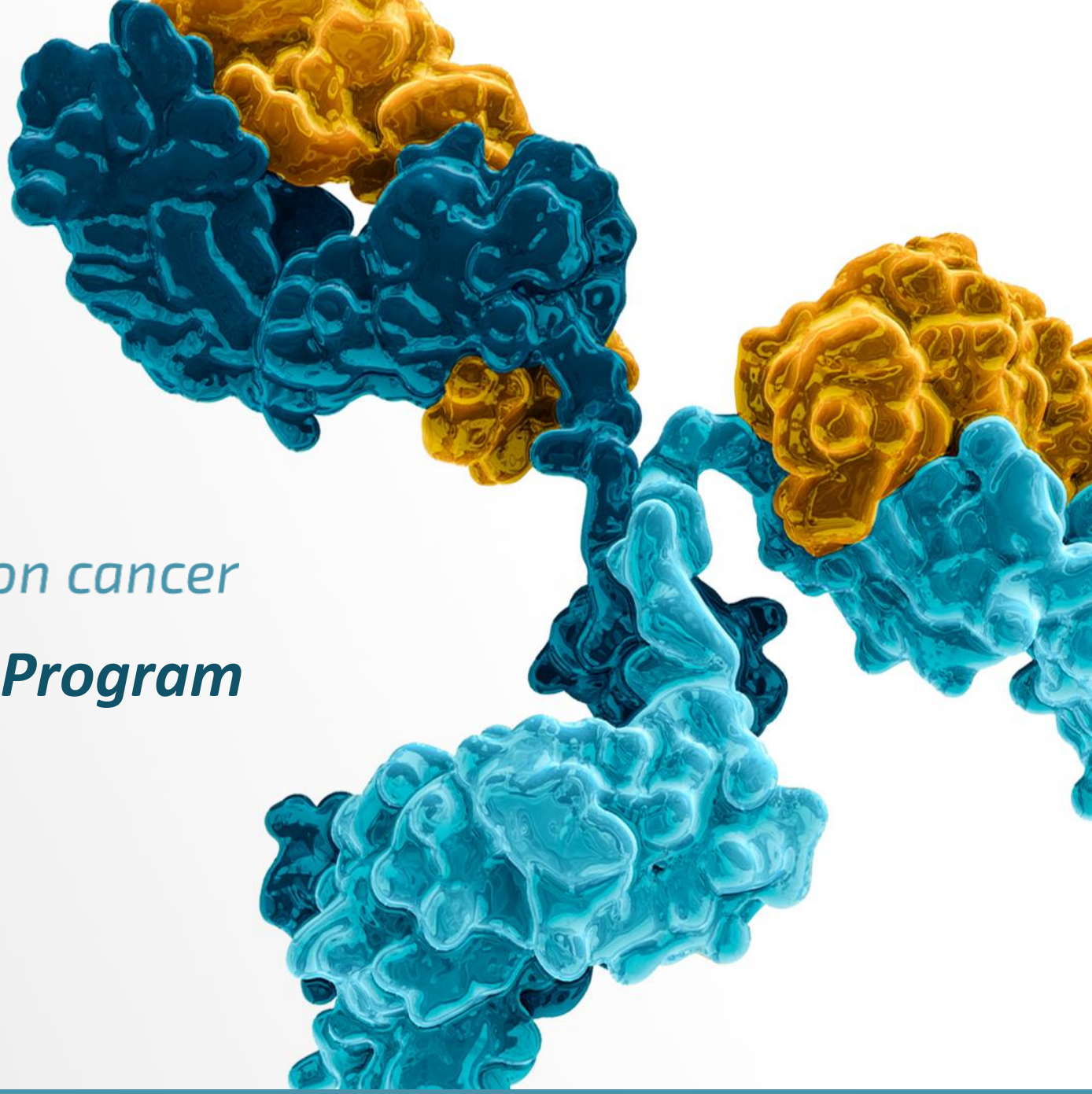
Merus closing in on cancer

ADClonics™ Bispecific ADC Program

Peter Lowe

14 May 2024



Disclaimer

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These and other important factors discussed under the caption “Risk Factors” in our Annual Report on Form 10-Q for the period ended March 31, 2024 filed on May 8, 2024 with the Securities and Exchange Commission, or SEC, and our other reports filed with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

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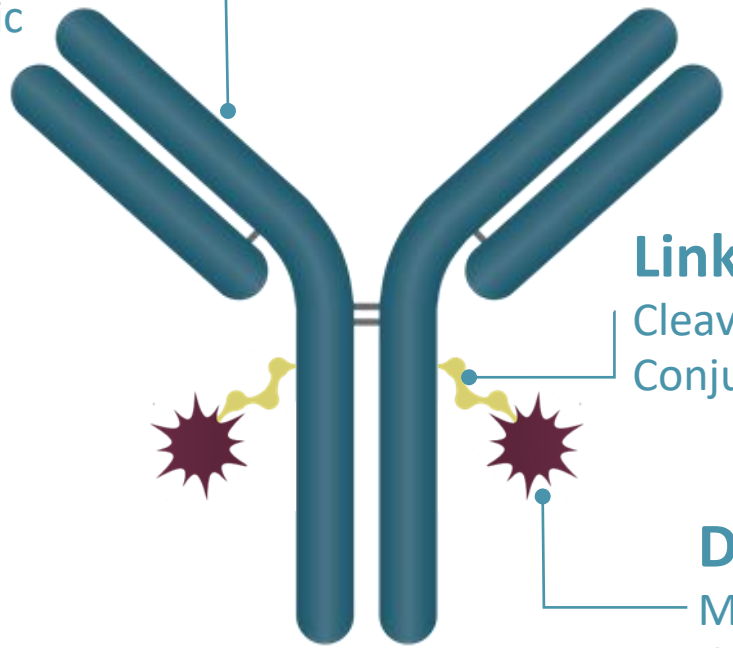
Antibody Drug Conjugates

A conventional ADC

Monoclonal Antibody
Bivalent monospecific
Human, humanized or chimeric



Linker
Cleavable/uncleavable
Conjugate to lysine or cysteine

Drug
Microtubule inhibitors or DNA damaging agents

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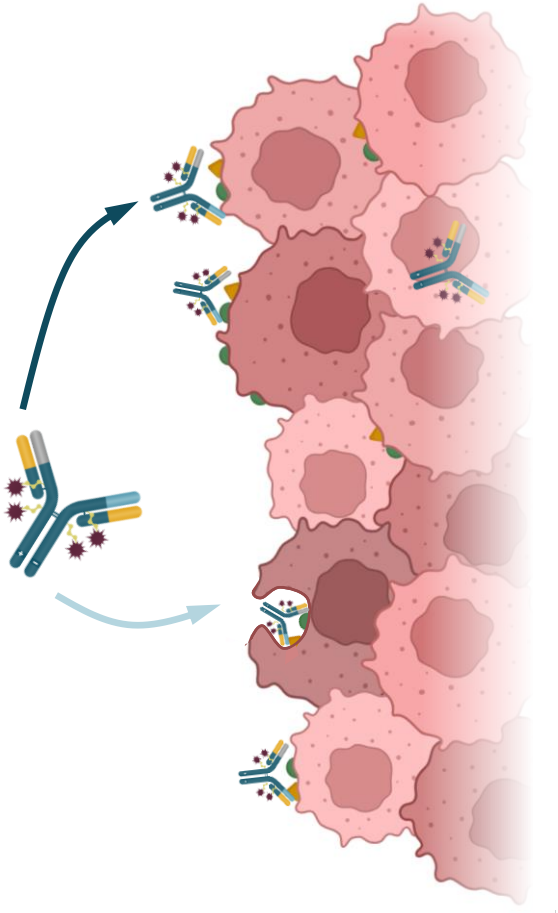
Antibody Drug Conjugates

Current monoclonal ADCs have limitations

	Limitations of conventional ADCs	**Opportunities** for bispecific ADCs
Selectivity	A single target on tumor and non-cancerous cells, leading to on target, off tumor tox	Increased selectivity for tumors that express two targets
Internalization	Drug delivery may be limited by internalization rate	Engaging two targets or epitopes to increase internalization
Cell killing	Limited selective tumor cell killing	Delivering drug to tumor cells expressing both targets



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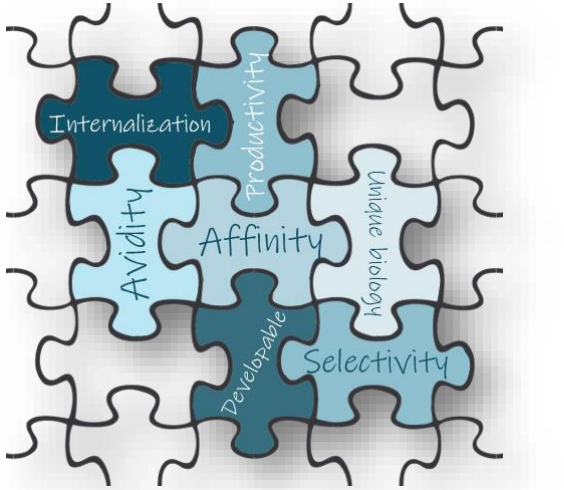
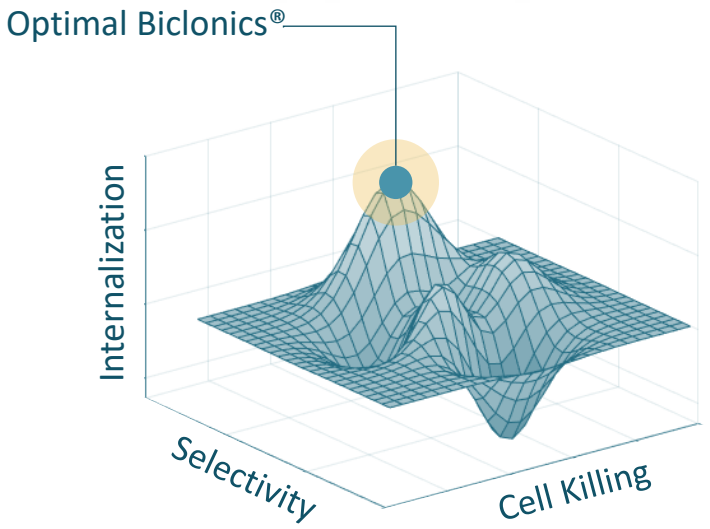
Bispecific Antibodies as ADCs

The optimal combination is a complex puzzle to solve

Screening a lot of clones is required to find the optimal characteristics

- Selectivity for target tissue
- Selective internalization
- Selective cell killing
- Ease of manufacturing





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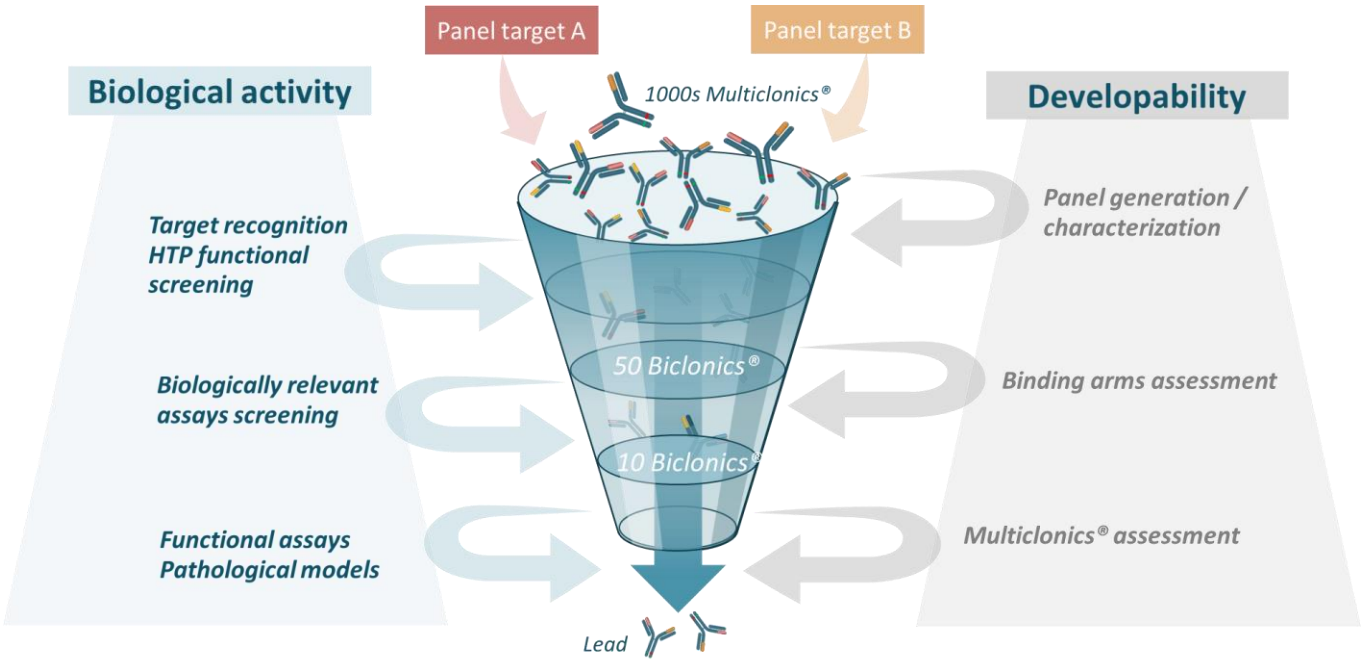
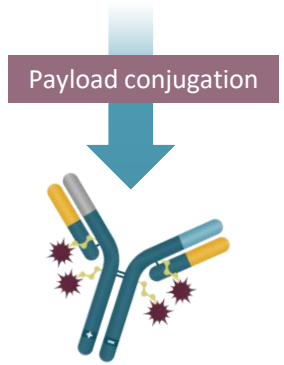
Merus Multiclonics® Platforms

Key elements

- Stable, fully human IgG1 scaffold validated in the clinic
- Large and diverse antibody Fab panels derived *in vivo*
- Large scale screening directly in the IgG1 format
- Select unique bispecific antibodies with optimal characteristics





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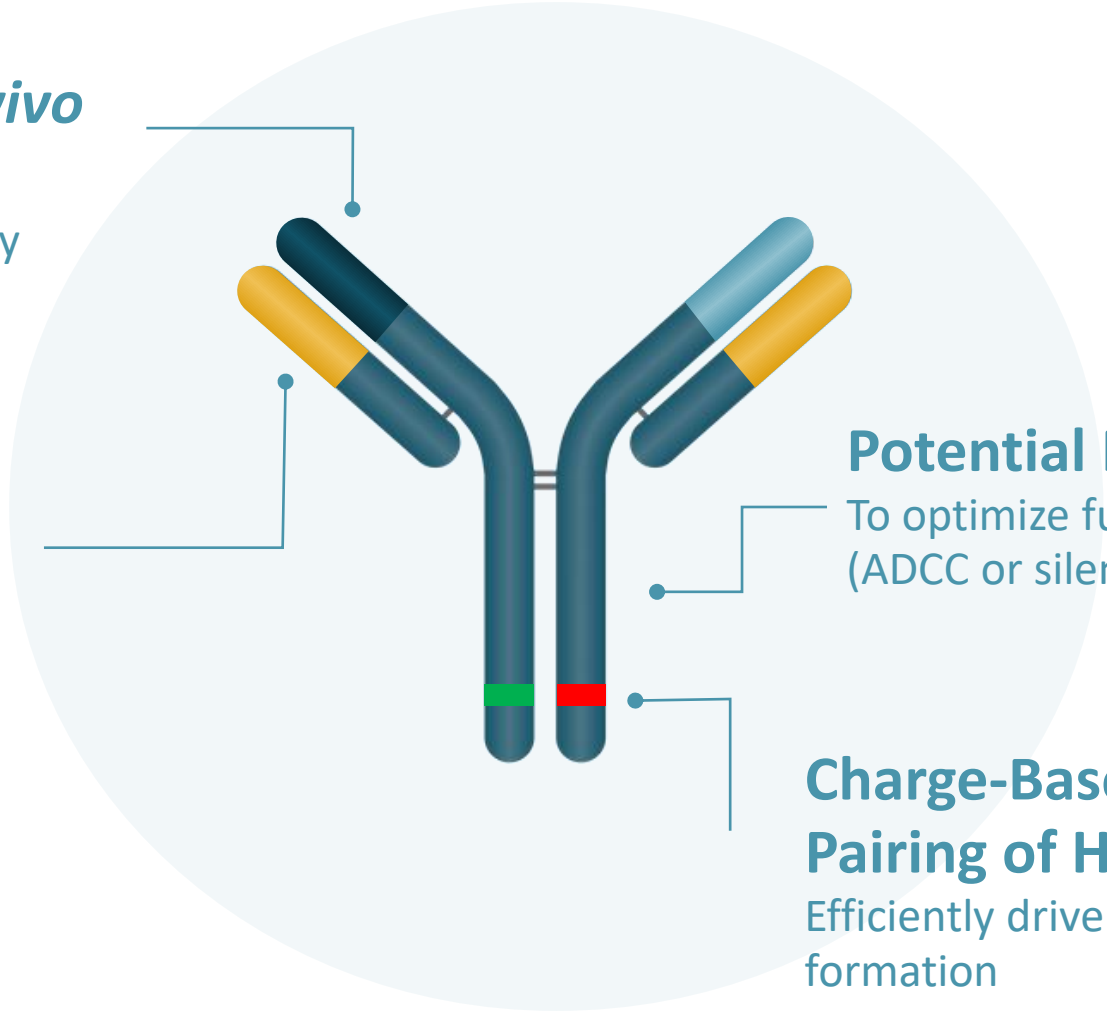
Merus Biclonics®: Fully Human IgG1 Bispecific Antibodies

Made essentially like monoclonal antibodies to facilitate discovery and development

Antibody Fab from *in-vivo* Discovery
For high diversity and specificity



Common Light Chain
To solve the light chain mispairing problem

Potential Fc Modification
To optimize functionality (ADCC or silencing)

Charge-Based (DEKK) Pairing of Heavy Chains
Efficiently drive heterodimer formation

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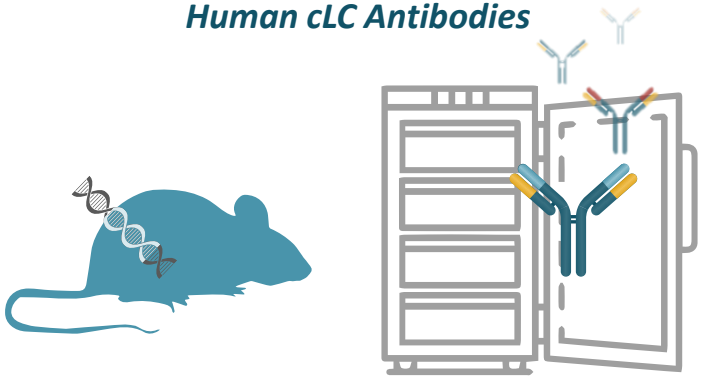
Screening for Optimal Capabilities in Multispecific Antibodies

Finding multispecifics at the speed and scale others find monoclonals

Generate

Human cLC Antibodies



Patented Mouse Technology

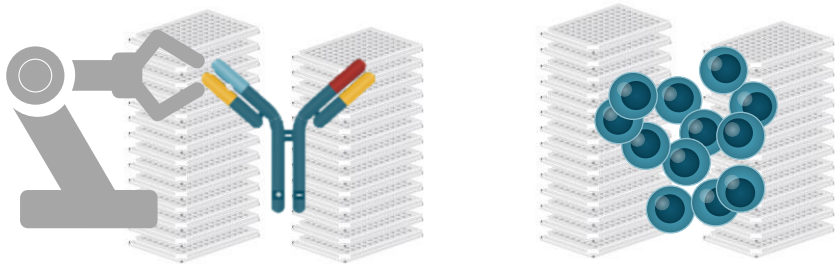
"Merus Mouse" (MeMo®) to generate diverse, high quality common light chain (cLC) antibody panels

Established Inventory

Diverse panels of cLC antibodies against numerous targets

Evaluate

Thousands of Multispecific Abs



Multiclonics® Libraries

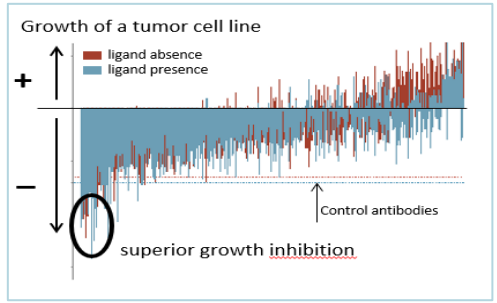
Robotics generate thousands of Multiclonics® by combining cLC antibody panels and our patented "DEKK" IgG heterodimerization technology

Unbiased Screening

In-format, unbiased functional screening in relevant cellular assays

Identify

Best Candidates



Identification of best candidates from thousands of different Biclonics® and Triclonics® against multiple different targets

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Biclonics® Manufacturing

Biclonics® can be manufactured similarly to normal IgGs

Leveraging standard mAb approaches:

- Single producer cell lines with up to in 1 - 4.5 g/L production
- Purified according to standard IgG1 procedures
- Stable liquid formulations to support clinical administration
- Drug product stability confirmed for up to 36 months

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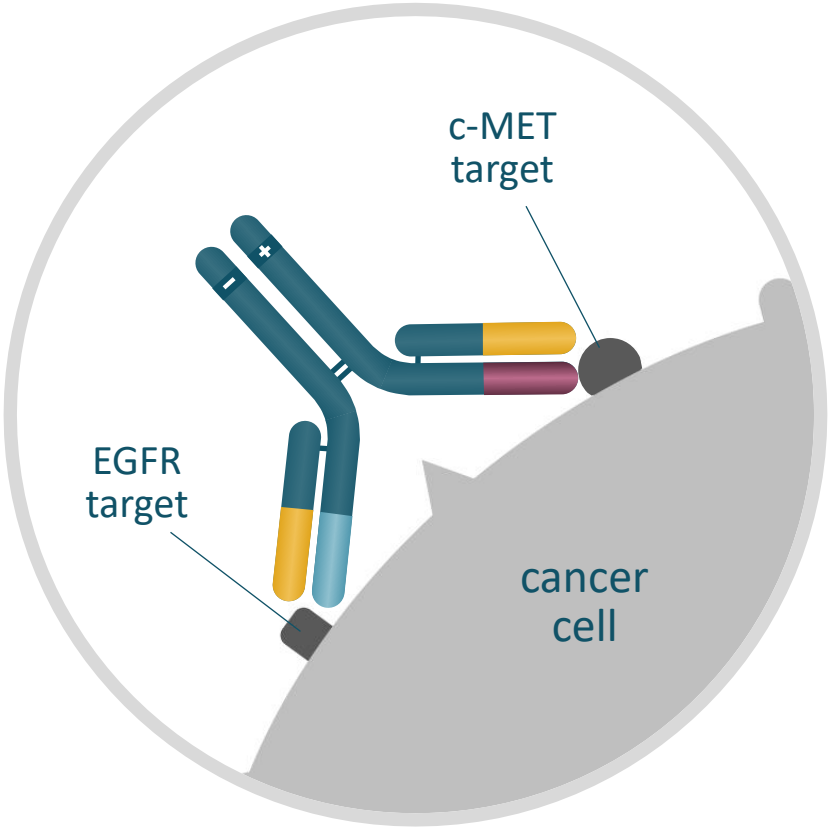
Clinically Validated Biclonics® Tested for ADC Compatibility

Clinical stage assets used to assess platform compatibility for ADClonics™

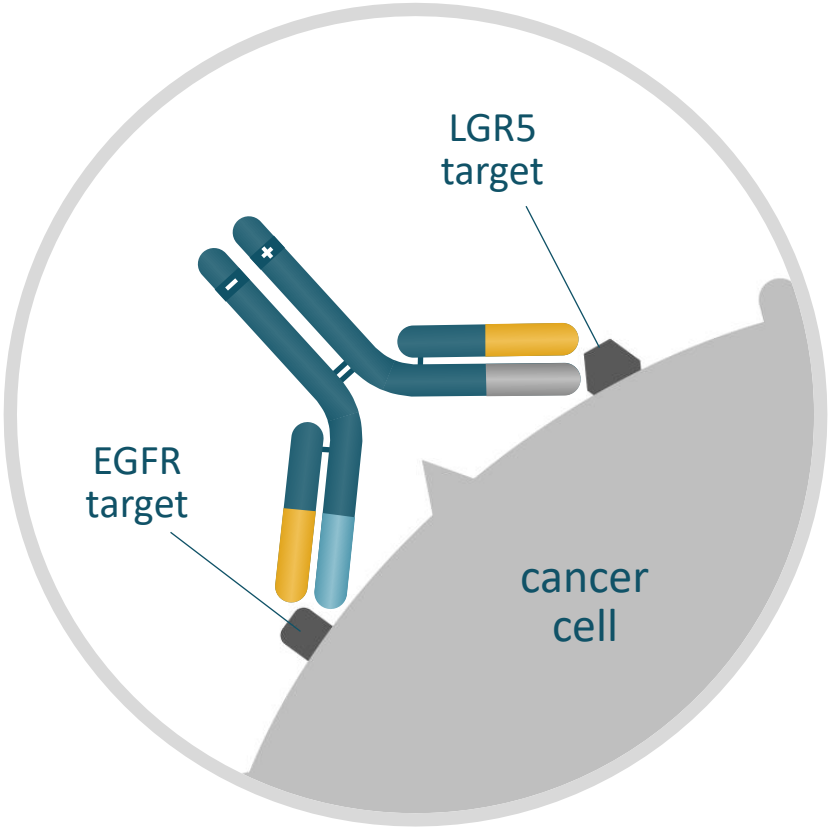
MCLA-129

EGFR x c-MET bispecific



Petosemtamab (MCLA-158)

EGFR x LGR5 bispecific



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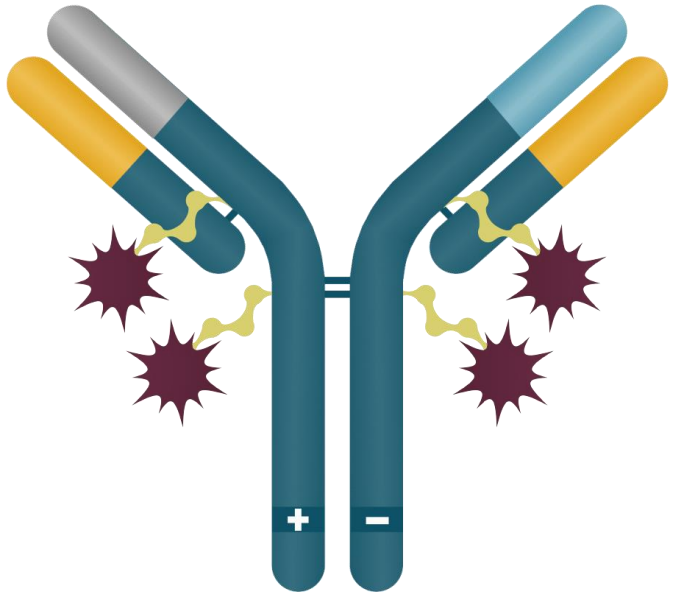
Evaluating MCLA-129 and MCLA-158 as ADClonics™

Fully human IgG1 bispecific antibodies

Can clinically validated drug-linkers be conjugated to Biclonics®?

- Are Biclonics® compatible with standard conjugation methods to make ADClonics™?
- Do ADClonics™ demonstrate favorable biophysical properties?
- Do they preferentially bind and internalize on dual target expressing cells?
- Do they selectively kill dual target-expressing cells?



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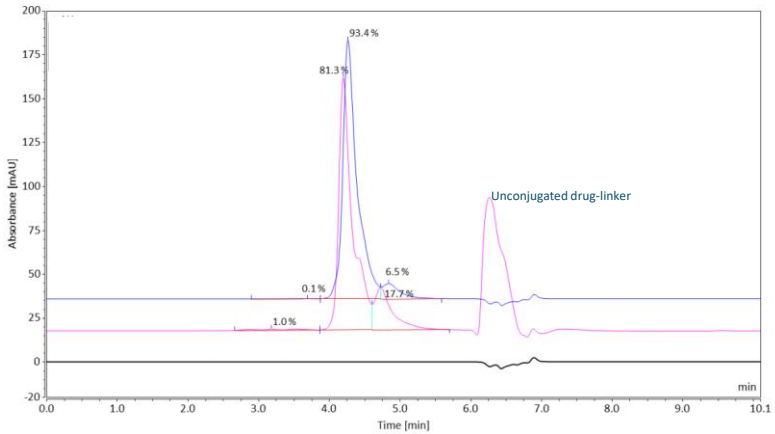
ADClonics™: Assessing Conjugation Efficiency

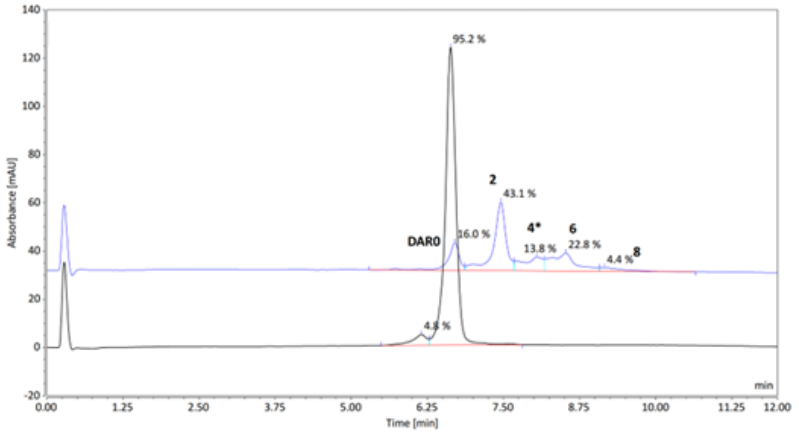
- High degree of protein monomer by SEC;
- Target DAR of ~4 demonstrated by HIC

Size **E**xclusion **C**hromatography (**SEC**)

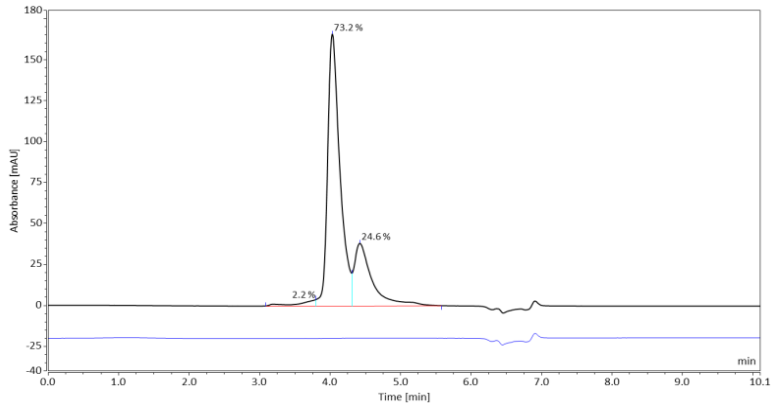
Hydrophobic **I**nteraction **C**hromatography (**HIC**)

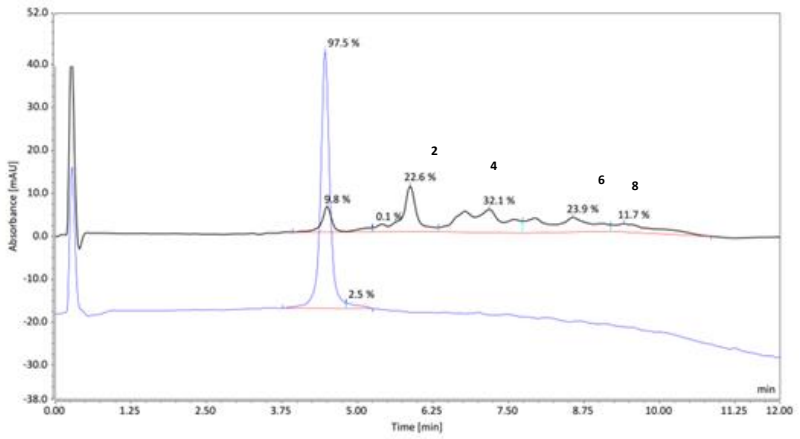
MCLA-129-MMAE





MCLA-158-MMAE





DAR, drug antibody ratio

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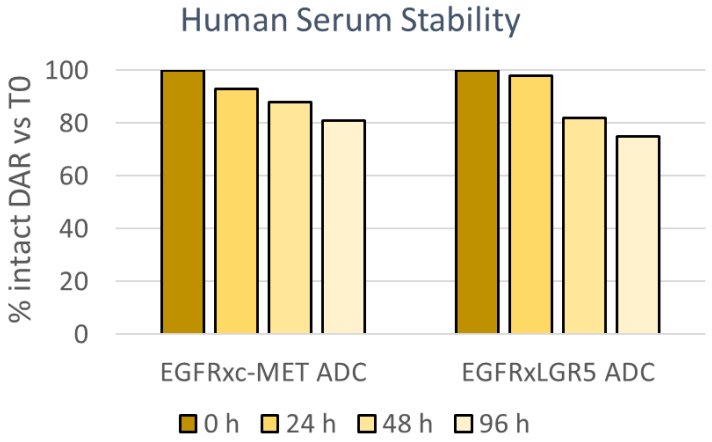
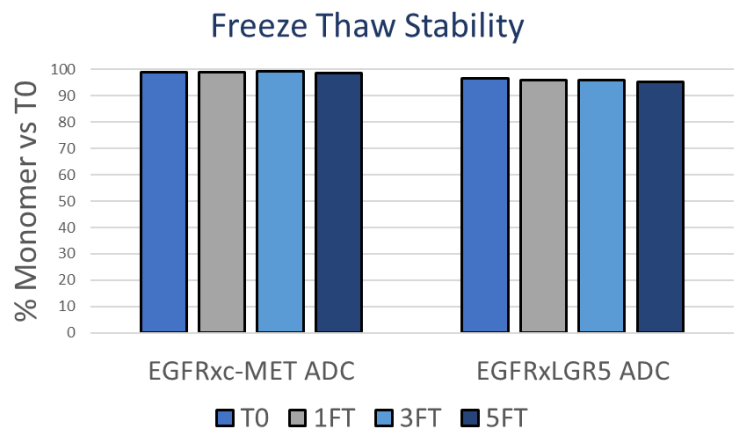
ADClonics™: Favorable Biophysical Properties

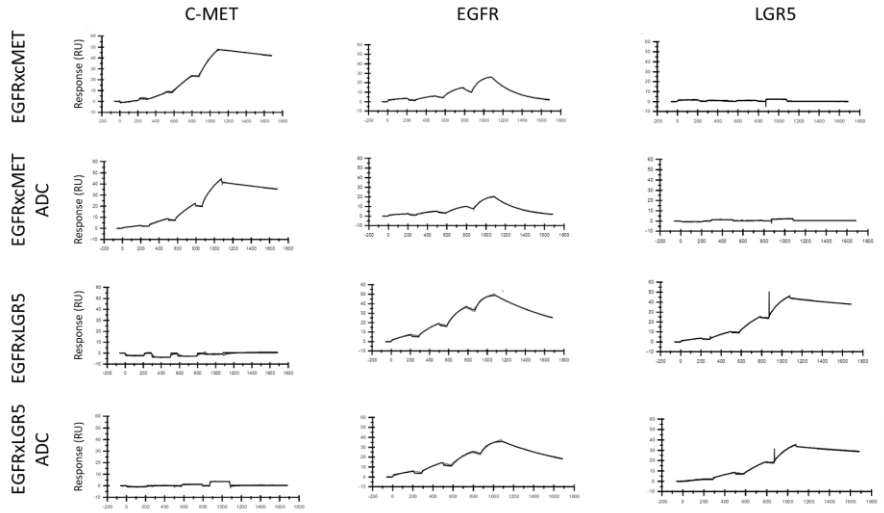
Stability and binding maintained

- Average intact DAR >75% after incubation in human serum over 96 hours at 37 °C
- Repeated freeze thaw cycles > 95% ADC monomer
- Target antigen binding retained in ADC format





Target binding SPR (Biacore)



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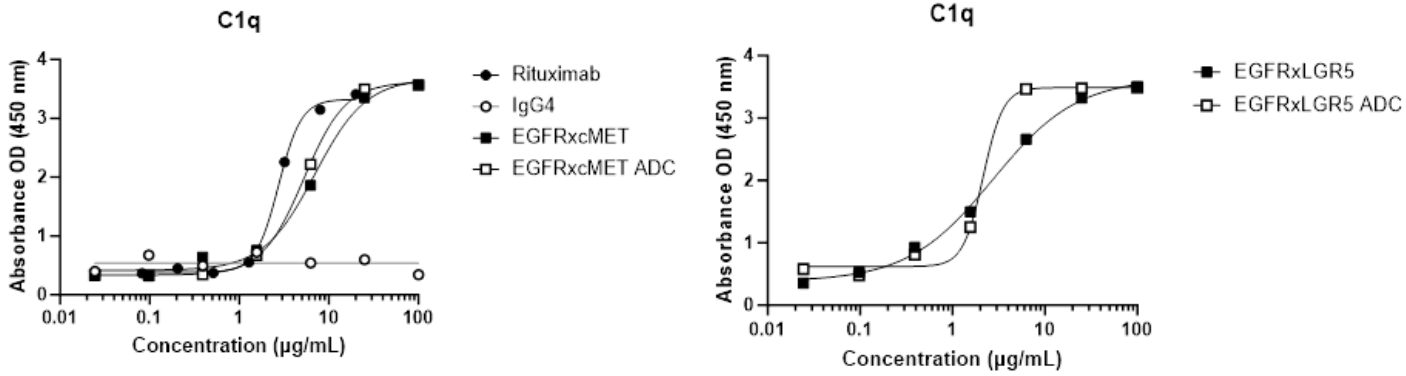
ADClonics™: Favorable biophysical properties

IgG Fc domain function maintained

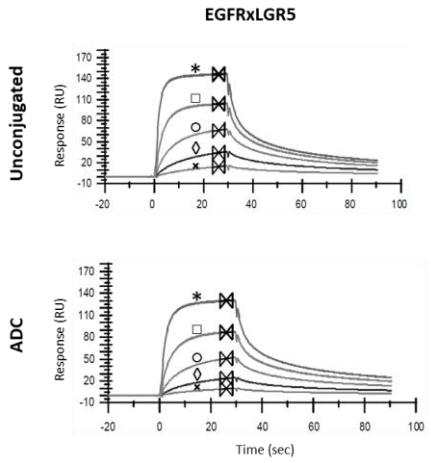
- C1q binding retained in ADC format
- FcRn binding retained in ADC format
- FcγR binding retained in ADC format

C1q binding ELISA

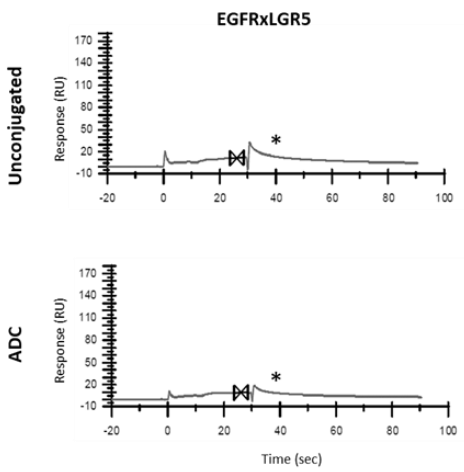


FcRn binding SPR (Biacore)

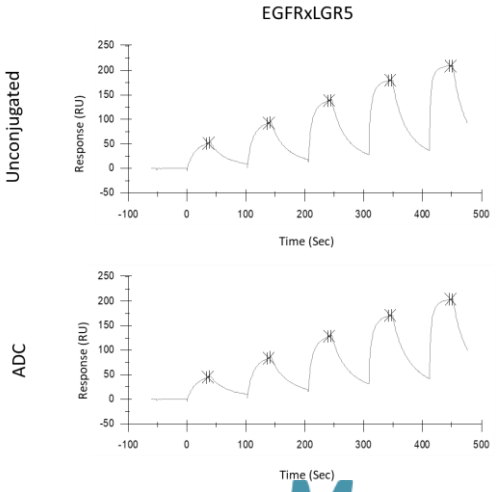
pH 6.0



pH 7.4



FcγR binding SPR (Biacore)



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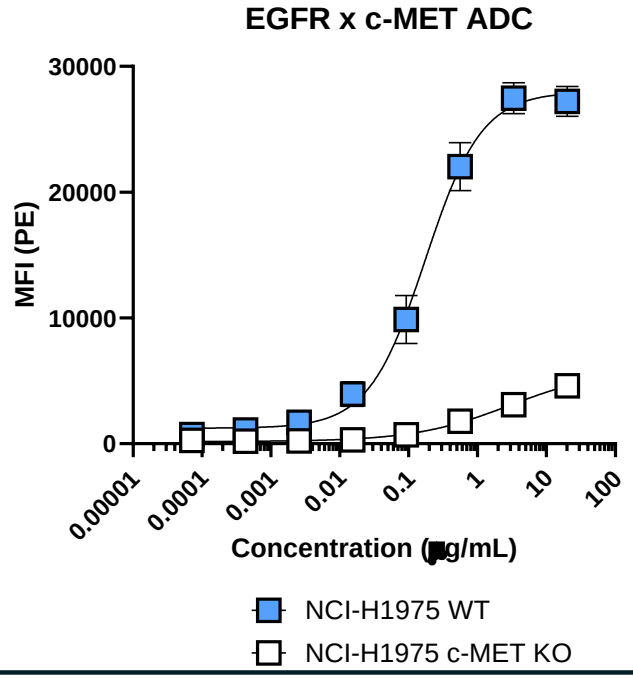
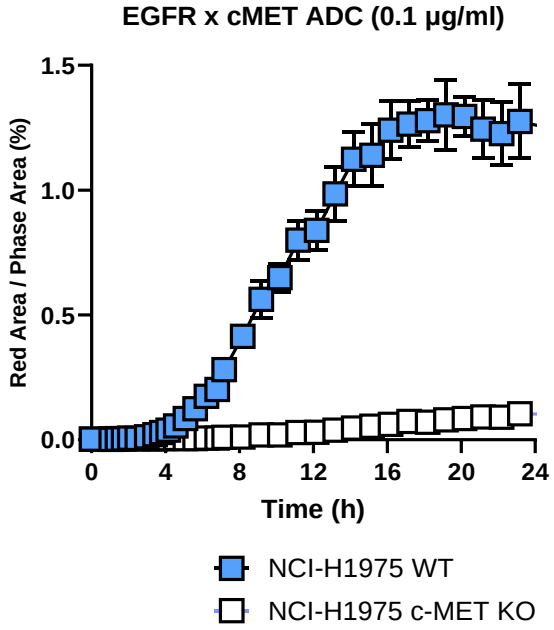
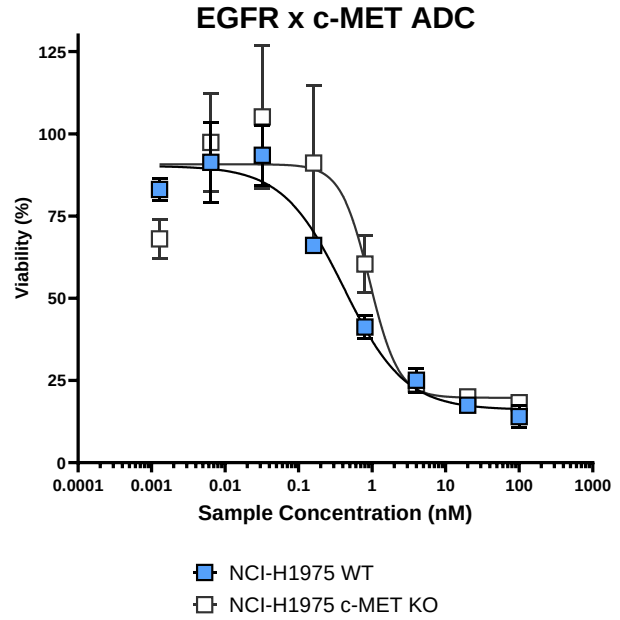
ADClonics™: Preferentially Bind, Internalize & Kill Dual-Target Expressing Cells

Selective cell binding, internalization and cell killing with EGFR x c-MET (MCLA-129) ADC

Cell binding	Internalization	Cell killing







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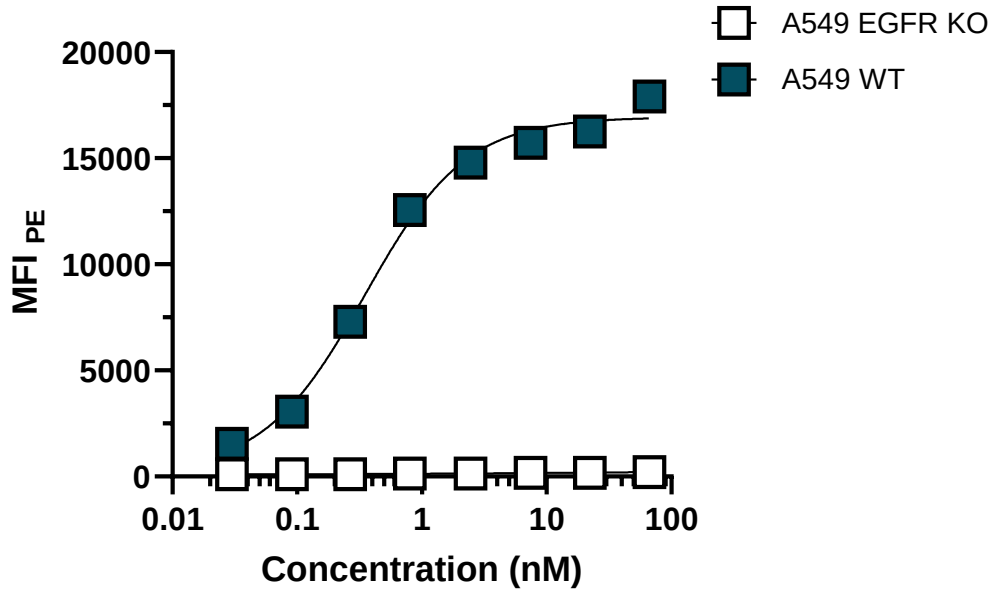
ADClonics™ Preferentially Kill Target Expressing Cells

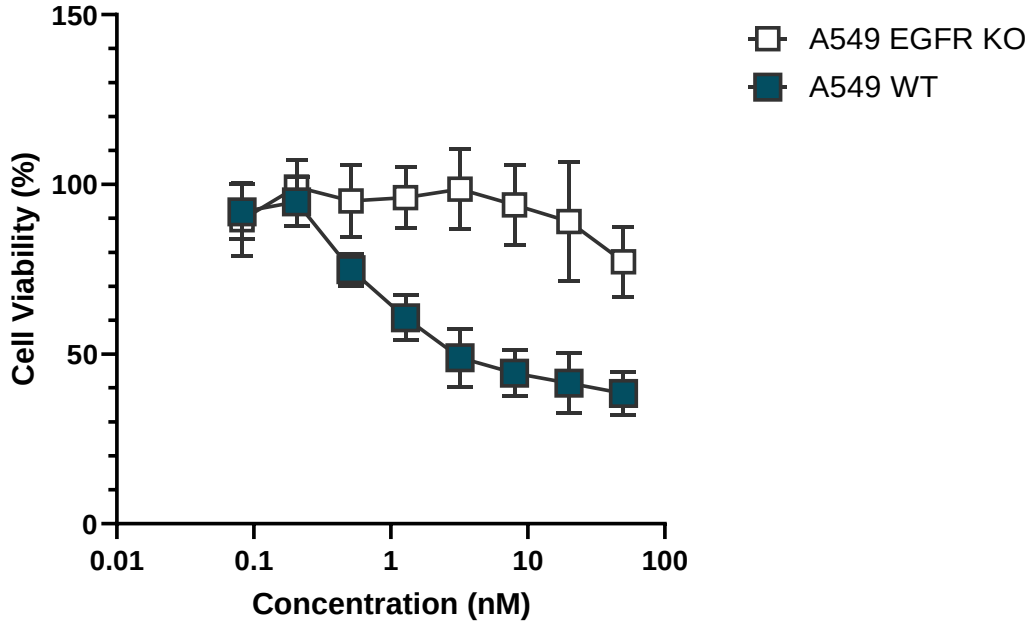
Selective cell binding and cell killing with EGFR x LGR5 (MCLA-158) ADC

Cell binding



The A549 cell line is not known to express LGR5

Cell killing



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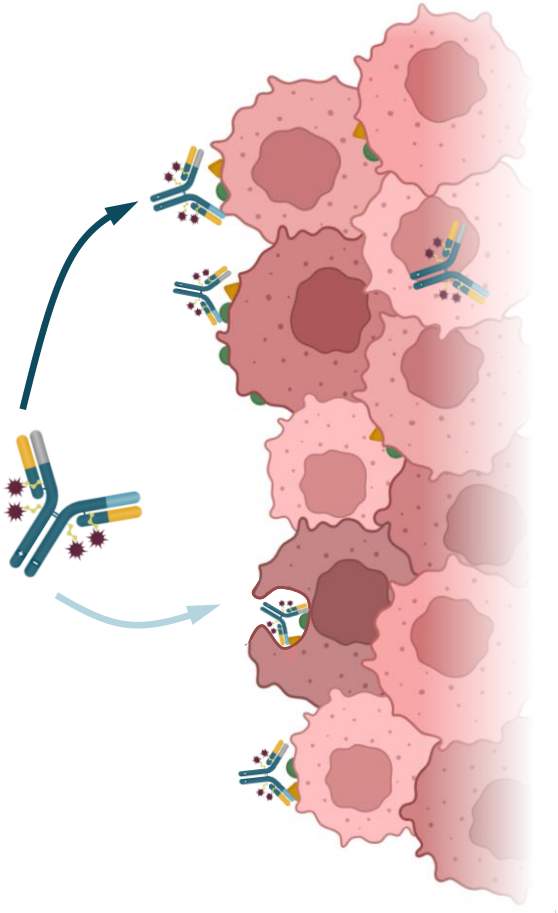
Antibody Drug Conjugates

Merus' Biclonics® ADCs may solve current limitations

	Limitations of conventional ADCs	**Opportunity** for bispecific ADC
Selectivity	A single target on tumor and non-cancerous cells, leading to on target, off tumor tox	Increased selectivity for tumors that express two targets
Internalization	Drug delivery may be limited by internalization rate	Engaging two targets or epitopes to increase internalization
Cell killing	Limited selective tumor cell killing	Delivering drug to tumor cells expressing both targets



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Conclusions

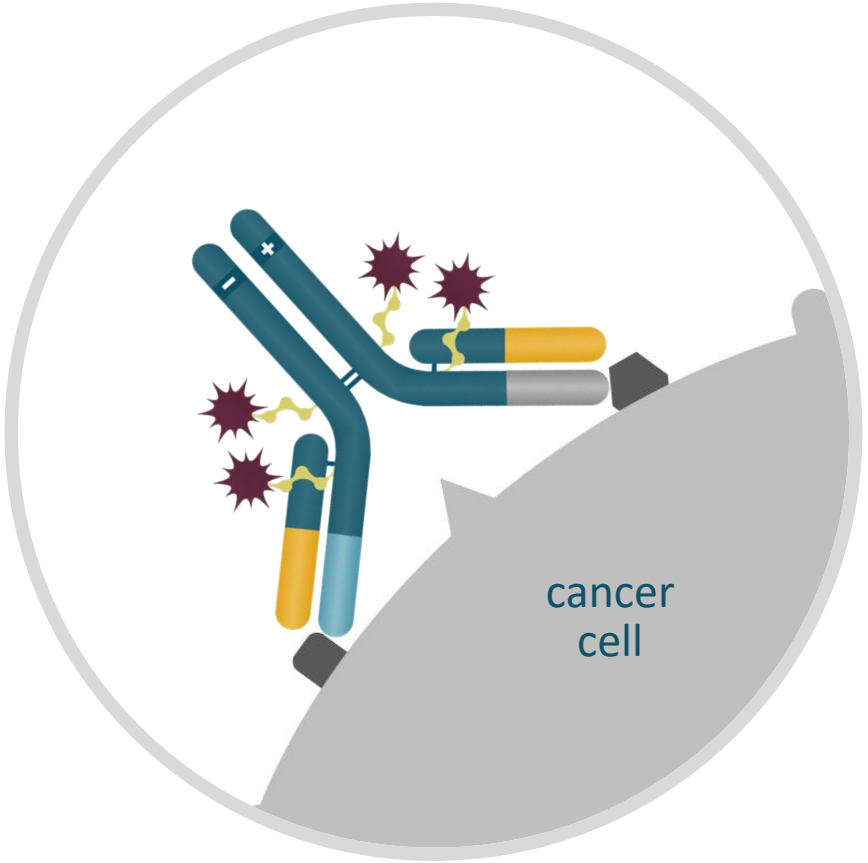
Merus ADClonics™ can address limitations of conventional monoclonal antibody-based ADC:

- Selectivity from binding two targets
- Selective internalization
- Selective cell killing

The Merus Multiclonics® platforms are ideally suited to generate ADClonics™- bispecific ADC with the Biclonics® format and platform

- Large, diverse panels and high throughput screening
- Robust and developable as ADC

MCLA clinical candidates as ADClonics™ offer potential advantages to monospecific ADCs



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closing in on cancer

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