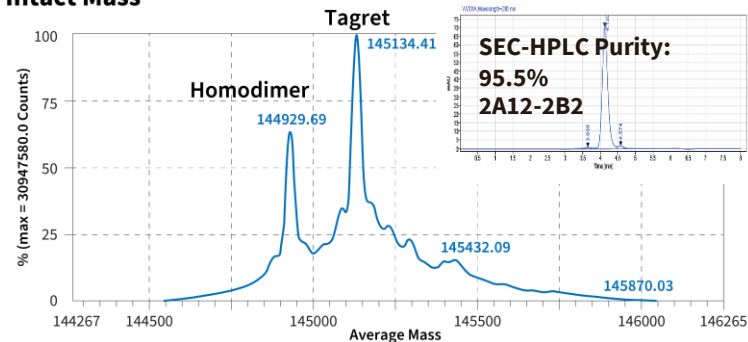
# Case Study 1: Mixed Mode + CEX

## Purification

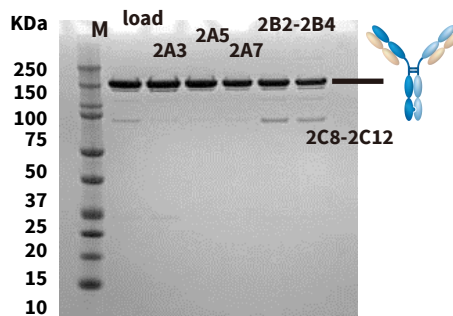
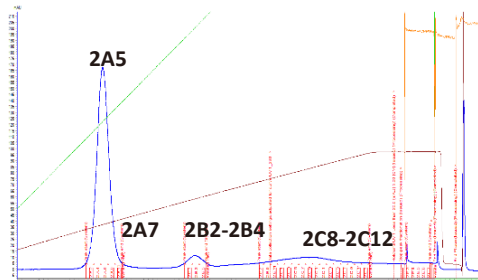
### 1) Mixed mode gradient



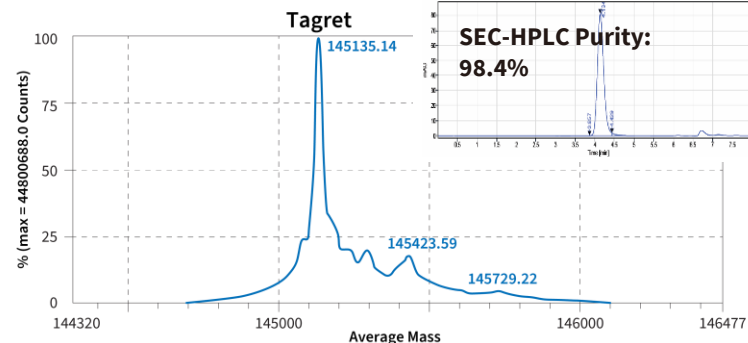
### Intact Mass



### 2) CEX gradient

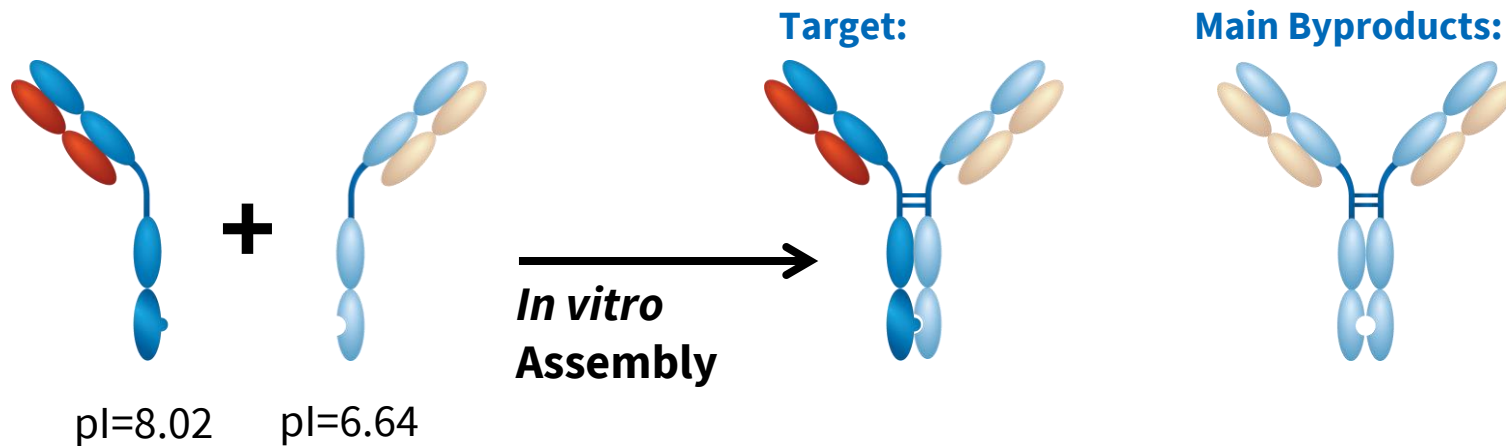


Control: 20196W210812C4P-2A42A7-DM-20210816.raw



Mixed mode + CEX could remove half antibody and homodimer.

## Case Study 2: Two Different LCs in KiH BsAb



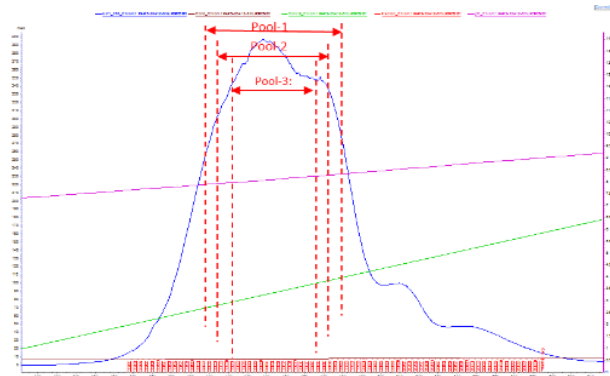
### BsAb Analytics TIP:

Use enzyme to turn IgG to (Fab')<sub>2</sub> for better separation of homodimer and heterodimer in LC-MS

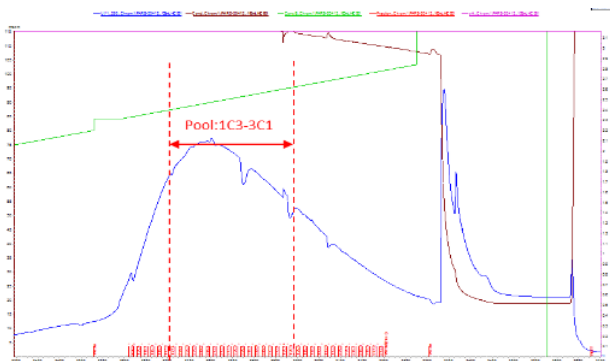


# Case Study 2: Two Different LCs in KiH BsAb

## 1) CEX



## 2) HIC



Mini pool 1

Mini pool 2

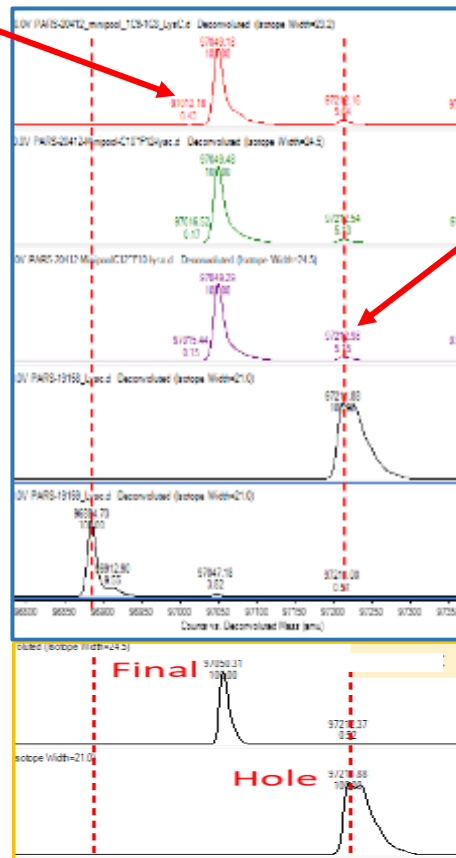
Mini pool 3

Hole control

Knob control

HIC Pool

Hole Control



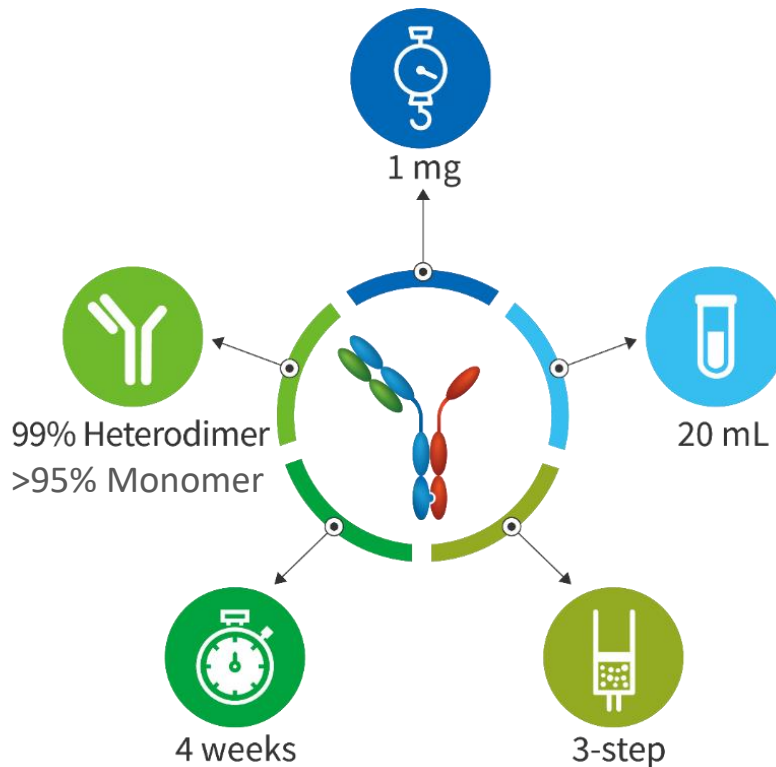


# **Quick 'n' Clean** 02

**Customized HTP BsAb Production**

# Quick 'n' Clean - Unlock the Optimal Pairings of BsAb

Automated **3**-  
step Purification



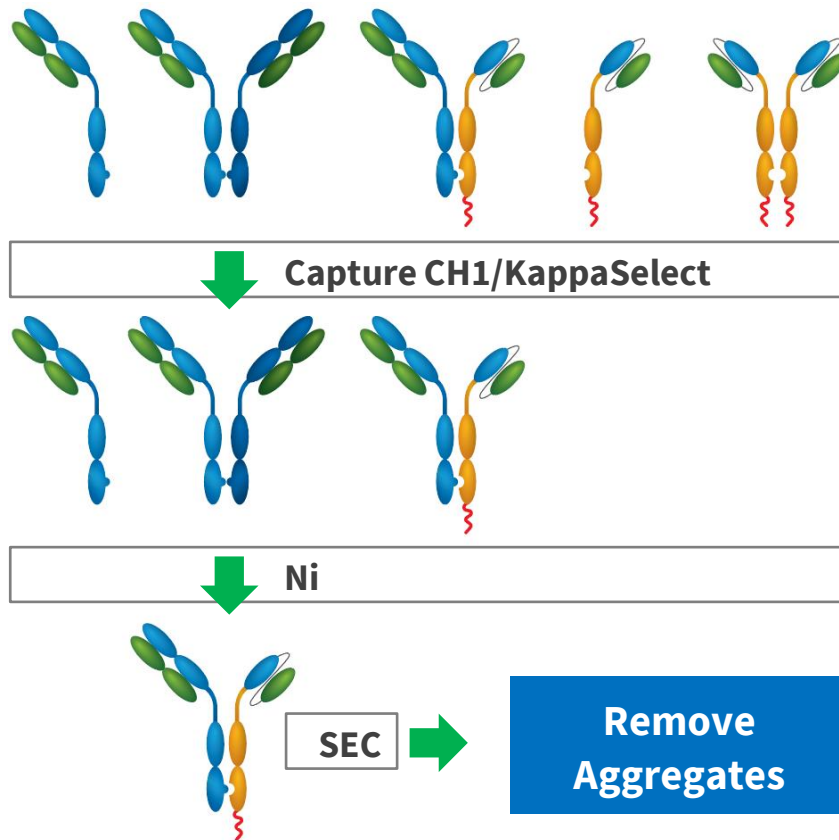
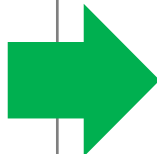
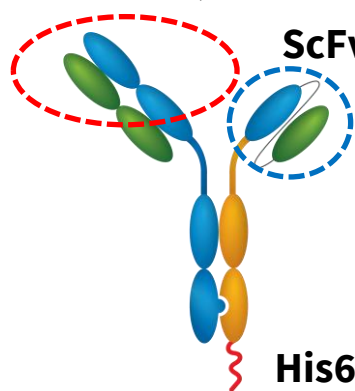
Customized HTP BsAb Production at the Discovery Stage



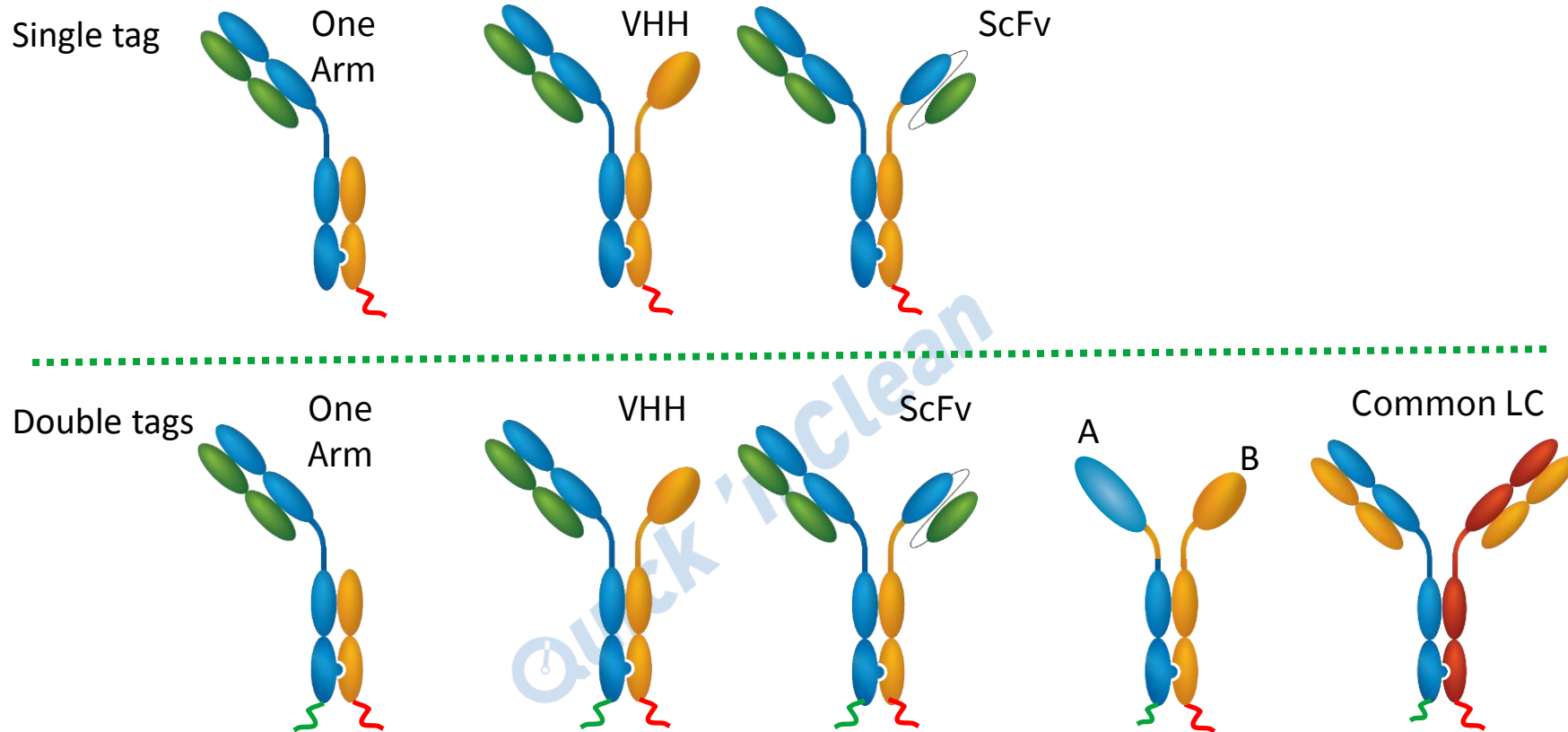
# Quick 'n' Clean - An Example Format

Bind to  
KappaSelect, etc

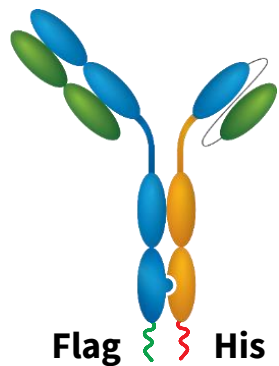
Does not bind to  
ScFv KappaSelect, etc



# Customized Formats to Screen Large Number of BsAb at Early Stage



# Quick 'n' Clean - Case Study: 25 Fab-ScFv with Double Tags (20 ml)



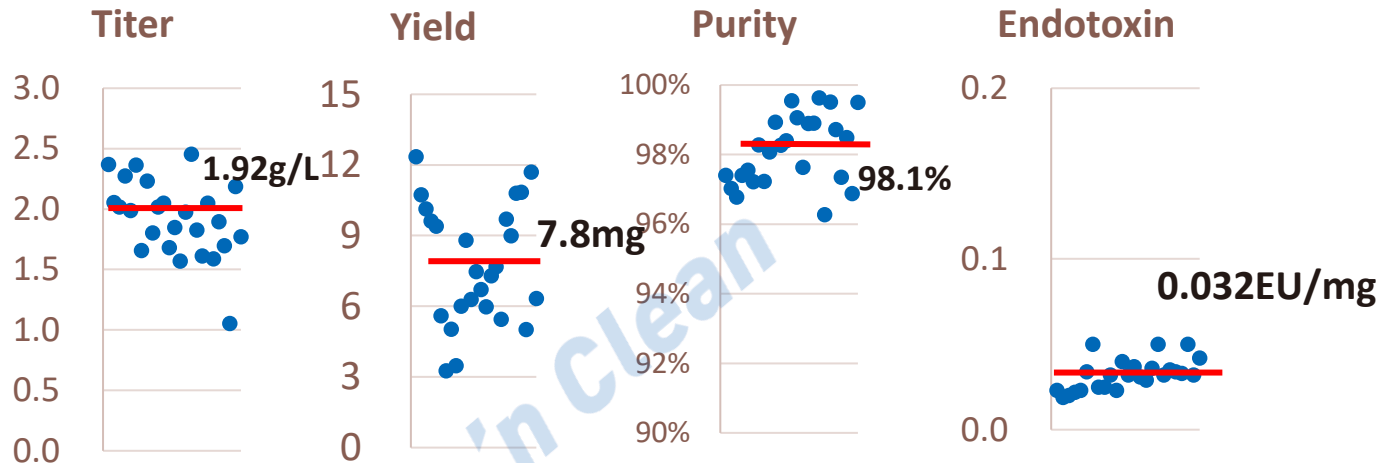
Ni



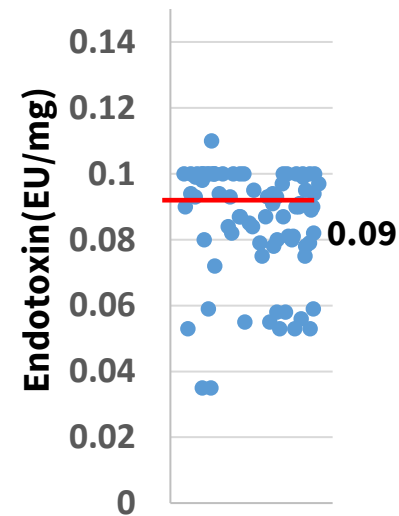
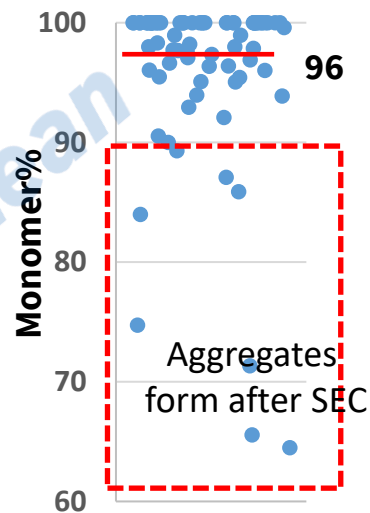
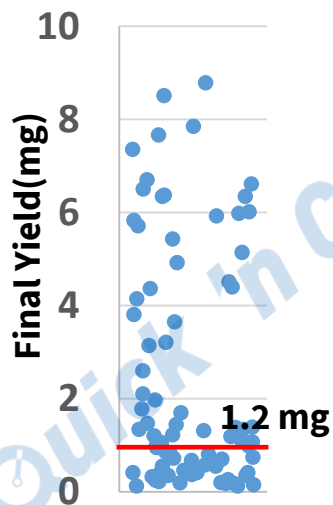
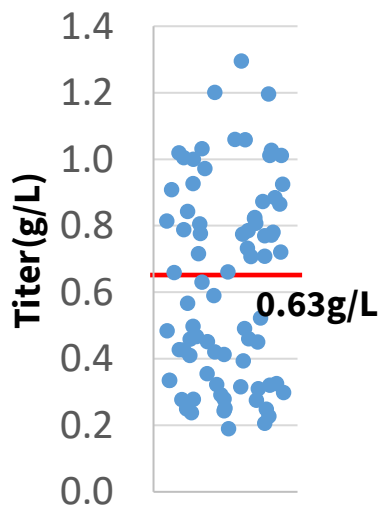
Anti-Flag



SEC



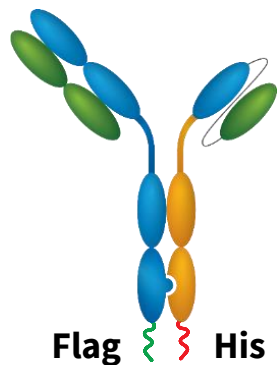
# Case Study: 65 One Arm ScFv (20 ml)



When **Quick 'n' Clean**

Meets **Ultra 96+**

# Quick 'n' Clean - Case Study: 25 ScFv-Fab with Double Tags(1 ml)

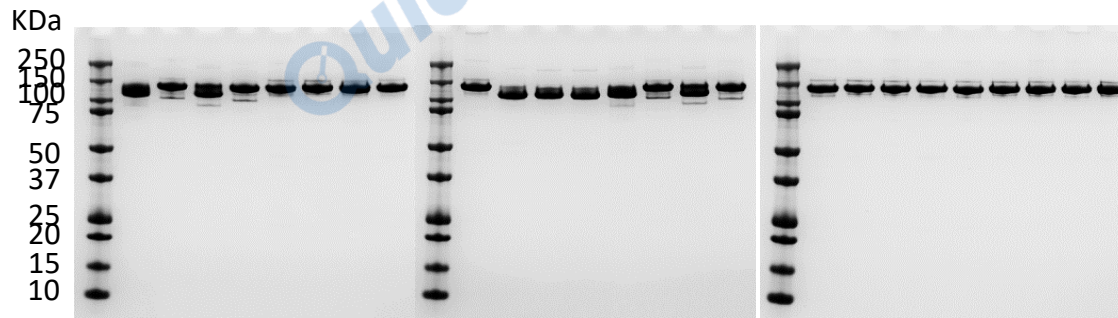
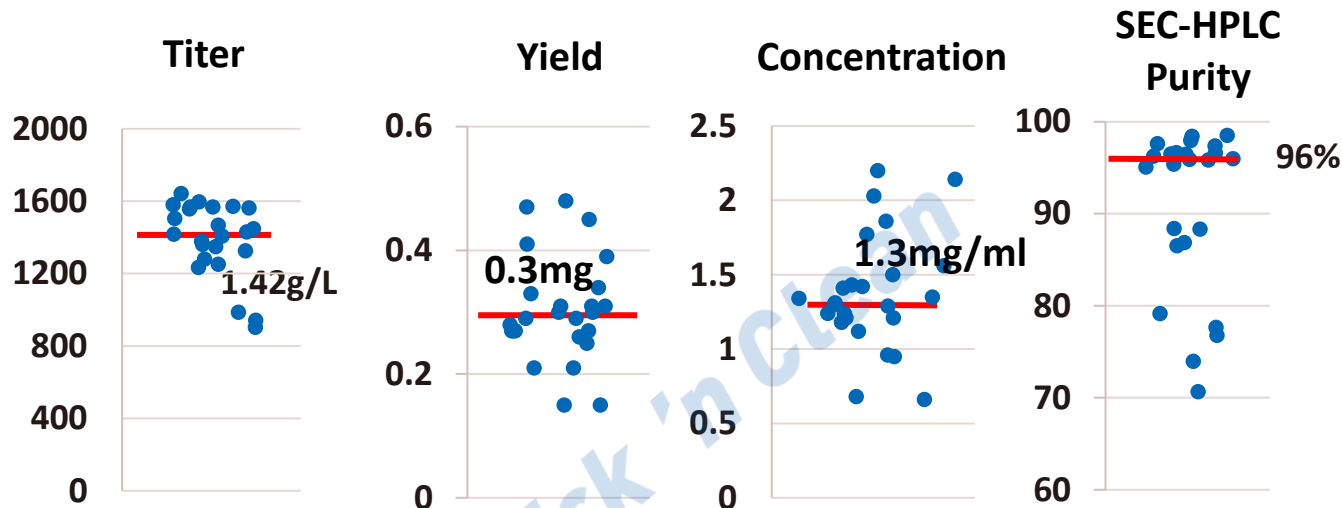


Ni

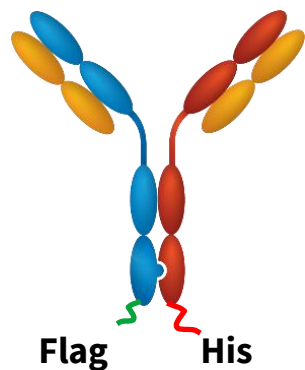


Anti-Flag

In 96 well plate



# Case Study: 25 Common LC BsAb with Double Tags(1 ml)

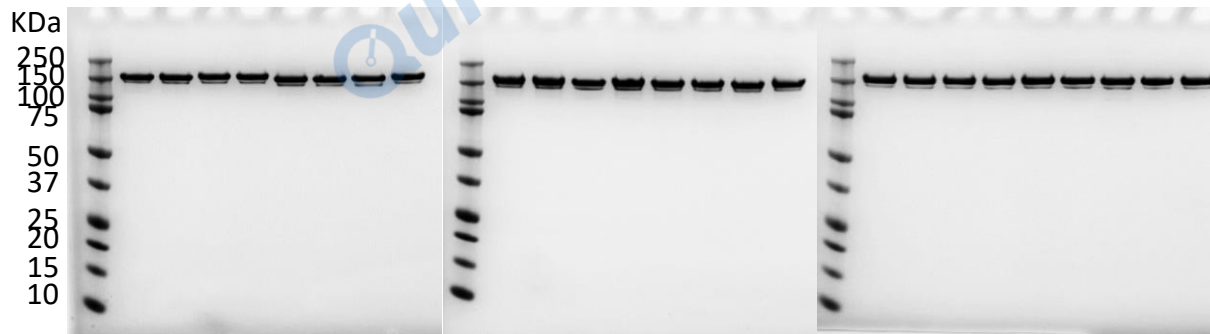
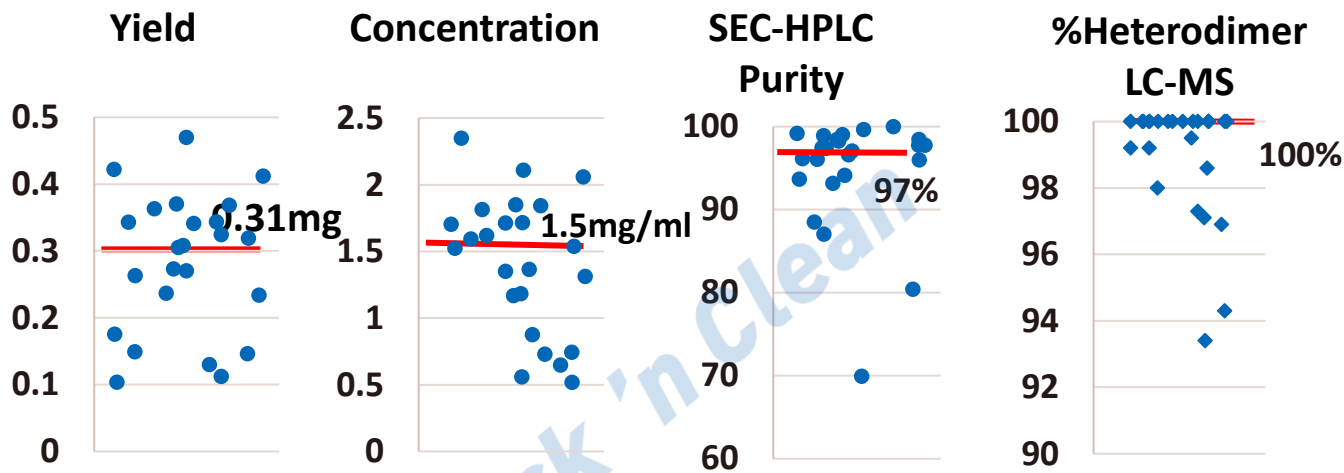


Ni



Anti-Flag

In 96 well plate



## Premium BsAb

- Extensive experience on most BsAb formats
- **No tag**, extensive scouting and optimization of purification
- Delivers 10 mg to grams of BsAb in 4-6 weeks
- **BsAb verified by intact mass**
- High quality for *in vitro* and *in vivo* studies

## Quick 'n' Clean

- Optimized for screening large number of BsAb at the early stage
- Customized designs with His/Flag tags
- Automated 3-step purification including SEC
- 1-5 mg BsAb from 20 ml cell culture, 4 weeks timeline
- **99% heterodimer**, >95% monomer, <0.5EU/mg endotoxin
- High quality for generating consistent data in most *in vitro* studies
- Plate based Quick n Clean can generate thousands of BsAb





*Thank You*

*Drug Development Expertise,  
Protein Production Excellence*

