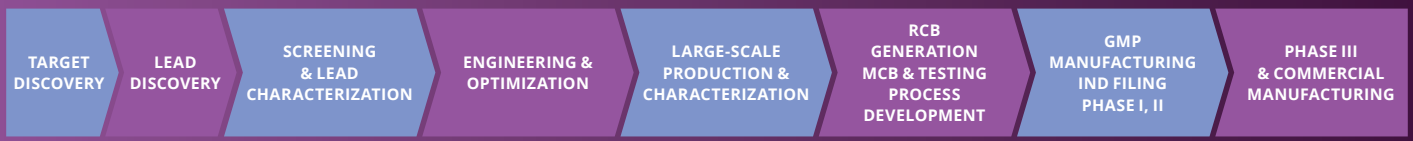
curia

REPORT

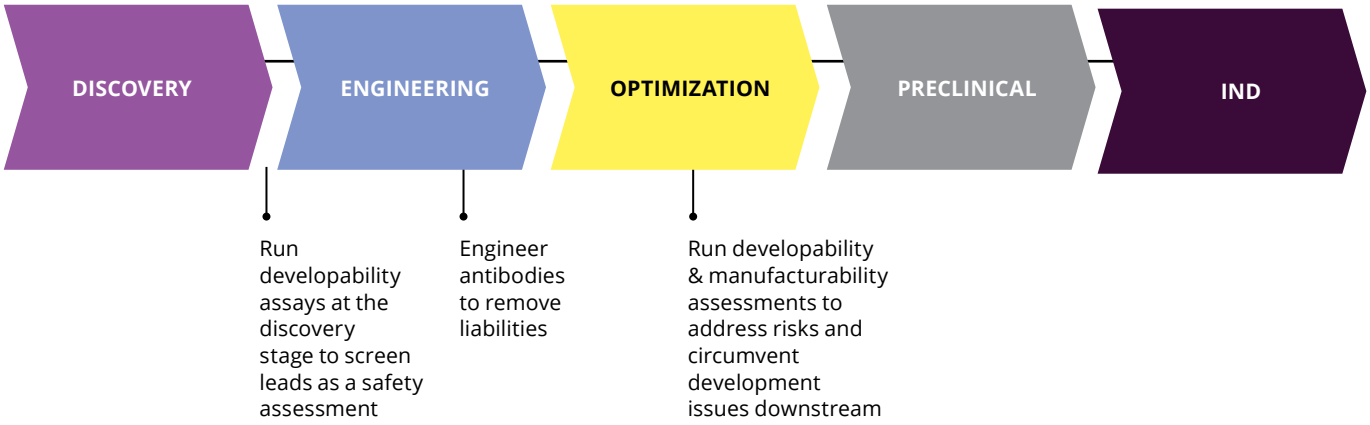
Developability assessment services

- **Curia 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!**
- **Curia has contributed to the development of 200+ therapeutic or diagnostic products and strives to do hundreds more.**
- **Curia is ISO 9001:2015 certfied and ISO 13485:2016 certified.**



Developability: Assess the path to product

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



Curia's developability assessment packages

RAPID AND SMALL-SCALE ASSESSMENT OF DRUG CANDIDATES

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

FORMULATION AND STABILITY STUDY

DEVELOPABILITY PACKAGE 3

- Buffer exchange
  - » Curia standard panel formulations
  - » Client may opt to choose their buffers
- Forced degradation
  - » Thermal stress
  - » Freeze thaw
- Available optional stress services
  - » 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 analysiss

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

DEVELOPABILITY PACKAGE 3

1. Buffer exchange
   - » Curia 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

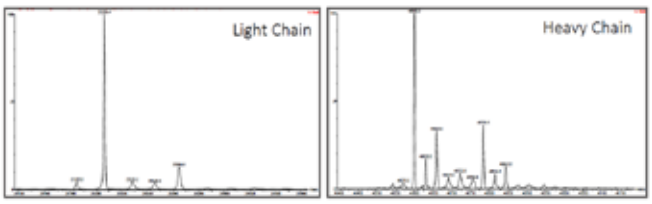
KEY FEATURES:

- 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
  - » Curia standard panel includes common formulations used for commercial antibodies
  - » Various bioanalytical and stability tests are provided

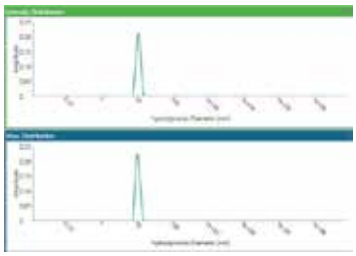
Developability assessment checklist

- *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

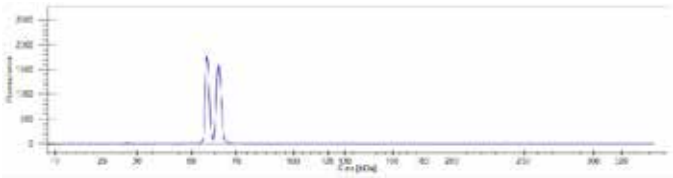
Intact Mass



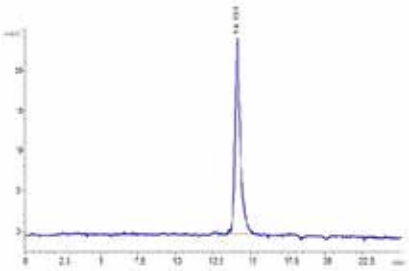
DLS



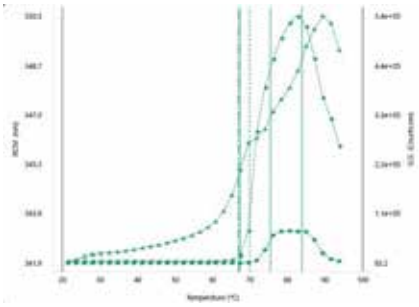
CE-SDS

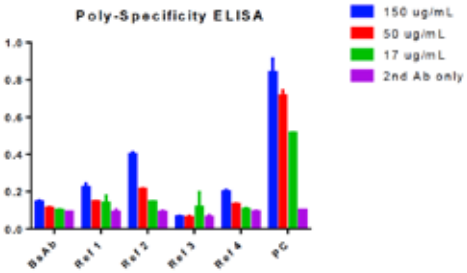


HPLC

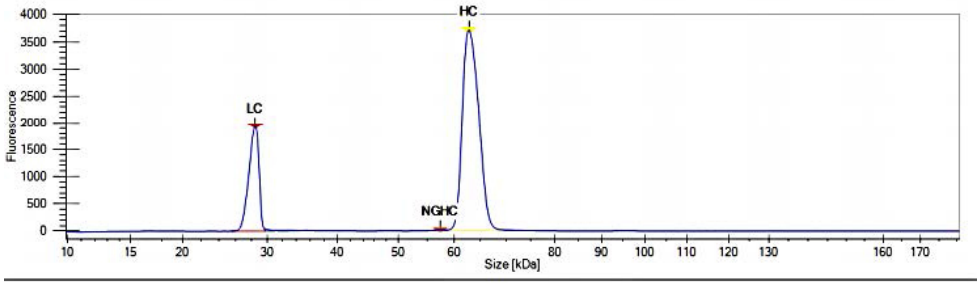


DSF/SLS

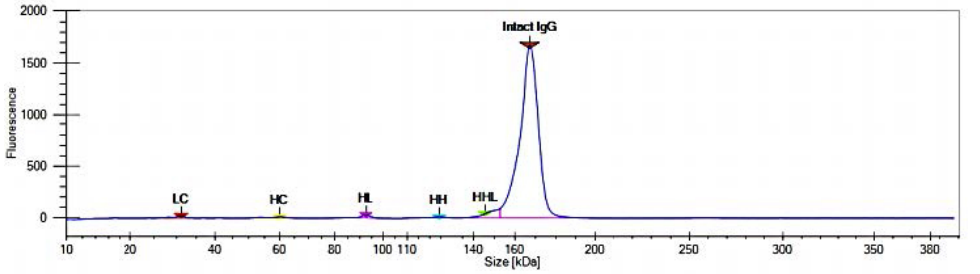




A therapeutic mAb candidate ready to move forward



Purity requirement
rCE >95%



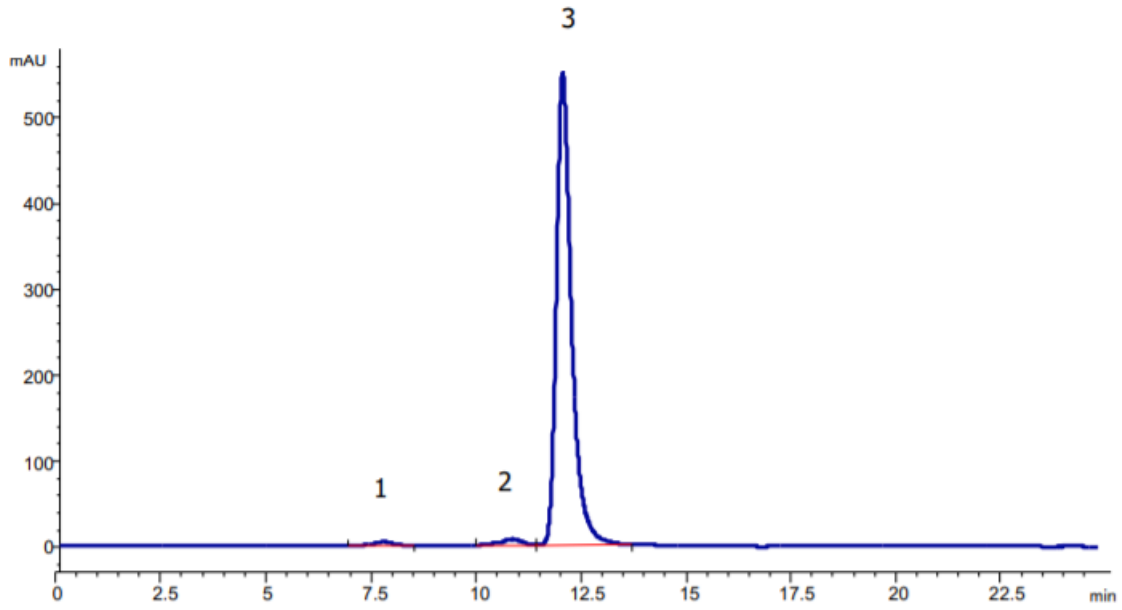
Purity requirement
nrCE >90%

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

SE-HPLC monomeric state

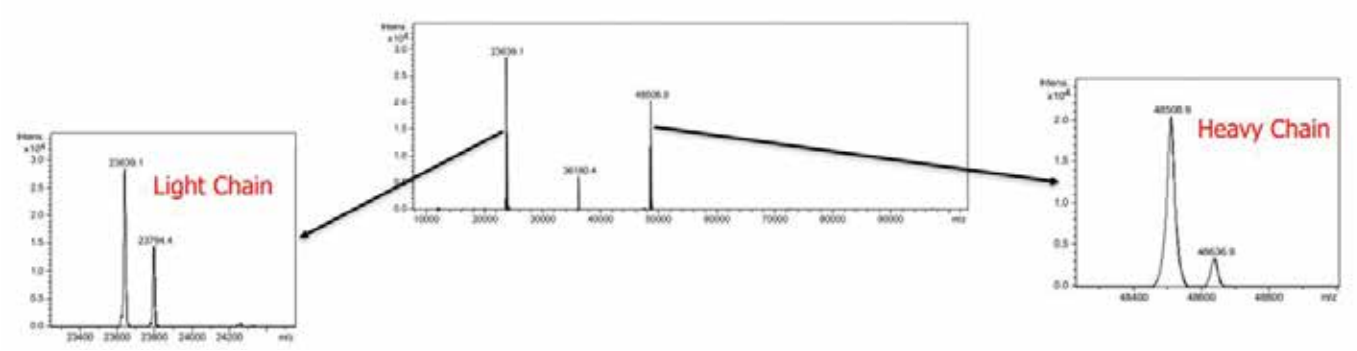


The mAb is ready to move forward as results show >90% peak area for the monomer peak.

Peak #	Peak Size (kDa)	Peak Area %	Peak ID
1	~1500	1.4	Aggregate
2	6.5	93.5	N/A
3	~150	96.3	Monomer

Waters® ACQUITY® UPLC System

Intact mass measurement – integrity of the molecule

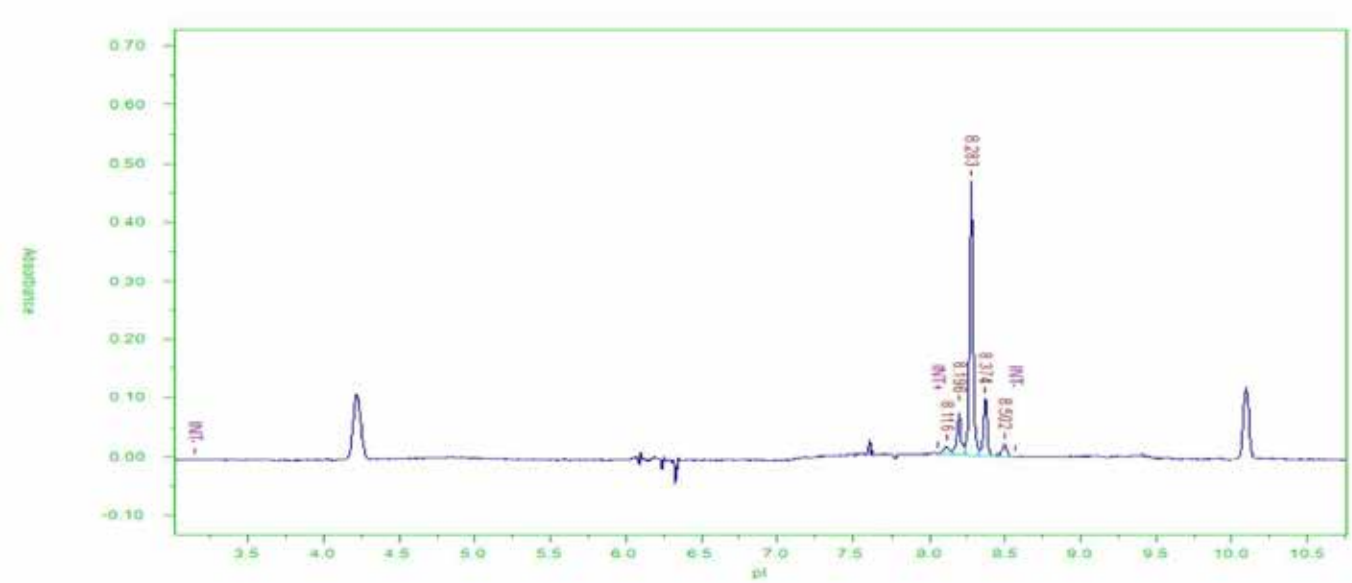


The mAb is ready to move forward based on intact mass data. The heavy and light chain mass was confirmed to match the sequence's expected mass differences.

	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

Xevo® G2-XS QToF Mass Spec System

cIEF charge variants profiling

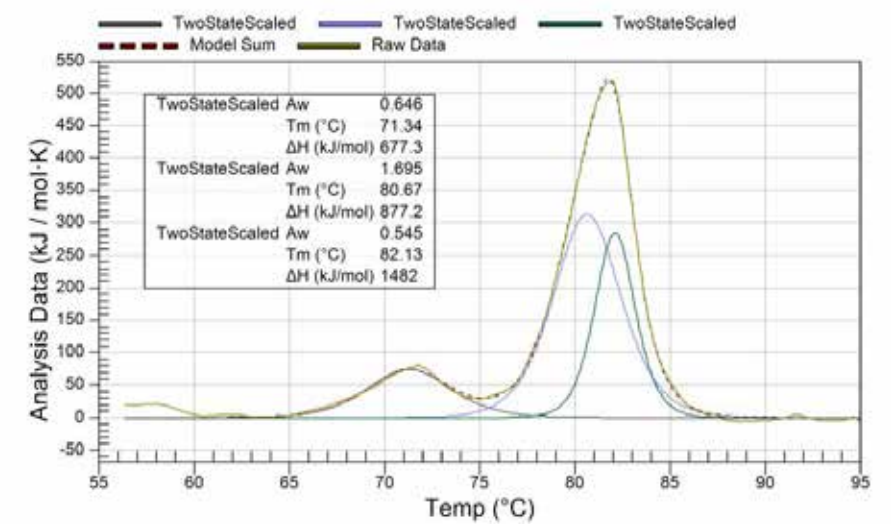


The mAb is ready to move forward as two pI markers are observed and a charge profile of the mAb is produced with a main peak observed

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

iCE3® system

DSC thermostability

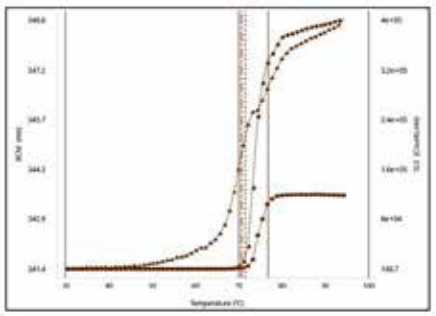


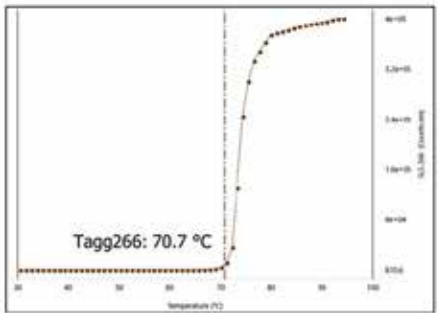
Peak Notes	pI	Peak Area %
1	71.3	438
2	80.7	1487
3	82.1	808

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.

Nano DSC

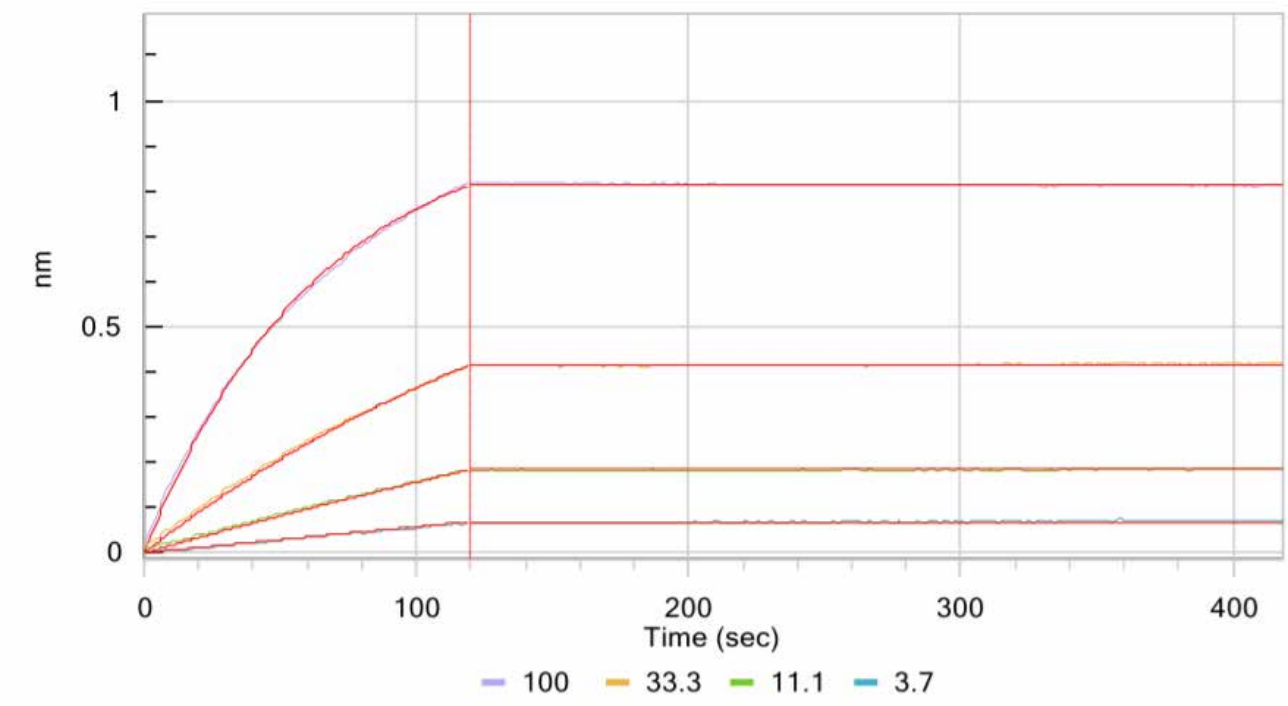
DSF thermostability





UNcle® platform

Affinity measurement against antigen in BLI or SPR – affinity requirement

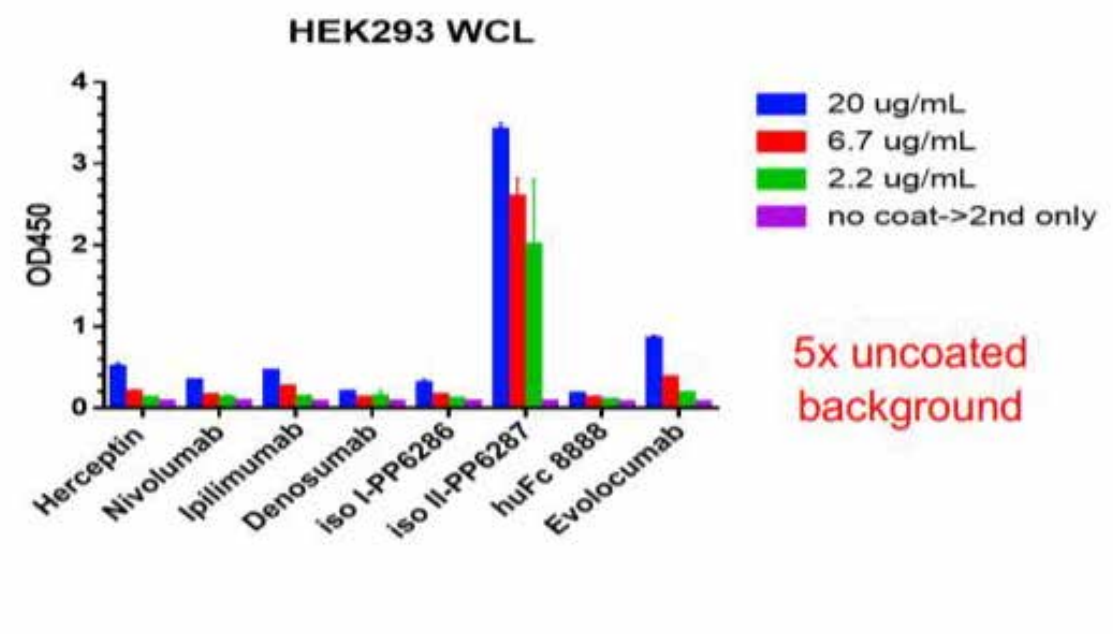


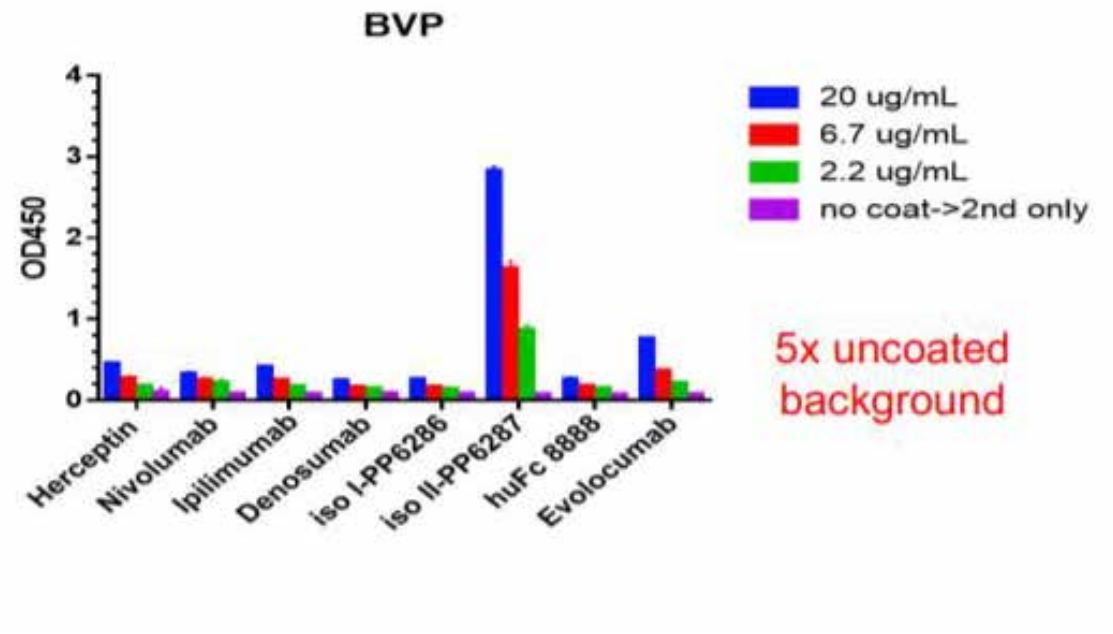
The mAb is ready to move forward as a binding affinity of 1.3E 11 was observed

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

Octet® system

Polyspecificity ELISA – specificity requirement





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

WORKING WITH CURIA

- Complete technology platform
- Technical consultation with experts specialized in antibody discovery and development
- Curia's online client portal — the Data & Process Management System — allows 24/7 access to project information (timelines, data, team communications)
- Strong project management with regular project updates

ABOUT CURIA

Curia is a Contract Development and Manufacturing Organization with over 30 years of experience, an integrated network of 29 global sites and over 3,500 employees partnering with customers to make treatments broadly accessible to patients. Our biologics and small molecule offering spans discovery through commercialization, with integrated regulatory and analytical capabilities. Our scientific and process experts and state-of-the-art facilities deliver best-in-class experience across drug substance and drug product manufacturing. From curiosity to cure, we deliver every step to accelerate and sustain life-changing therapeutics. ***Learn more at curiaglobal.com***

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