

# Development of a versatile, synthetic, heavy chain-only platform for the discovery of monoclonal and multispecific therapeutic antibodies

# ADIMAB

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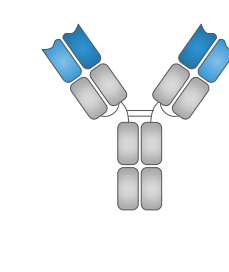
\*indicates co-author status

## Background

**140+** Pharma/Biotech Partners    **650+** Therapeutic Programs    **80+** Clinical Advancements    **6** Commercial Products

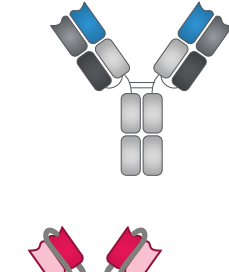
- Heavy chain-only antibodies (HCAbs) are an emerging therapeutic modality
- Traditional HCAb discovery uses animal immunization, which can produce candidates with developability problems requiring further optimization
- We developed a novel human, synthetic HCAb discovery platform in yeast to avoid this
- HCAbs from this library are highly developable and well-suited as building blocks for Fc-containing multispecific antibodies
- Resulting antibody architectures span from 1+1 bispecific to 2+1+1 trispecific formats

## Adimab's synthetic diversities



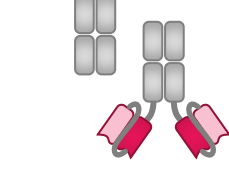
**IgG-k**

10<sup>10</sup> synthetic IgG library utilized in Adimab proprietary yeast strain with kappa light chain diversity, and boutique options (short and long CDRH3)



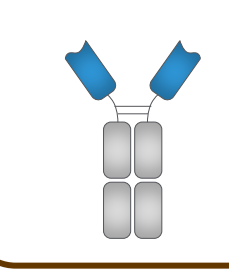
**IgG-lambda**

10<sup>10</sup> synthetic IgG library utilized in Adimab proprietary yeast strain with lambda light chain diversity



**scFv**

10<sup>6</sup> synthetic diversity library utilizing VHV1 or VLVH diversities and using N-term or C-term Fc-based formats



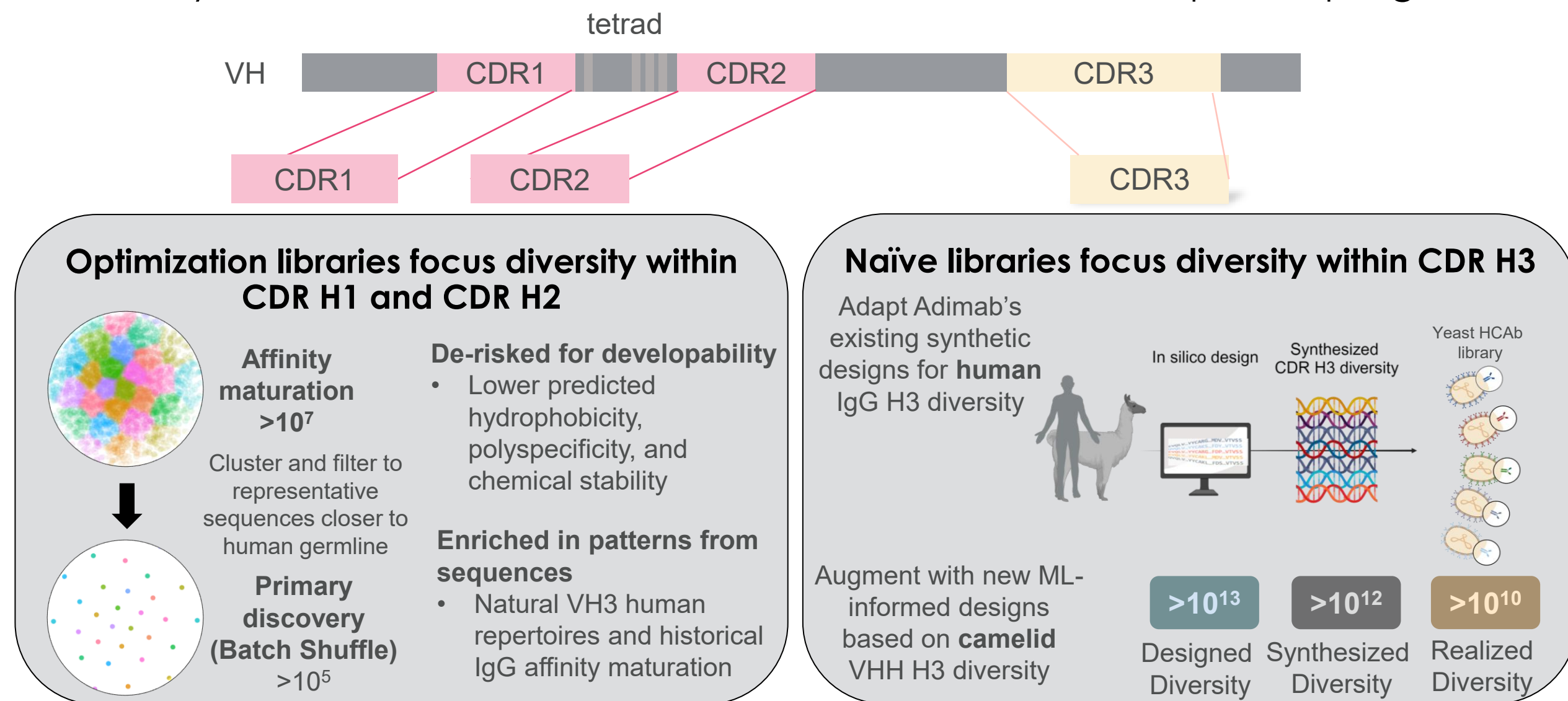
**HCAb**

Synthetic HC-only and *in vivo* VHH diversity within the Adimab proprietary yeast strain

## Design objectives for HCAb discovery platform

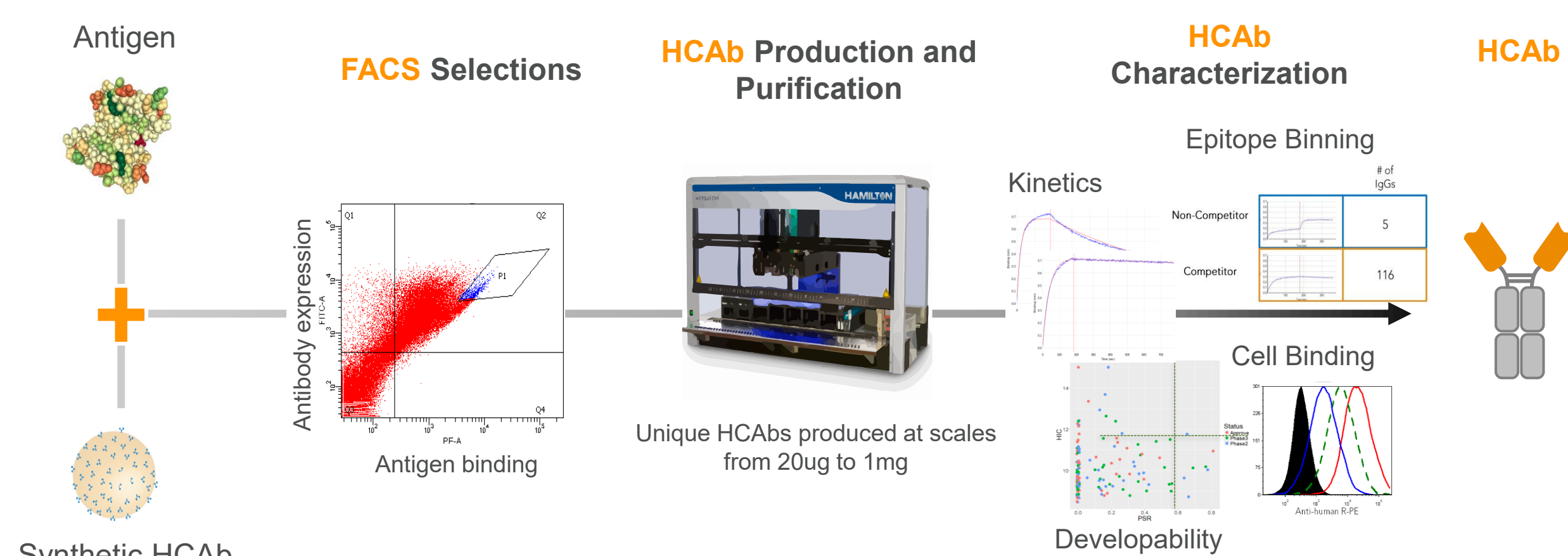
### Figure 1: Library design principles

Adimab's synthetic HCAb libraries have been used in >20 therapeutic programs.



### Figure 2: HCAb discovery project flow

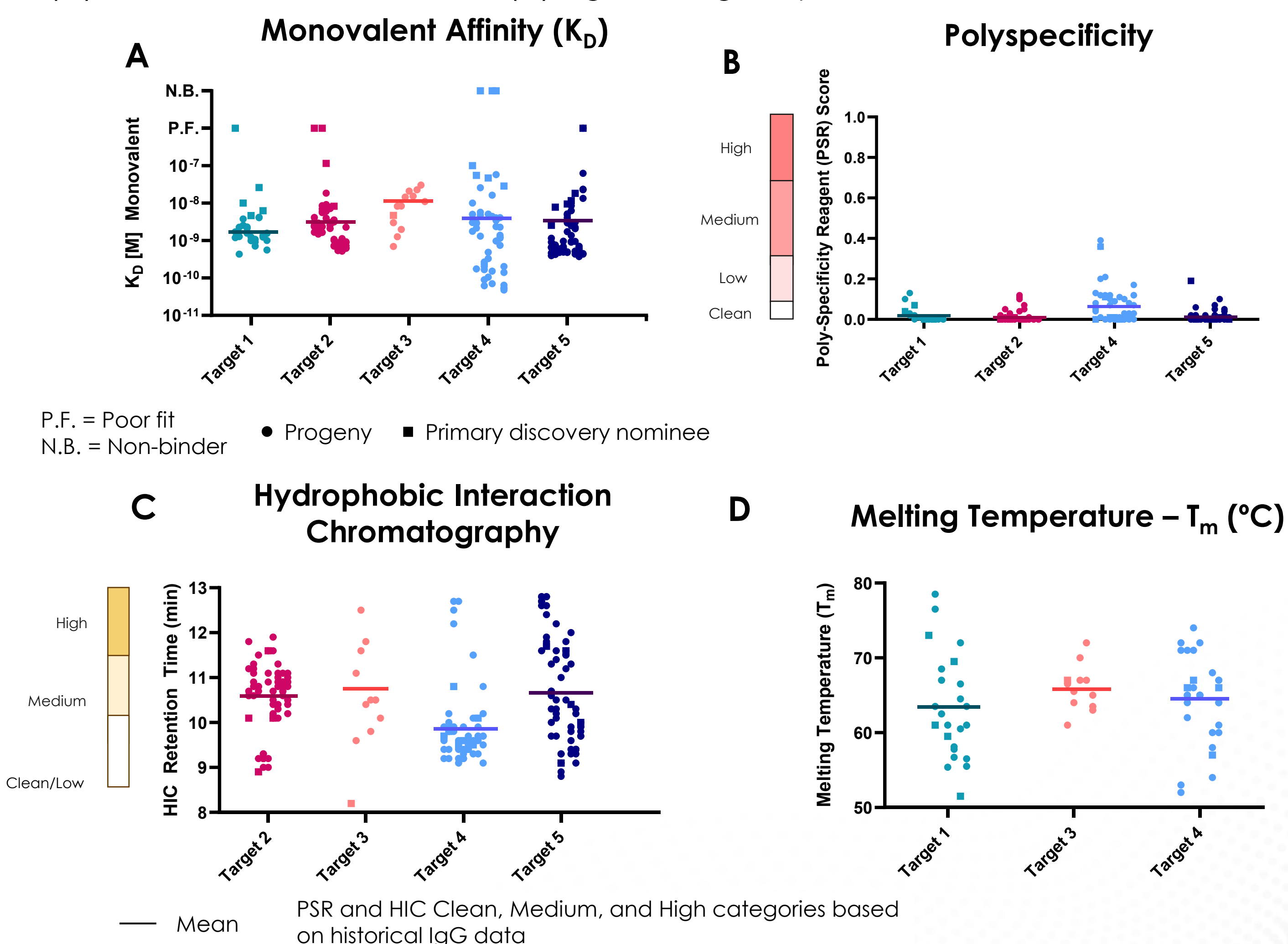
Adimab's platform allows for delivery of HCAbs with desired specificity profile within 4-5 months from selection start.



## Characterizing output HCAbs

### Figure 3: HCAbs show high affinity and favorable developability across multiple Adimab campaigns.

Delivered HCAbs show (A) a range of monovalent affinities, (B) low polyspecificity, (C) low HIC retention times, and (D) high melting temperatures.

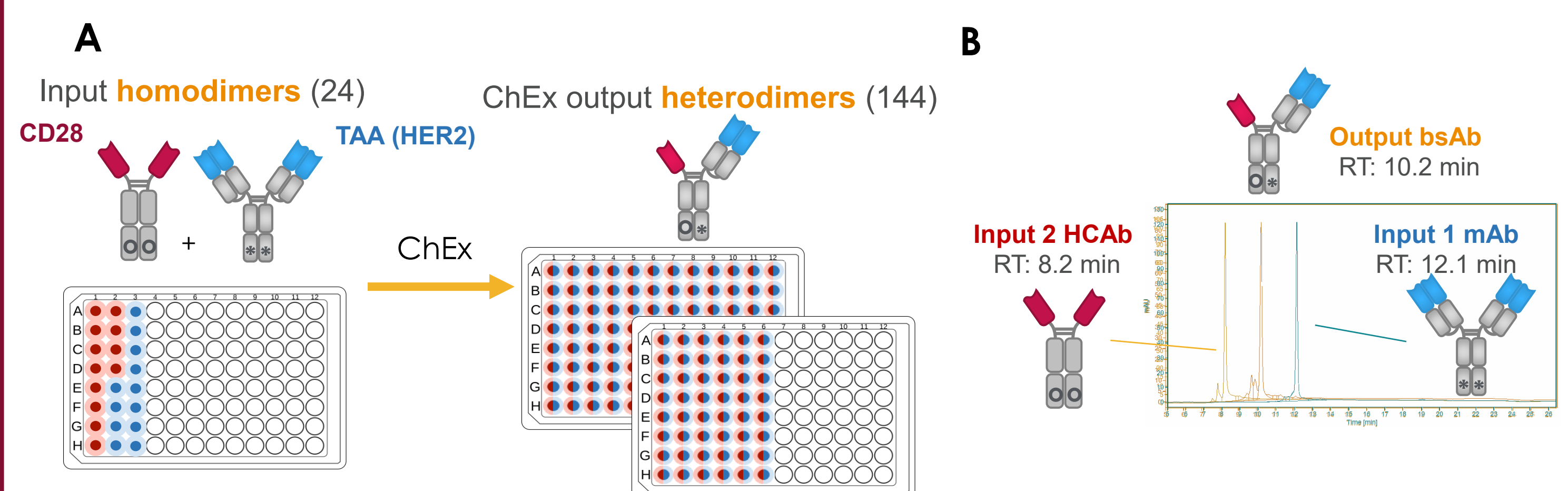


## Generation of VHH-based multispecifics

### Chain exchange (ChEx)

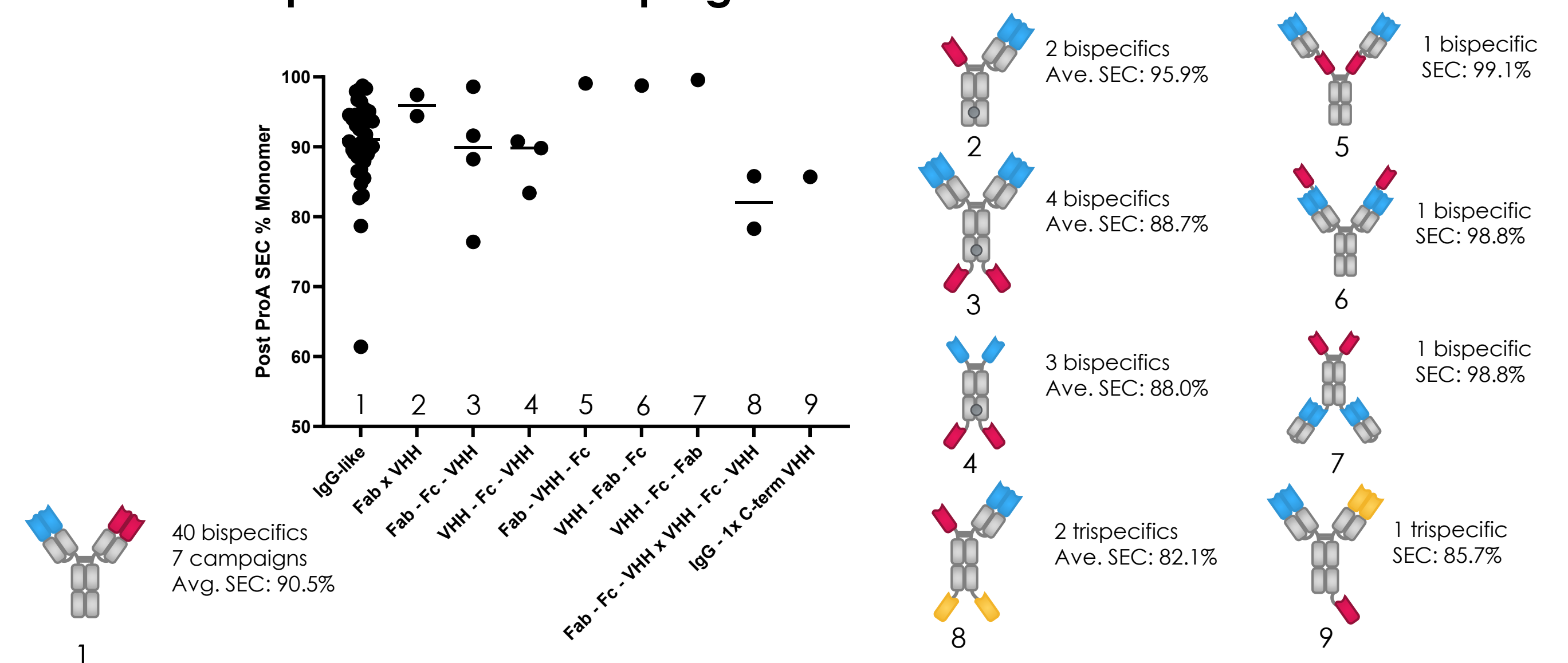
### Figure 4: Adimab Chain Exchange (ChEx) is applied to generate panels of VHH containing multispecifics.

(A) ChEx generates panels of multi-specific antibodies for functional assays. (B) Analytical Ion Exchange (aEX) output of CD28 x HER2 bispecific shows high purity.

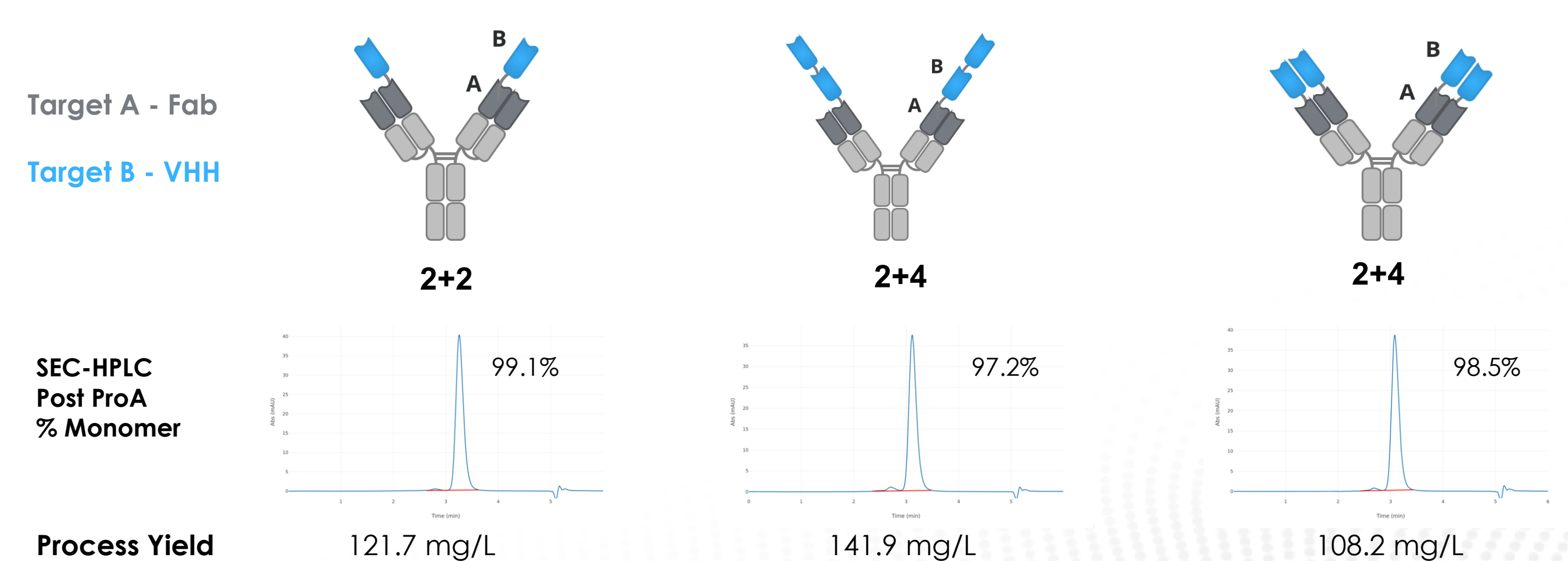


## VHH-based multispecific formats

### Figure 5: VHH-based bispecifics and trispecifics exhibit high purity across multiple Adimab campaigns.



### Figure 6: Multispecifics with up to 6 binding arms can be produced with good titers and high purity.



## Conclusions

- Synthetic, yeast-based heavy chain-only antibody (HCAb) platform enables rapid discovery of diverse, developable monovalent binders
- HCAbs derived from our platform show high affinity, low polyspecificity, and favorable biophysical properties across various targets
- VHH-based multispecific formats are efficiently generated with high purity using Adimab-developed chain pairing solutions, including chain exchange (ChEx)
- Our platform supports scalable discovery of monospecific and multispecific antibody therapeutics with flexible architectures

**Acknowledgments:** We thank the many teams within Adimab that contributed to this work including High-throughput Expression, Protein Analytics, Computational Biology/Platform Technologies, Core, Mammalian, and Antibody Engineering.

### Contact Adimab

If you are interested in partnering with Adimab, please reach out to our Business Development department at [bd@adimab.com](mailto:bd@adimab.com).

The QR code on the right links to Adimab posters and other resources.

