

# *Merus* closing in on cancer

## SPEAKERS

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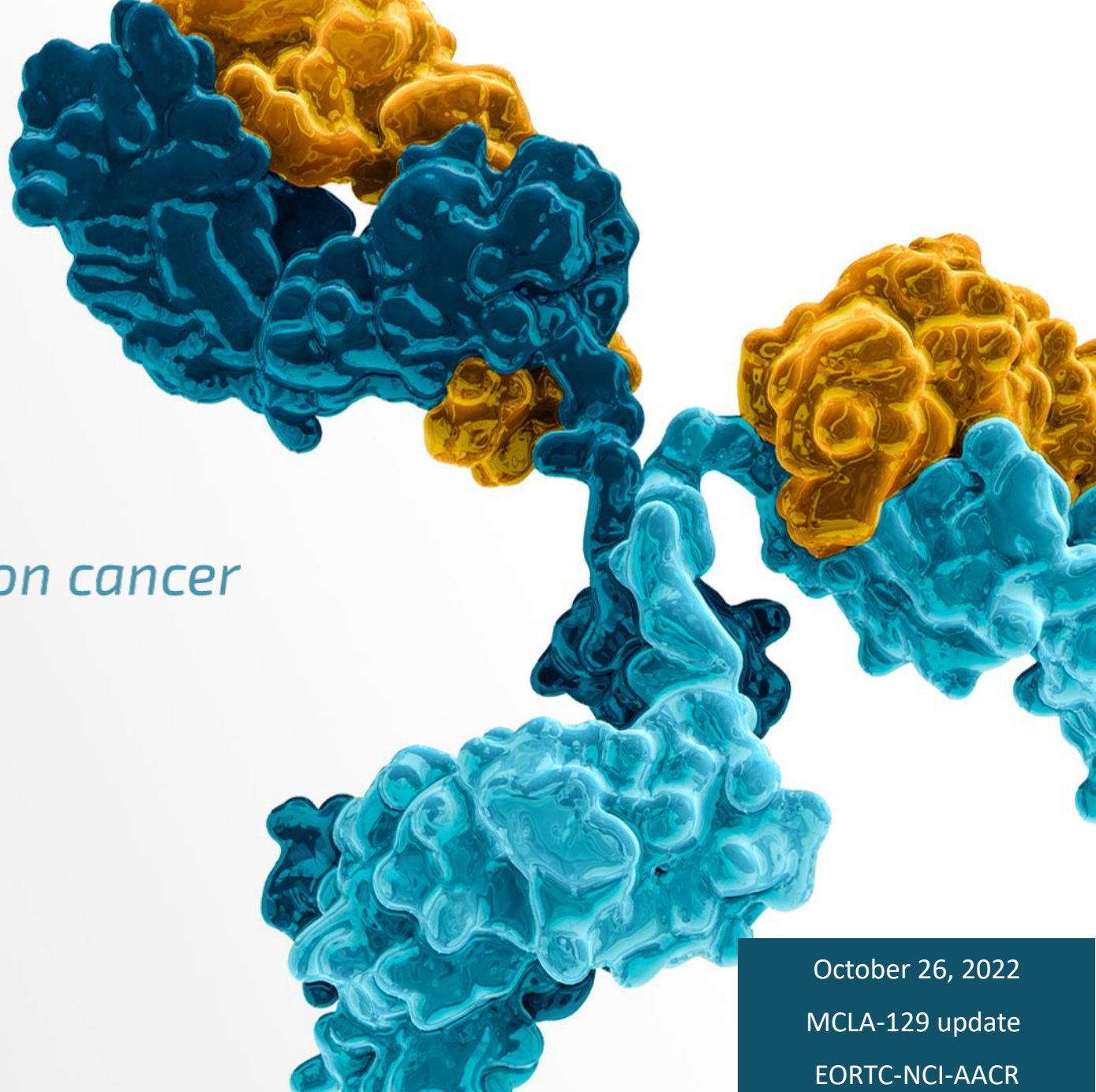
**Andrew Joe, MD**  
CHIEF MEDICAL OFFICER

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IR/CORP COMMS

October 26, 2022

MCLA-129 update

EORTC-NCI-AACR



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# Disclaimer

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This presentation (including any oral commentary that accompanies this presentation) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the impact our Biclomics® and Triclomics® platforms can have on cancer, our product candidates' potential to treat certain types of tumors, the timing of regulatory filings and the timing and impact of and anticipated data read outs or results from our clinical trials and our collaborations, and anticipated cash runway. These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding, which may not be available and which may require us to restrict our operations or require us to relinquish rights to our technologies or antibody candidates; potential delays in regulatory approval and impacts of the COVID-19 pandemic, which would impact our ability to commercialize our product candidates and affect our ability to generate revenue; the unproven approach to therapeutic intervention of our Biclomics®, and Triclomics® technology; our limited operating history; economic, political, regulatory and other risks involved with international operations; the lengthy and expensive process of clinical drug development, which has an uncertain outcome; the unpredictable nature of our early stage development efforts for marketable drugs; potential adverse public reaction to the use of cancer therapies; potential delays in enrollment of patients, which could affect the receipt of necessary regulatory approvals; failure to obtain marketing approval internationally; failure to compete successfully against other drug companies; potential competition from other drug companies if we fail to obtain orphan drug designation or maintain orphan drug exclusivity for our products; our reliance on third parties to conduct our clinical trials and perform clinical development and the potential for those third parties to not perform satisfactorily; our reliance on third parties to manufacture our product candidates, which may delay, prevent or impair our development and commercialization efforts; protection of our proprietary technology; our patents being found invalid or unenforceable; potential lawsuits for infringement of third-party intellectual property; our ability to attract and retain key personnel; managing our growth could result in difficulties.

These and other important factors discussed under the caption “Risk Factors” in our in our Annual Report on Form 10-Q for the period ended June 30, 2022 filed on August 8, 2022 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.

# Agenda

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Welcome &  
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& Pipeline

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Q & A

## On the call



**Bill Lundberg, MD, MBA**  
CHIEF EXECUTIVE OFFICER



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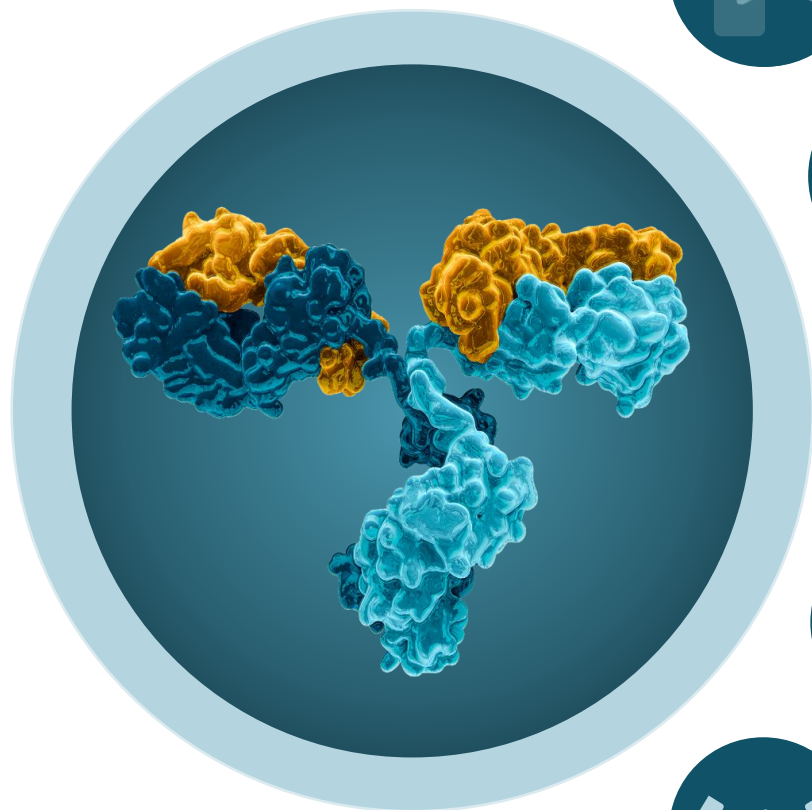


**Andrew Joe, MD**  
CHIEF MEDICAL OFFICER



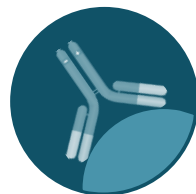
**Kathleen Farren**  
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# Merus Overview



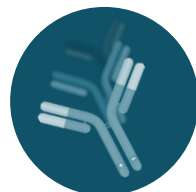
## Oncology-focused Company Developing Multispecific Antibody Therapies

Bispecific and trispecific cancer therapeutic candidates based on the human IgG format



## Established Clinical Pipeline

Four clinical stage assets with proof of concept data on Zeno in NRG1-fusion (NRG1+) cancer<sup>1</sup>, and early encouraging data on Peto in Head and Neck cancer<sup>2</sup> and MCLA-129 in solid tumors<sup>3</sup>



## Leading Multispecific Antibody (Multiclonics®) Platforms

Common light chain format permits broad high throughput evaluation of Biclonics® and Triclonics®, to develop clinical stage assets with meaningful clinical responses in patients



## Near Term Trial Updates and Strong Cash Position Beyond 2024\*

Upcoming clinical milestones and program updates planned over the next 12-18 months: Zeno registration-directed program, MCLA-129 initial clinical data, and Peto clinical update



## Strategic Collaborations to Unlock Platform Value

Multiple strategic collaborations and license agreements

<sup>1</sup> Schram et al., ASCO 2022, efficacy data cutoff April 12, 2022 and safety data cutoff January 12, 2022

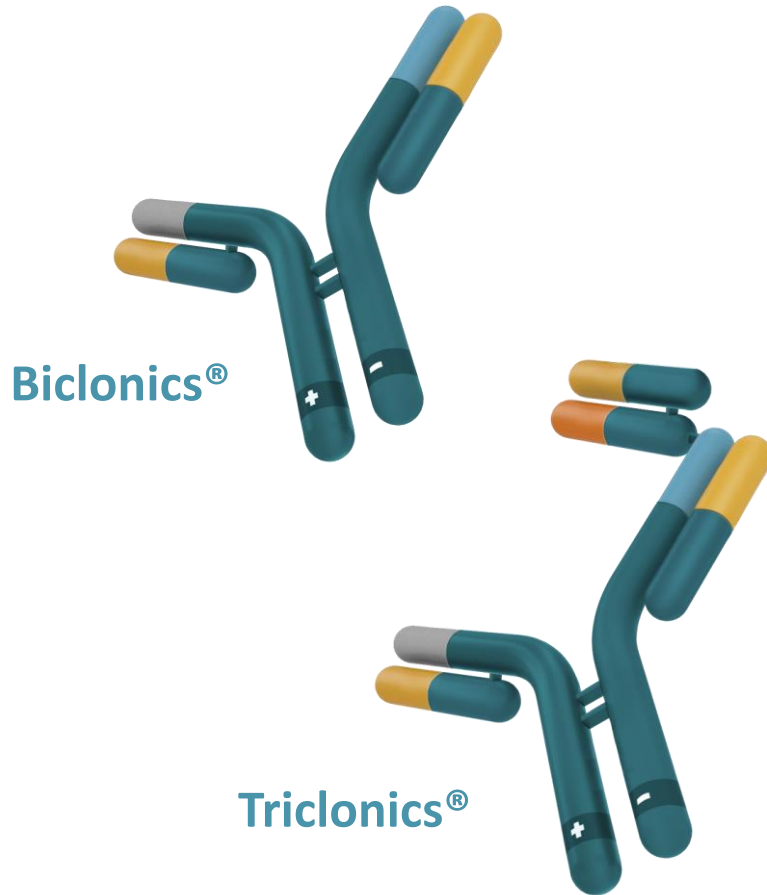
<sup>2</sup> Hollebecque et al., AACR-NCI-EORTC 2021, data cutoff August 9, 2021

<sup>3</sup> Ou et al., EORTC-NCI-AACR 2022, data cutoff August 15, 2022

5 \*See August 8, 2022 10-Q noting our belief that our cash, cash equivalents and marketable securities, will fund our operations beyond 2024.

# Merus Multiclonics®

*Bispecific and Trispecific therapeutic candidates for cancer  
with broad application for human disease*



## Large-scale screening

- *To select the best Biclonics® and Triclonics® from up to 1,000s of candidates*

## Fully human IgG format

- *Ease of manufacturing*
- *Low immunogenicity risk*
- *Predictable in vivo behavior*
- *Durable, consistent half life*
- *Potential for ADCC enhancement and Fc silencing*

## Robust IP portfolio

Patents covering Multiclonics® technology, including

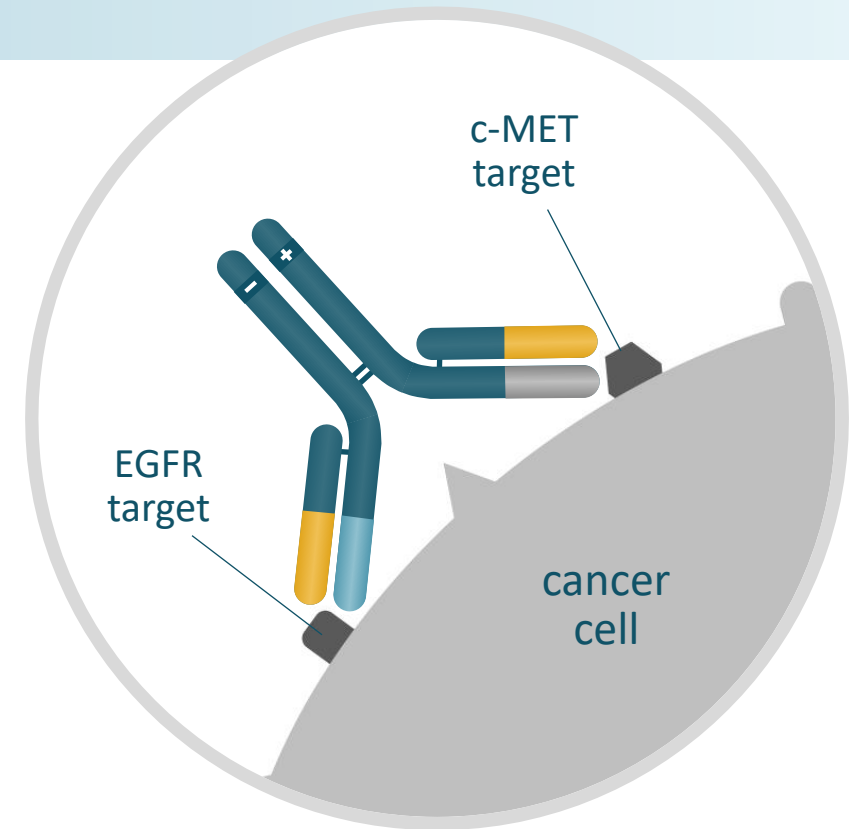
- *Common light chain antibody generation and screening*
- *Dimerization by charge engineering*



***Designed to target lung cancer  
and other solid tumors  
expressing EGFR and c-MET***

**MCLA-129**  
EGFR x c-MET Bispecific

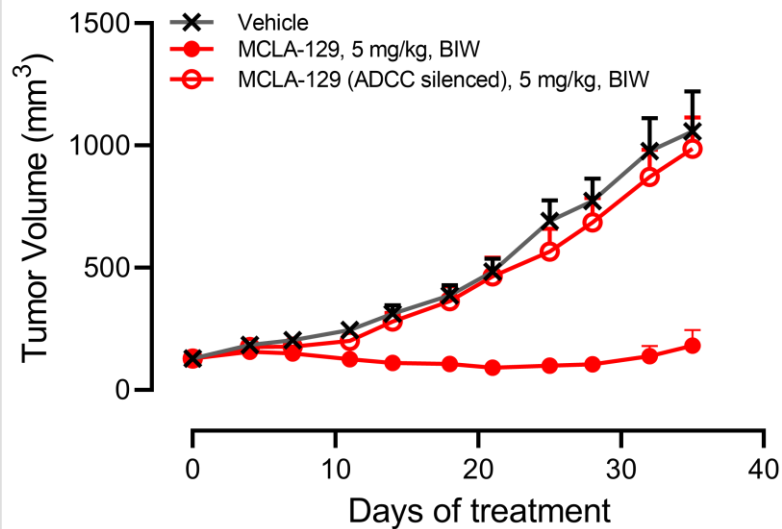
- Targets both EGFR and c-MET on cancer cells
- Modifications to enhance ADCC
- Significant opportunity in lung cancer and other solid tumors
- Phase 1/2 trial ongoing; clinical update provided in 2H22
- Expansion cohorts ongoing, including in combination with a third generation EGFR TKI



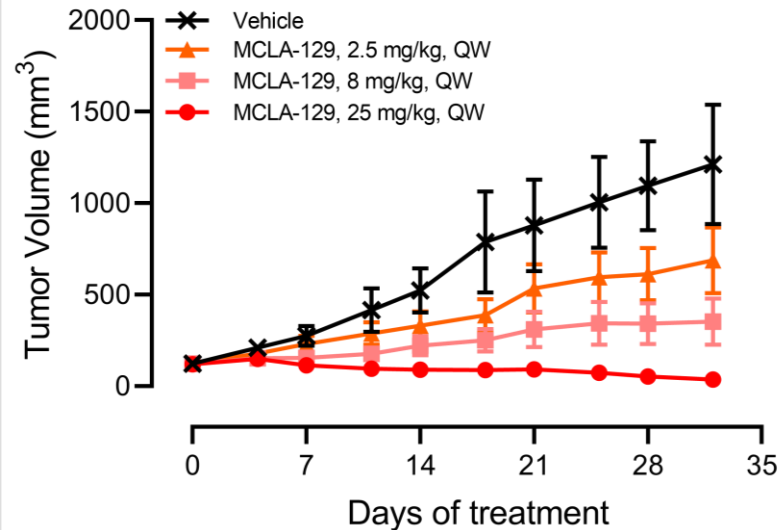
# MCLA-129 — Targets both EGFR and c-MET

*Demonstrated tumor growth inhibition and potent ADCC in preclinical studies\**

## Inhibition of NSCLC EGFR<sup>del19</sup> tumor growth



## Inhibition of NSCLC EGFR<sup>exon20</sup> tumor growth



## Potent Bispecific Antibody

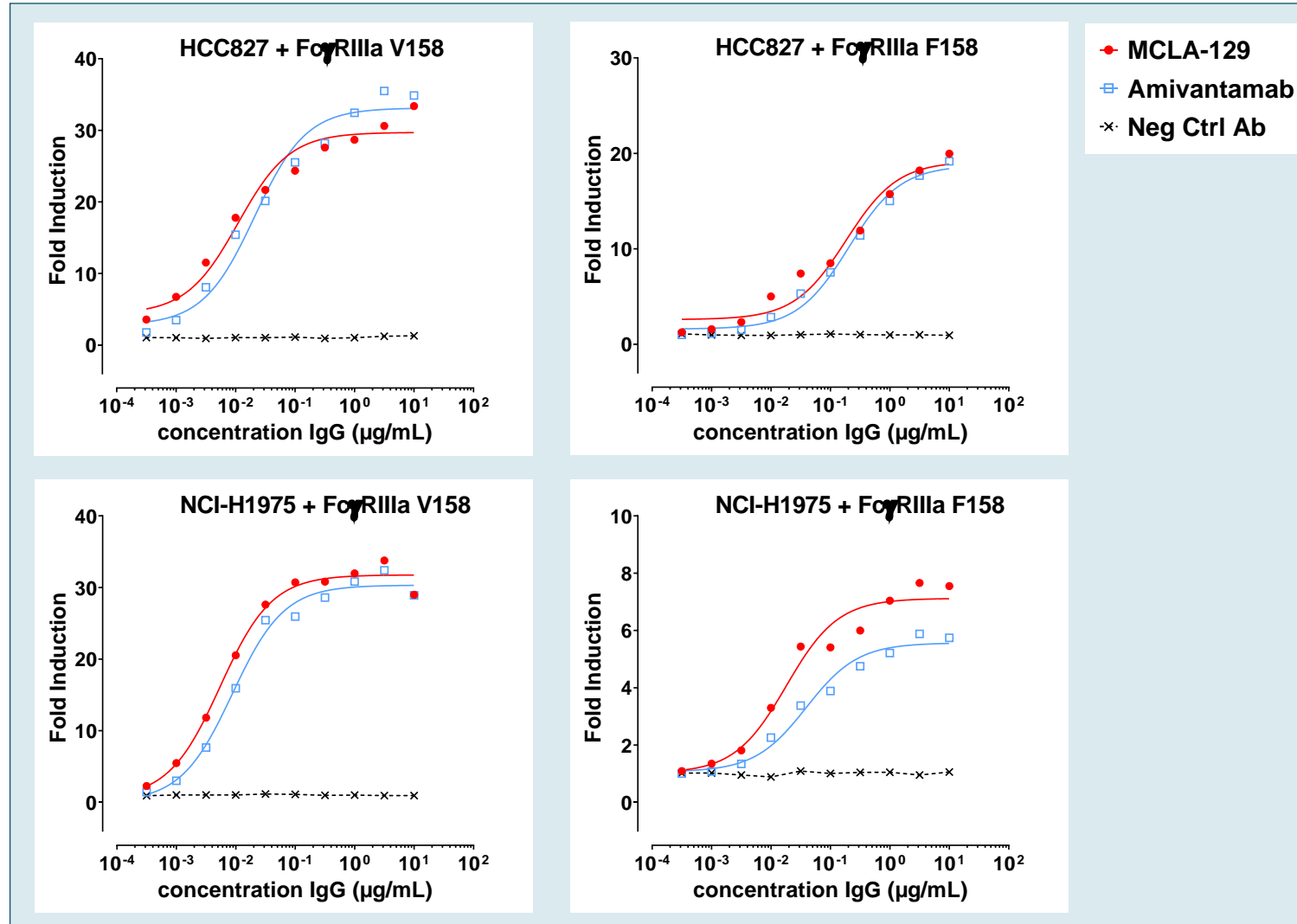
- Blocks EGF and HGF binding to EGFR and c-MET
- Fc enhanced to promote ADCC and ADCP
- Potently inhibit NSCLC tumor growth as monotherapy and in combination with EGFR TKI in preclinical models
- Overcome HGF-mediated EGFR-TKI resistance in preclinical models

\* Sources: Geuijen et al. (AACR 2019 Poster presentation) <https://merus.nl/wp-content/uploads/2019/10/AACR-NCI-EORTC-Poster-LBC07-MCLA-129.pdf>;  
de Gorter et al. (AACR 2021 Poster presentation) [https://merus.nl/wp-content/uploads/2021/04/Merus\\_poster\\_MCLA-129\\_AACR2021.pdf](https://merus.nl/wp-content/uploads/2021/04/Merus_poster_MCLA-129_AACR2021.pdf);  
de Gorter et al. (AACR 2022 Poster presentation) [https://merus.nl/wp-content/uploads/2022/04/Merus\\_poster\\_MCLA-129\\_AACR2022-FINAL.pdf](https://merus.nl/wp-content/uploads/2022/04/Merus_poster_MCLA-129_AACR2022-FINAL.pdf)



# ADCC Function Against EGFRm NSCLC Cell Lines

## *MCLA-129 ADCC activity compared to amivantamab*

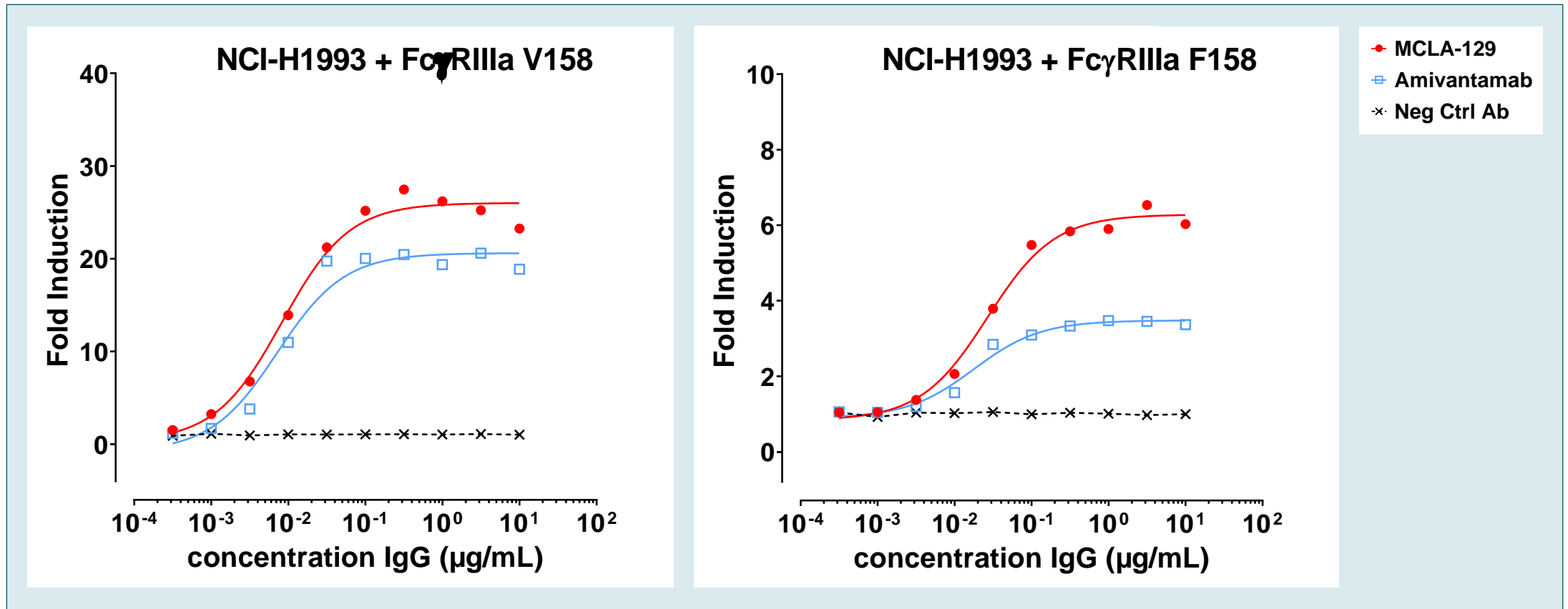


Cell line	EGFR mutation	Amplification
NCI-HCC827	del (E746,A750)	EGFR
NCI-H1975	L858R, T790M	NA

V158: High affinity FcγRIIIa receptor; F158: Low affinity FcγRIIIa receptor

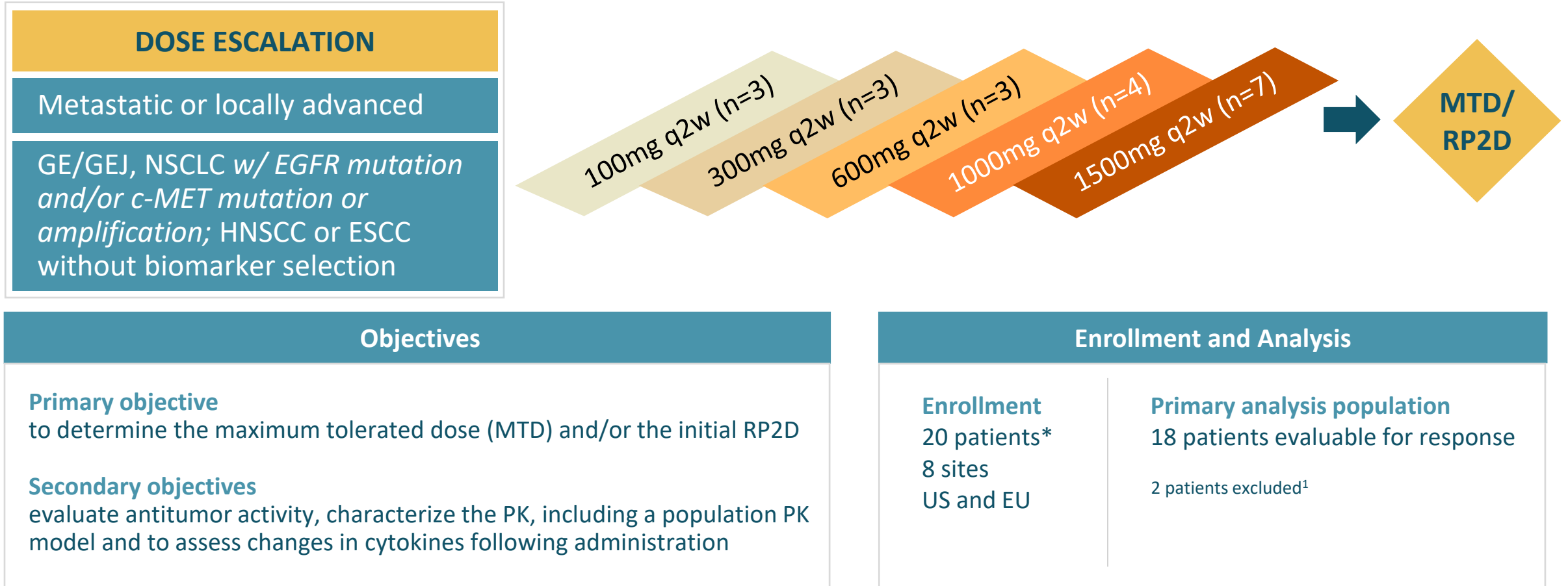
# ADCC Function Against MET Amp NSCLC Cell Lines

## *MCLA-129 ADCC activity compared to amivantamab*



V158: High affinity Fc $\gamma$ RIIIa receptor; F158: Low affinity Fc $\gamma$ RIIIa receptor

# MCLA-129 Phase 1 Dose Escalation Trial



<sup>1</sup>20 patients enrolled as of the May 8, 2022 data cutoff date. As of the August 15, 2022 data cutoff date, 18 patients were evaluable for response with two discontinuing before the second infusion (1 patient due to investigator decision, clinical progression; and 1 patient passing away due to an unrelated AE).

# Patient Characteristics

Patient Characteristics	N=20
Age (years), median (range)	65.5 (43–79)
Female / Male (%)	60% / 40%
ECOG 0 / 1 (%)	65% / 35%
Race (%)	
Caucasian	75%
Asian	25%
Tumor Type	N=20
Non-small cell lung cancer (NSCLC)	16
Head and neck squamous cell carcinoma (HNSCC)	2
Gastroesophageal junction (GEJ)	1
Esophageal squamous cell carcinoma (ESCC)	1

Mutation status NSCLC, n= 16	
EGFR del19	8
EGFR L858R	4
c-MET exon 14	2
EGFR exon 20	1
EGFR other: G719A, R776C	1
N of Metastatic Sites, median (range)	2 (1-6)
Brain involvement	20%
N of Lines of Prior Therapies, median (range)	3 (1*–7)
Prior Osimertinib	12*
Prior anti-PD-(L)1 inhibitors	10
Prior c-MET inhibitors	3**

\* data updated post data cutoff date

\*\* including anti-EGFR/anti-c-MET bispecific antibodies

# Safety

## Most frequent adverse events (>10%)

Preferred term	Irrespective of causality		Suspected related	
	All grades n(%)	Grade 3-4 n(%)	All grades n(%)	Grade 3-4 n(%)
<b>-- Any event</b>	<b>19 (95%)</b>	<b>9 (45%)</b>	<b>19 (95%)</b>	<b>4 (20%)</b>
Infusion related reaction*	18 (90%)	1 (5%)	18 (90%)	1 (5%)
Dyspnea	11 (55%)	1 (5%)	9 (45%)	1 (5%)
Flushing	9 (45%)	-	9 (45%)	-
Nausea	9 (45%)	-	8 (40%)	-
Fatigue	6 (30%)	1 (5%)	3 (15%)	-
Back pain	5 (25%)	-	2 (10%)	-
Chills	5 (25%)	-	5 (25%)	-
Myalgia	5 (25%)	-	4 (20%)	-
Vomiting	5 (25%)	-	5 (25%)	-
Cough	4 (20%)	-	3 (15%)	-
Abdominal pain	3 (15%)	-	1 (5%)	-
Arthralgia	3 (15%)	-	2 (10%)	-
Dermatitis acneiform	3 (15%)	-	3 (15%)	-
Lipase increased	(15%)	-	2 (10%)	-
Oedema peripheral	3 (15%)	-	-	-
Pruritus	3 (15%)	1 (5%)	3 (15%)	1 (5%)

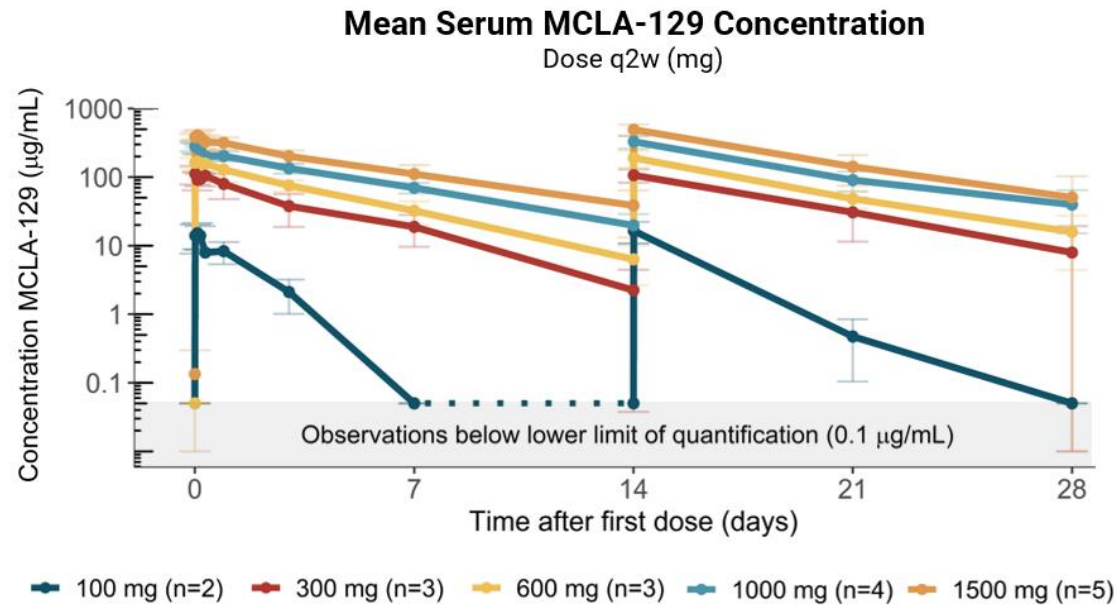
\* Grouped term covering all AEs occurring within 24 hours of the infusion considered by the investigator as an IRR

## Key Takeaways

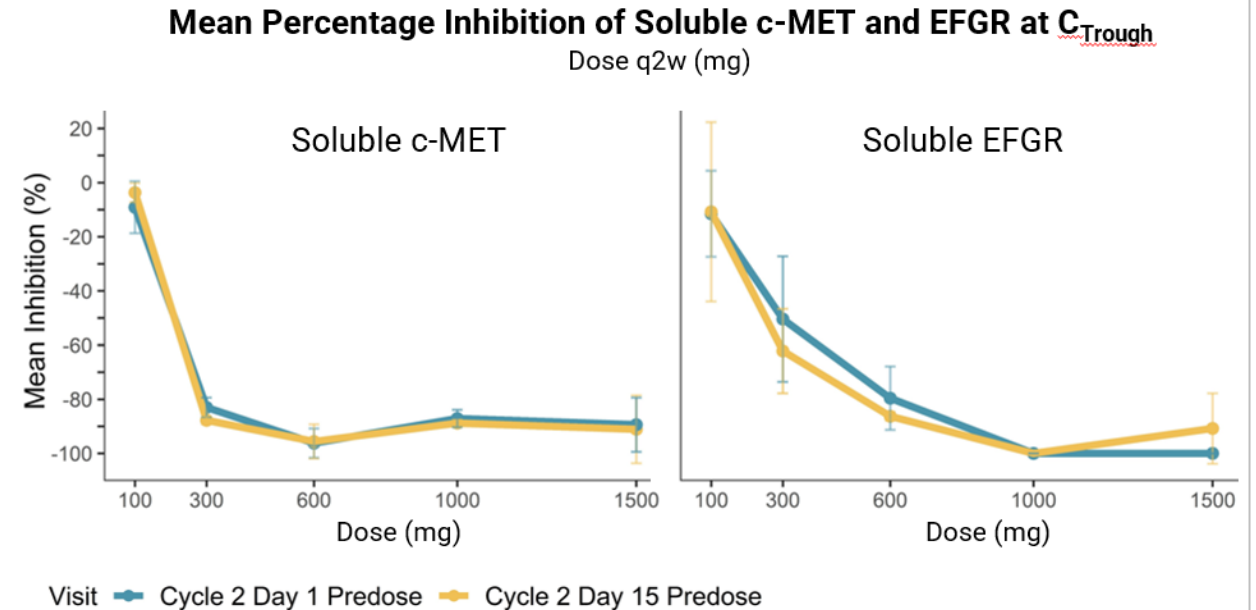
- Safety results are based on 20 patients who received one or more doses of MCLA-129 across all dose levels tested as of the August 15, 2022 data cutoff date
- No dose limiting toxicities (DLTs) reported
- Most frequent AEs were IRR (infusion-related reactions)
  - 90% any grade, one patient (5%) grade 3, no grade 4-5
  - The majority of events occurred during the first infusion
- No reported:
  - treatment-related grade 4 or 5 AEs
  - discontinuations due to toxicity
  - interstitial lung disease

# Pharmacokinetics and Pharmacodynamics

Estimated mean half-life at steady-state is ~200 hours based on population PK analysis



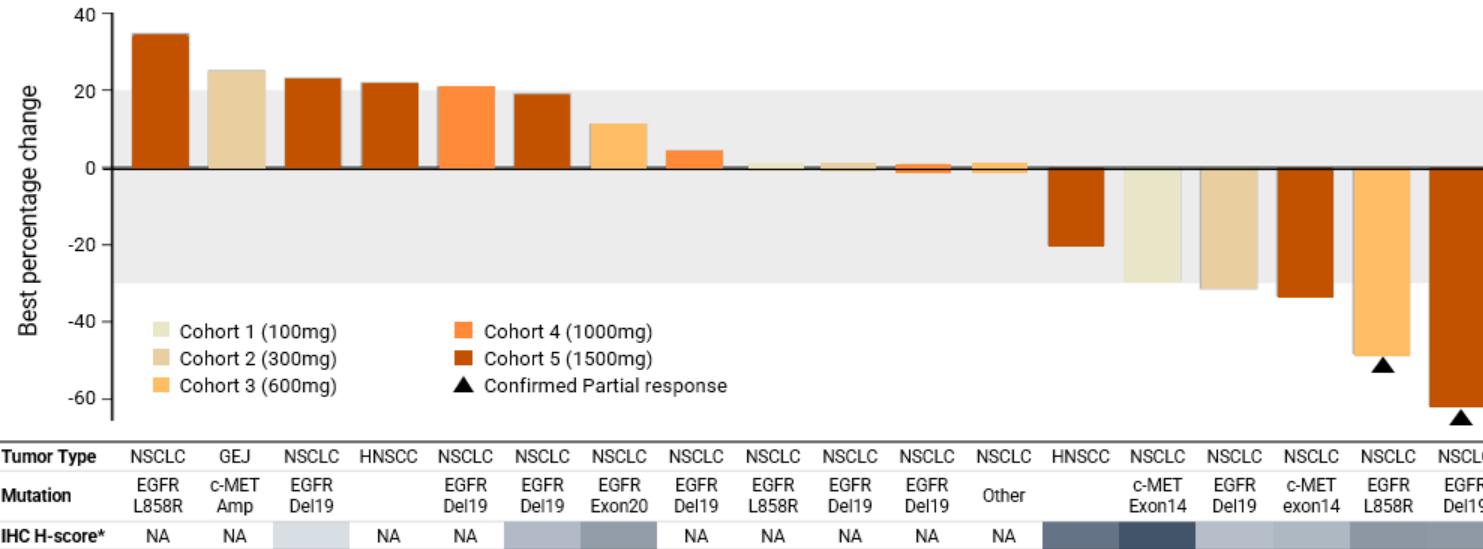
Maximal inhibition of soluble EGFR and soluble c-MET occurs at doses of 1000 mg q2w and higher





# Preliminary Anti-tumor Activity

*Two confirmed PRs and additional four tumors with >20% shrinkage*



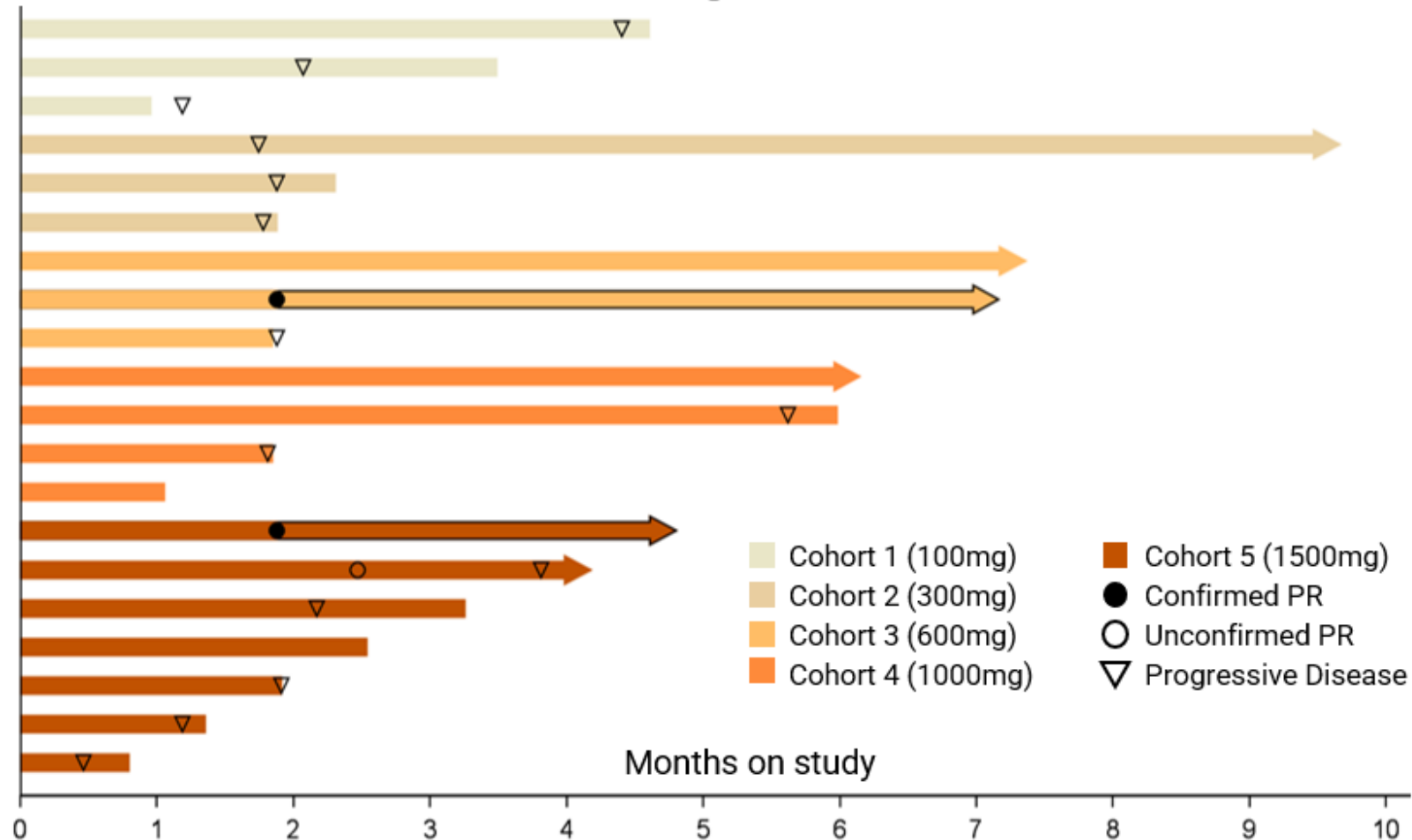
\*Combined EGFR and c-MET IHC H-score

Dose level (mg)	Tumor type	Mutation	Best response (Δ% target lesions)	Cycle received	Prior treatments *
1500	HNSCC		SD (-20%)	2	PB Cet N
100	NSCLC	c-MET exon 14	SD (-29.2%)	5	PB Cr Cap P
300	NSCLC	EGFR 19del	PD (-31.4%)	11 (+)	PB O P
1500	NSCLC	c-MET exon14	uPR (-33.3%)	3	PB Tep P
600	NSCLC	EGFR L858R	PR (-48.2%)	8 (+)	PB O P
1500	NSCLC	EGFR 19del	PR (-59.6%)	5 (+)	PB O N

\*PB: platinum based chemotherapy; O: osimertinib; N: nivolumab; P: pembrolizumab; Cr: crizotinib; Cap: capmatinib; Cet: cetuximab; Tep: tepotinib; (+) patient ongoing; PR partial response; uPR unconfirmed partial response; SD stable disease; PD progression disease

## Duration of Exposure

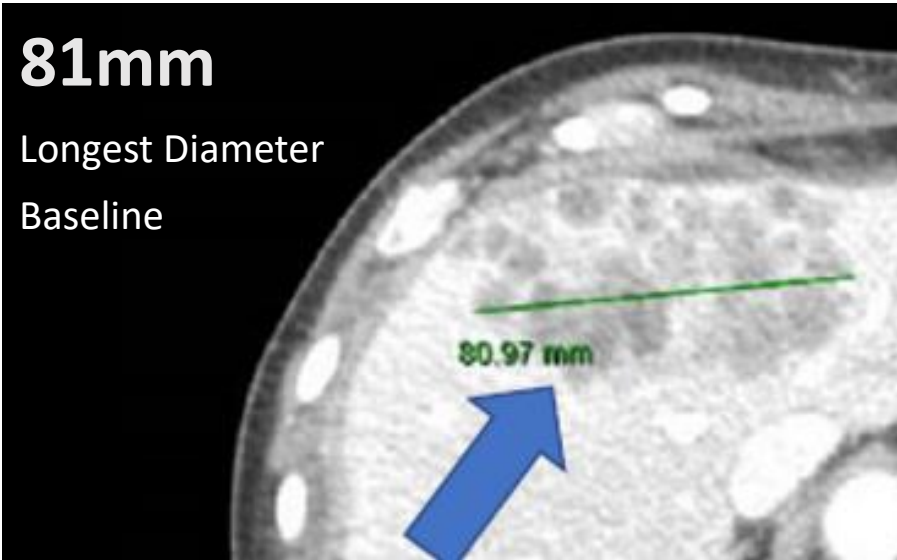
*Median duration of exposure was 12.6 weeks*  
*Six patients remain on-going as of August 15 data cutoff*



## Preliminary Anti-Tumor Activity

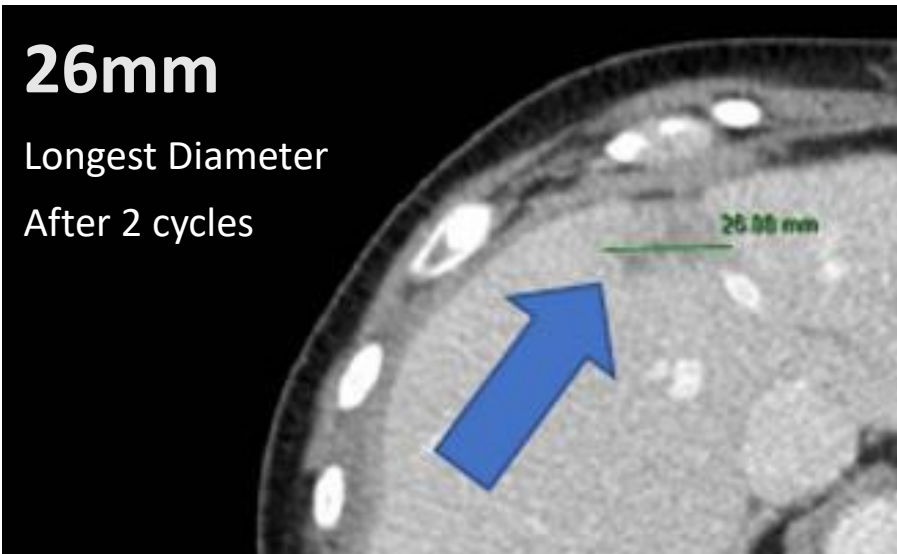
**81mm**

Longest Diameter  
Baseline



**26mm**

Longest Diameter  
After 2 cycles



### 65-year-old female patient with L858R EGFRm NSCLC

- Previously lines of therapy- doublet chemotherapy, immunotherapy, and TKI
- Received 600 mg q2w
- Patient achieved partial response with a 62% tumor reduction
- 8+ cycles and remains on treatment

# MCLA-129 Dose Escalation

## Conclusions



MCLA-129 was observed to be **well tolerated** with a **manageable safety profile**



**Maximal inhibition of soluble EGFR and soluble c-MET** was achieved at 1000 mg q2w



**Tumor target engagement** is predicted to be **>95%** throughout the dosing cycle at 1500 mg q2w



**Antitumor activity** was observed among heavily pretreated patients, across **multiple tumor types** and dose levels

Initial RP2D is **1500 mg IV q2w**; expansion cohorts are enrolling

As of October 2022, a total of 33 patients have been enrolled and treated with MCLA-129 in the dose escalation and dose expansion on this phase 1/2 trial.\*

*\*Since the May 8, 2022 cutoff, an additional 13 patients have been enrolled, none evaluable for response as of the August 15, 2022 data cutoff*

# Dose Expansion

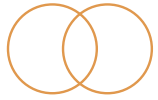
*At initial recommended phase 2 dose 1500mg q2w*



DOSE EXPANSION AT RP2D
Cohort A: NSCLC with EGFR exon20 insertion
Cohort B: NSCLC with c-MET exon14 skipping
Cohort C: HNSCC
Cohort D + 3 <sup>rd</sup> gen EGFR TKI: NSCLC 1L (EGFR sensitizing mutations)
Cohort E + 3 <sup>rd</sup> gen EGFR TKI: NSCLC post-Osimertinib

# MCLA-129: The Third Clinically Active Biclonics® from the Merus Platform

*Discovering and developing promising multi-specific antibody medicines is our core competency*



## **MCLA-129**

observed to be well tolerated with early, encouraging signs of anti-tumor activity in multiple tumor types



MCLA-129 **pre-clinical and clinical profile** suggest it successfully targets EGFR x c-MET bispecific, with ADCC activity



**Expansion Cohorts** are enrolling in key patient segments



Significant unmet clinical need in multiple solid tumor sub-groups supports large potential **commercial opportunity**



**Third current clinically active Biclonics® from Merus platform** which includes **Zeno** in NRG1+ cancer and **Peto** in HNSCC



## Q&A



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[www.merus.nl](http://www.merus.nl)

