LakePharma
The Biologics Company

Developability Assessment Services

LakePharma Hayward

NR-7041.20191223

About LakePharma

- LakePharma is a US-based Biologics CRDMO with operations in CA, MA, and TX
- Specializes in the production and evaluation of DNA vectors, viral vectors, cell lines, proteins, antibodies and conjugates, while providing integrated solutions bridging discovery, engineering, development, and GMP manufacturing. *Ask us about ISPs!*
- LakePharma has contributed to the development of 200+ therapeutic or diagnostic products and strives to do hundreds more.
- LakePharma Hayward is ISO 9001:2015 certified, and LakePharma Hopkinton is ISO 13485:2016 certified.

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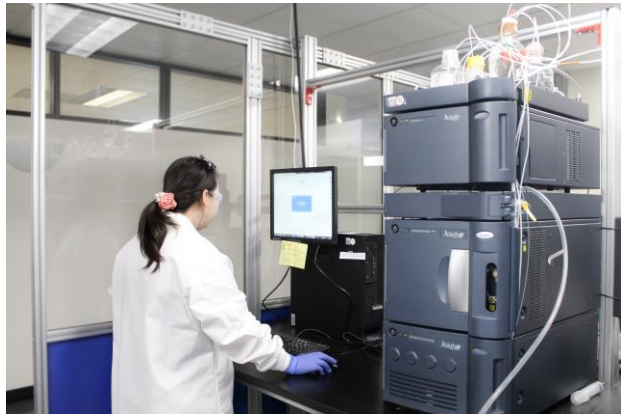
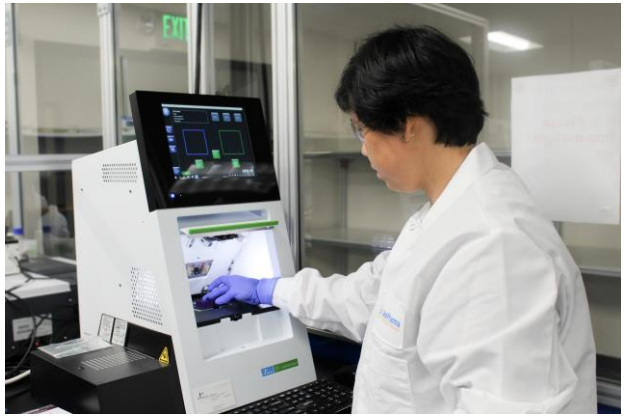
LakePharma Hayward

Dedicated facility for upstream and downstream process development, research cell bank (RCB) generation, and GMP manufacturing of analyte specific reagents.

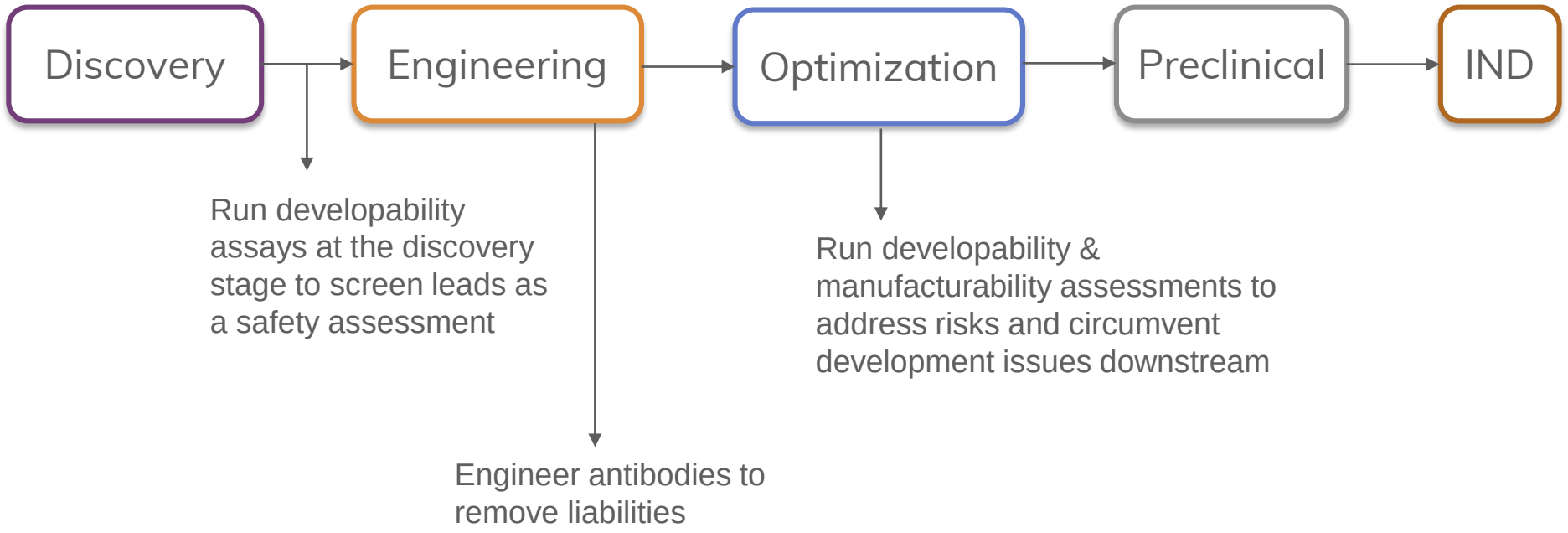
- All developability assessments are performed at this site





Developability: Assess the Path to Product

LakePharma offers developability studies for antibody drug candidates with promising biochemical and biophysical properties.



LakePharma's Developability Assessment Packages

Rapid and small-scale assessment of drug candidates

Formulation and stability study

Developability Package 1

- *In silico* Sequence Liability analysis
- *In silico* Immunogenicity analysis
- Turnaround time: 1 week

Developability Package 2

- Polyspecificity Assessment
- Integrity and Stability Assessment
  - Aggregation
  - Purity
  - Charge Variant
  - Thermostability
  - Post-translational modifications
- Turnaround time: 2-3 weeks

Developability Package 3

- Buffer Exchange
  - LakePharma standard panel formulations
  - Client may opt to choose their buffers
- Forced Degradation
  - Thermal stress
  - Freeze thaw
- Integrity and Stability Assessment following stress conditions
- Additional available stress conditions
  - Agitation
  - Oxidation
  - Photostability (Light)
  - pH acid/base

Therapeutic Developability Assessment Packages 1 and 2

Developability Package 1

In silico predictive tools are employed to serve as selection criteria for better and safer therapeutic leads.

1. *In silico* sequence liability analysis
2. *In silico* immunogenicity analysis

Developability Package 2

A series of fast and small-scale bioanalytical tests will be performed to determine the feasibility and liability of the drug candidates prior to drug development.

1. Polyspecificity assessment
2. Integrity and stability assessment

Key Features:

- Rapid and small-scale assessments for drug candidates
  - *In silico* analysis can be completed in 1 week
  - Polyspecificity and integrity assessment can be completed in 2-3 weeks
- Only a small amount of materials is needed for stability and liability determination

Therapeutic Developability Assessment Package 3

The goal of this package is to assess the stability of the molecule and identify a suitable formulation for the antibody.

Developability Package 3

1. Buffer Exchange
    - LakePharma standard panel formulation
    - Client may opt to choose their buffers
2. Forced Degradation
    - Thermal stress
    - Freeze thaw
3. Integrity and Stability Assessment
    - Aggregation
    - Purity
    - Charge Variant
    - Thermostability
    - Post-translational modifications
4. Additional available stress conditions
    - Agitation
    - Oxidation
    - Photostability (Light)
    - pH acid/base

Key Features:

- Rapid formulation studies for drug candidates
    - 2 weeks incubation time for standard forced degradation
    - Formulation studies can be completed in 5 - 6 weeks
- Robust formulation assessments with minimal materials
    - LakePharma standard panel includes common formulations used for commercial antibodies
    - Various bioanalytical and stability tests are provided

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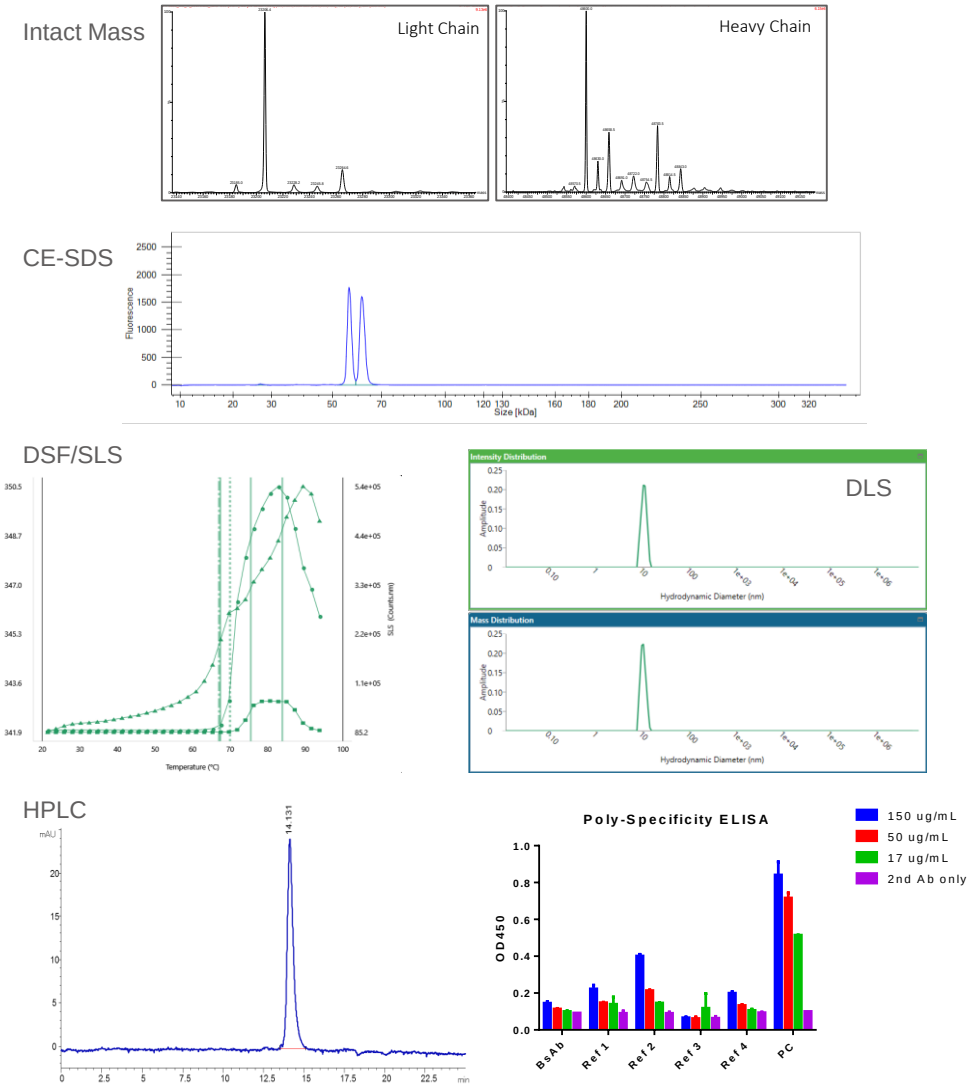
Developability Assessment Checklist

- *In silico* sequence liability analysis and immunogenicity analysis
  - Heavy and light chain variable liability analysis
  - VH and VL analysis
  - Nine core residues with potential affinity to MHC class II identified
- Productivity readiness check
  - Transient production in HEK293 or CHO system
- Integrity and stability check (to demonstrate whether the antibody is stable biochemically)
  - Intact mass/peptide mapping/ PTM by mass spec
  - DSF/DLS – thermostability assessment
  - Aggregation/fragmentation/PTM and glycan profiling over 2 weeks incubation under stressed conditions
  - SE-HPLC/LabChip CE-SDS
- PK readiness check
  - Poly-specificity ELISA, surface hydrophobicity assay – specificity requirement



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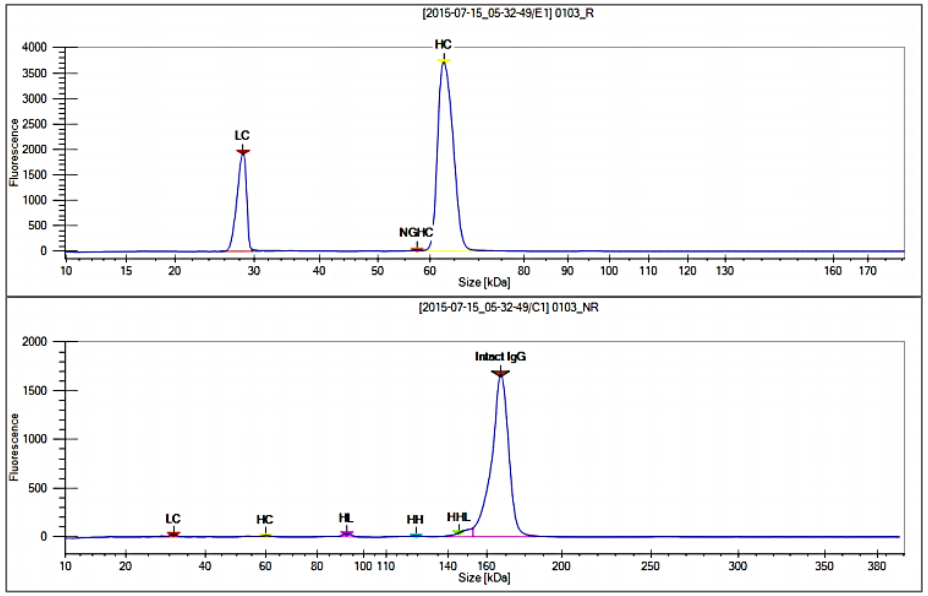
CASE STUDY

Assessing a mAb Candidate Utilizing Package 2

A Therapeutic mAb Candidate Ready to Move Forward



Purity requirement rCE>95%

Purity requirement nrCE>90%

The mAb is ready to move forward as results show >95% purity by reduced CE-SDS analysis and >90% purity by non-reduced CE-SDS analysis

Sample ID	%LMWC	%(HC+LC)	%MMWC	%HMWC
mAb reduced	N/A	99.3	0.7	N/A
mAb non-reduced	6.5	93.5	N/A	N/A

LabChip® GXII Touch HT

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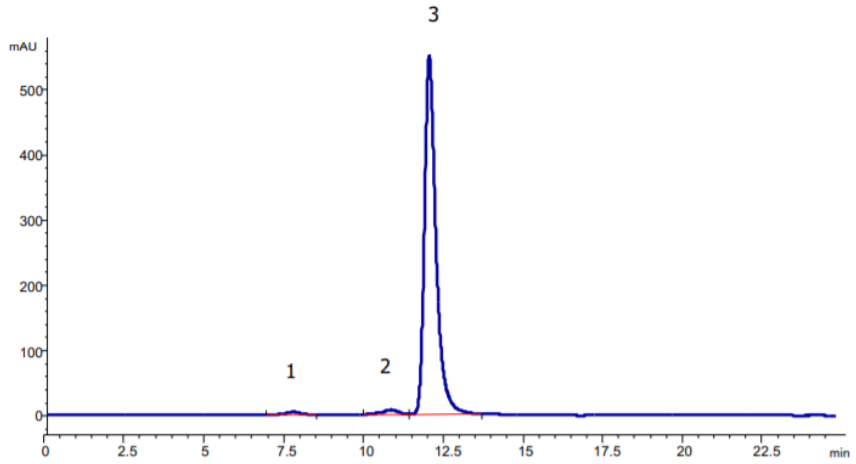
A Therapeutic mAb Candidate Ready to Move Forward

SE-HPLC – monomeric state



Peak #	Peak Size (kDa)	Peak Area %	Peak ID
1	~1500	1.4	Aggregate
2	~250	2.3	Aggregate
3	~150	96.3	Monomer

The mAb is ready to move forward as results show >90% peak area for the monomer peak.

Waters® ACQUITY UPLC® System

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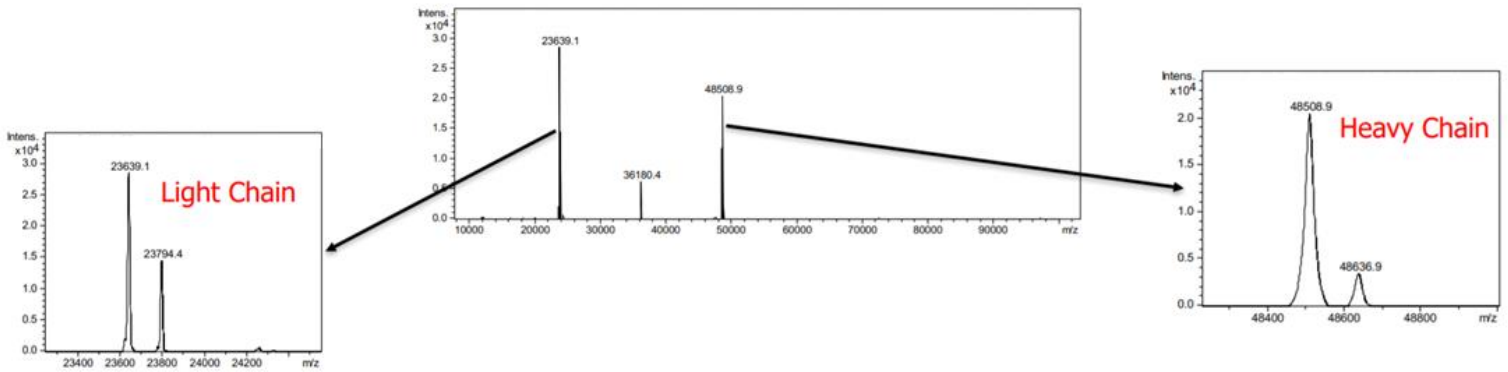
A Therapeutic mAb Candidate Ready to Move Forward

Intact mass measurement – integrity of the molecule



	Heavy Chain	Light Chain
Measured Mass	48636.90 Da	23794.40 Da
Calculated Mass	48634.90 Da	23794.53 Da
Delta Mass	+2.00 Da	-0.13 Da

The mAb is ready to move forward based on intact mass data. The heavy and light chain mass was confirmed to match the sequence's expected mass differences.

Xevo™ G2-XS QToF Mass Spec System

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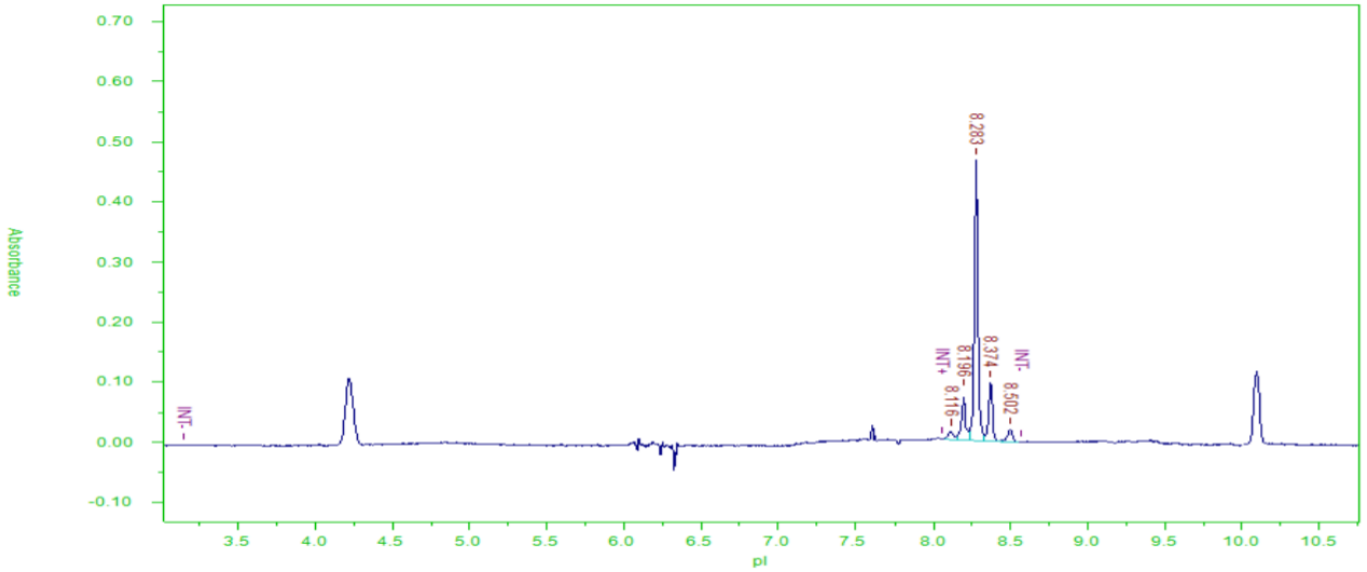
A Therapeutic mAb Candidate Ready to Move Forward

cIEF – Charge variants profiling



Peak Notes	pI	Peak Area %	# Peak ID
1-2	---	15.38	Acidic Peak Group
3	8.28	65.28	Main Peak
4-5	---	19.34	Basic Peak Group

The mAb is ready to move forward as two pI markers are observed and a charge profile of the mAb is produced with a main peak observed

iCE3™ system

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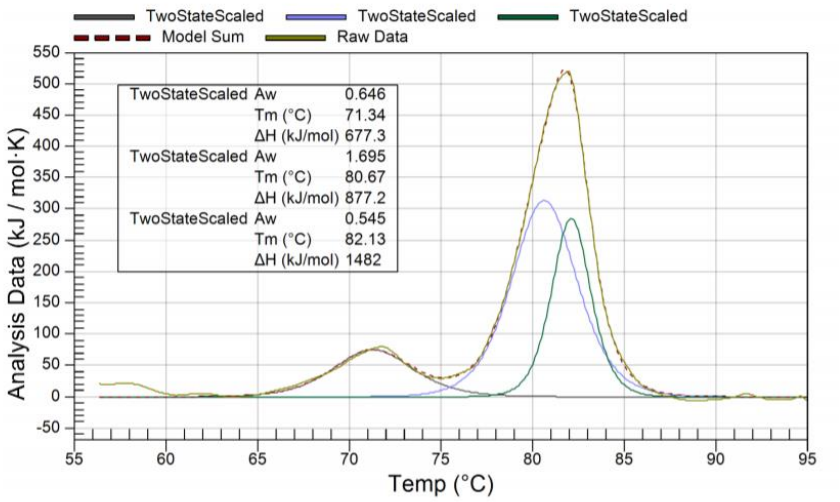
A Therapeutic mAb Candidate Ready to Move Forward

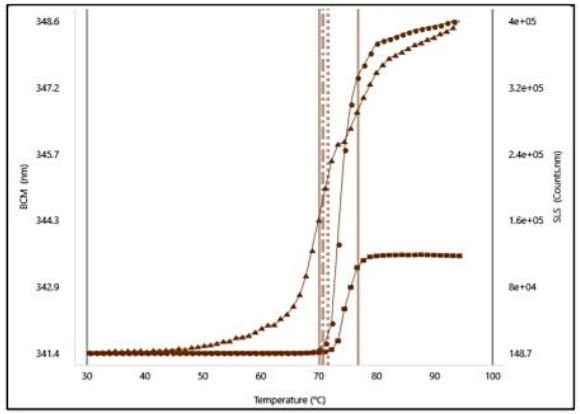
- DSC – Thermostability

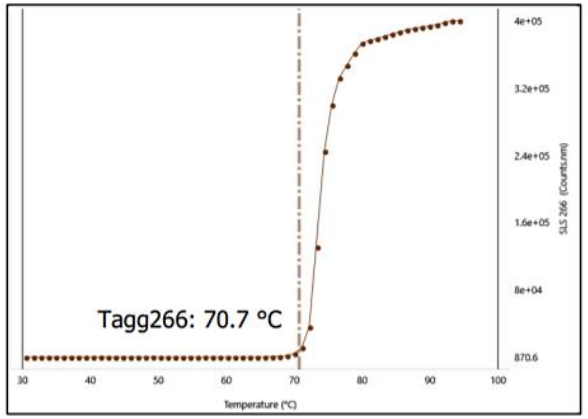


Peak #	Tm (°C)	ΔHcal (kJ/mol)
1	71.3	438
2	80.7	1487
3	82.1	808

Nano DSC

- DSF – Thermostability and Aggregation onset





UNcle

The mAb is ready to move forward as melting temperatures of 71.3°C, 80.7°C, and 82.1°C were observed. The three peaks signify the Fc (C_H2, C_H3) and Fab regions of the mAb.

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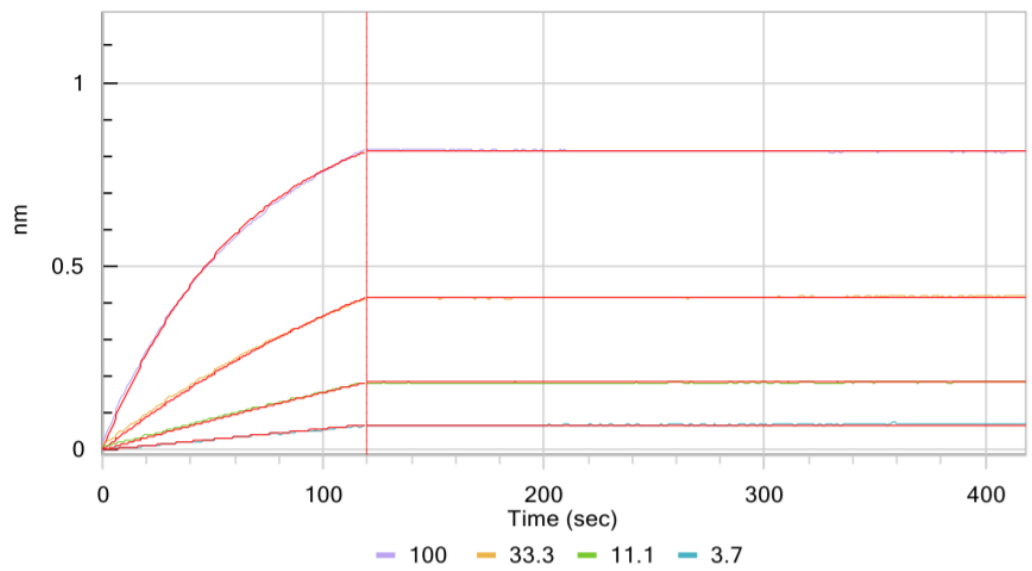
A Therapeutic mAbCandidate Ready to Move Forward

Affinity measurement against antigen in BLI or SPR – affinity requirement



The mAb is ready to move forward as a binding affinity of 1.3E-11 was observed

Method	Loading Sample ID	Sample ID	KD (M)	kon(1/Ms)	kdis(1/s)	Full X^2	Full R^2
Octet	Antigen	mAb #1	1.3E-11	1.6E+05	2.0E-06	0.0217	0.9998

Octet®

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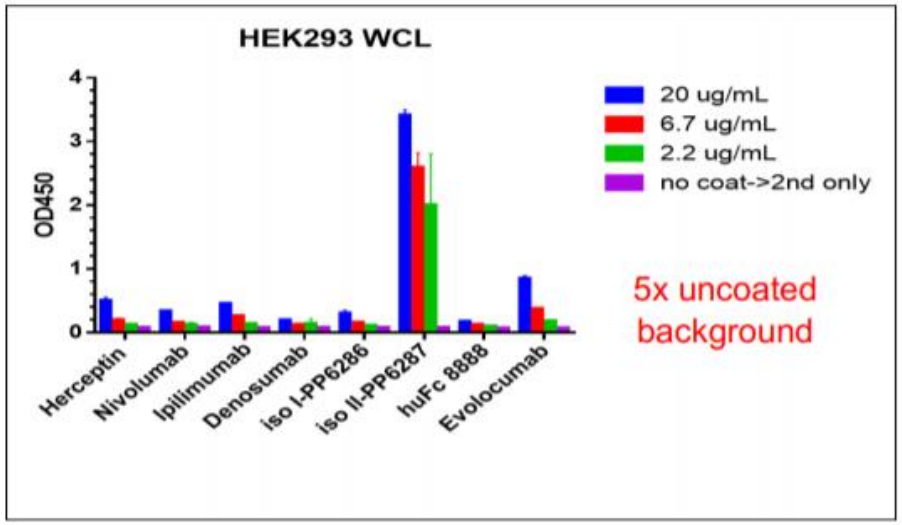
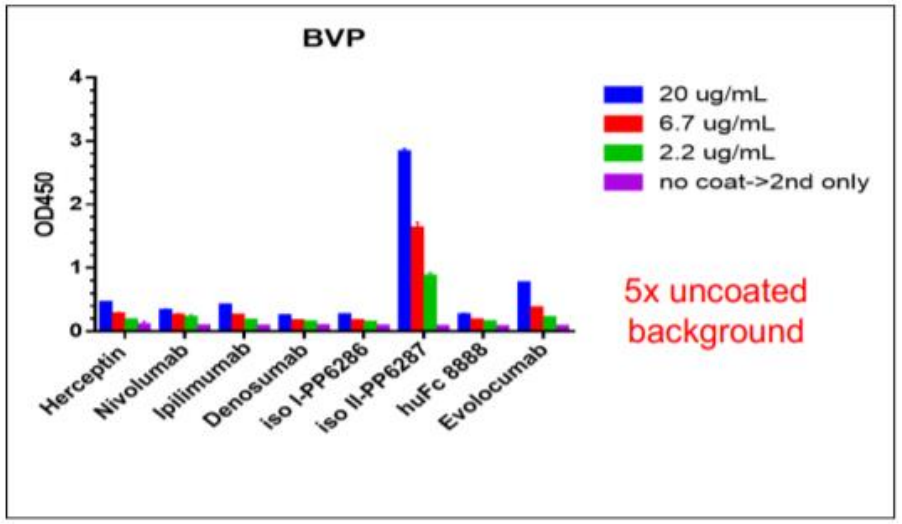
Commercial mAb Polyspecificity Assessment

Polyspecificity ELISA– Specificity requirement





HEK293 whole cell lysate (WCL) and BVP ELISA showed consistent results, which serve as good PK indicators.

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Working with LakePharma

- Comprehensive technology platform
- Technical consultation with experts in antibody discovery, protein production, and GMP manufacturing
- Online data system for 24-hour access to project information (timelines, data, team communications)
- Strong project management with regular project updates (email and teleconferences)

For more information, please contact Inquiries@LakePharma.com