# Merus closing in on cancer Frery Day.

**Corporate Presentation** 

January 2025



# **Disclaimer**

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 Biclonics® and Triclonics® platforms can have on cancer, our intellectual property, our product candidates' potential to treat certain types of tumors, the timing of regulatory filings and the timing and anticipated data read-outs, updates 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 out operations or require us to relinquish rights to our technologies or antibody candidates; potential delays in regulatory approval and impacts of the market volatility, and global conflict in Russia, Ukraine and the Middle East, 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 Biclonics<sup>®</sup>, and Triclonics<sup>®</sup> 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 stage of 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 Quarterly Report on Form 10-Q for the period ended September 30, 2024 filed on October 31, 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.



# **Merus Overview**



- Compelling clinical data in 1L and 2L+ recurrent/metastatic head and neck squamous cell cancer (r/m HNSCC)<sup>1,2</sup>
- Global r/m HNSCC opportunity expected to exceed \$5B in 2028<sup>3</sup>
- Phase 3 trials: 1L (LiGeR-HN1) and 2/3L (LiGeR-HN2) HNSCC enrolling
- 2L metastatic colorectal cancer (mCRC) in combination with standard chemotherapy and 3L+ petosemtamab monotherapy enrolling; 1L in combination with standard chemotherapy planned

### **Progress Across our Clinical Pipeline**

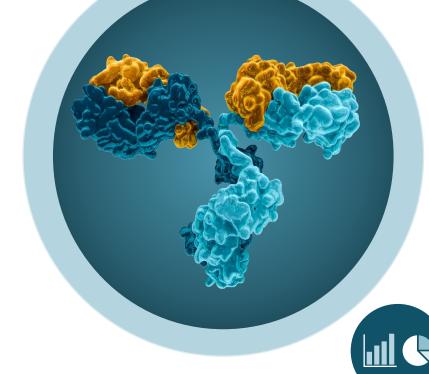
- Merus' first product approval: Bizengri® (zenocutuzumab) approved by U.S. FDA under accelerated approval for NRG1+ pancreatic adenocarcinoma and non-small cell lung cancer (NSCLC)<sup>4</sup>
- MCLA-129 demonstrated strong clinical activity in EGFRm NSCLC and METex14 NSCLC<sup>5</sup>; 2L+ EGFRm NSCLC in combination with chemotherapy enrolling
- Multiple collaboration programs developed from our Multiclonics® platforms advancing into the clinic

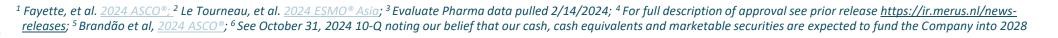
### **Unique Platform Technology Validated by Key Strategic Collaborations**

- Using novel, proprietary Multiclonics® platform technologies to discover and develop bispecific and trispecific antibodies essentially like monoclonal antibodies
- Validating discovery collaborations; potential future milestones and royalties
- Versatile platforms with opportunities for expansion beyond oncology focus

### **Strong Cash Position into 2028**<sup>6</sup>

- Cash and cash equivalents of \$783M
- Well capitalized, expected to be funded through multiple corporate milestones







# **Merus Ambitious Goals**

# Achieved in 2024



# **FDA**

Breakthrough Therapy
Designation:
Petosemtamab monotherapy
in 2L+ r/m HNSCC<sup>1</sup>

Petosemtamab in 1L r/m HNSCC 2024 ASCO ANNUAL MEETING





# 2024 and Beyond



against milestones and on clinical trial progress



### **2L+ HNSCC**

petosemtamab monotherapy at ESMO® ASIA 2024

### 1L PD-L1+ HNSCC

petosemtamab with pembrolizumab (clinical data update planned 2025)

### **mCRC**

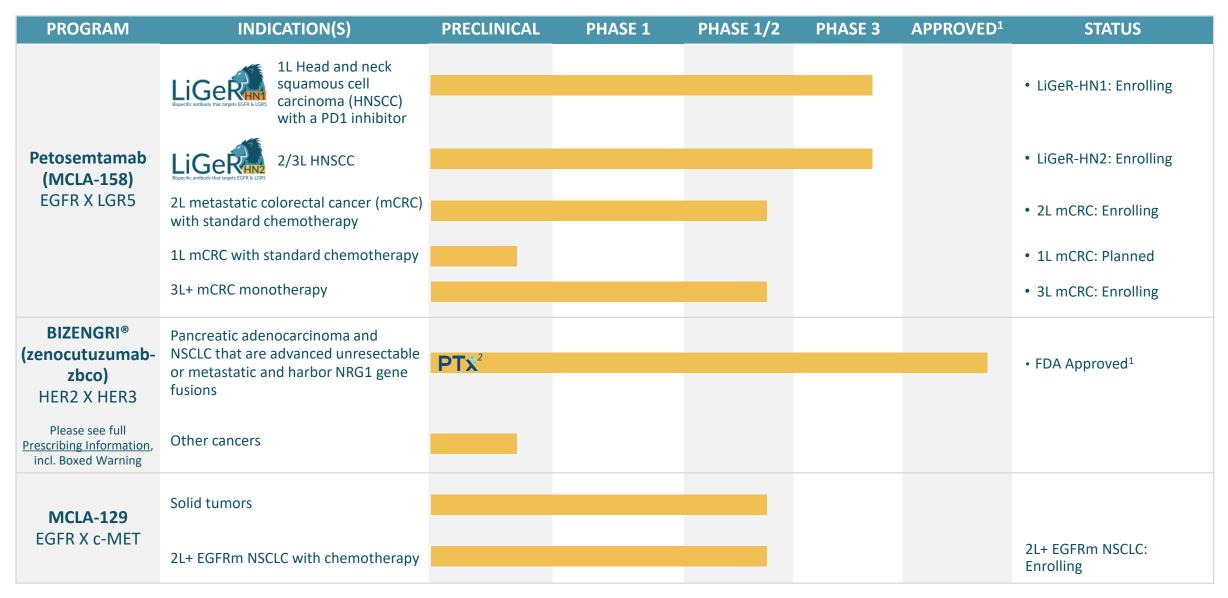
petosemtamab monotherapy and with chemotherapy (initial clinical data planned 2025)

# **Expansion Opportunities**

potential for additional exploratory indications



# **Merus Clinical Pipeline**



Merus

<sup>&</sup>lt;sup>1</sup> Approved under accelerated approval by the U.S. FDA for pancreatic adenocarcinoma or non-small cell lung cancer that is advanced unresectable or metastatic and harbors the NRG1 gene fusion—not approved in any other jurisdiction of Merus is eligible to receive milestones and royalty payments for commercialization of Zeno in the U.S. for the treatment of NRG1+ cancer. see prior release <a href="https://ir.merus.nl/news-releases">https://ir.merus.nl/news-releases</a>

# **Strategic Relationships**

# Funding the company and providing expansion opportunities













# CASE STUDY: Multi-Target Collaboration with Biohaven to Co-Develop Bispecific ADCs<sup>1</sup>

- Research and development collaboration and license agreement to co-develop three novel bispecific antibody drug conjugates (ADCs), leveraging Merus' Biclonics® technology platform, and Biohaven's next-generation ADC conjugation and payload platform technologies
- Unlocks the power of Merus' Biclonics® bispecific antibody technology with Biohaven's proprietary linker and payload, with the potential to generate novel therapeutics having enhanced specificity and potency



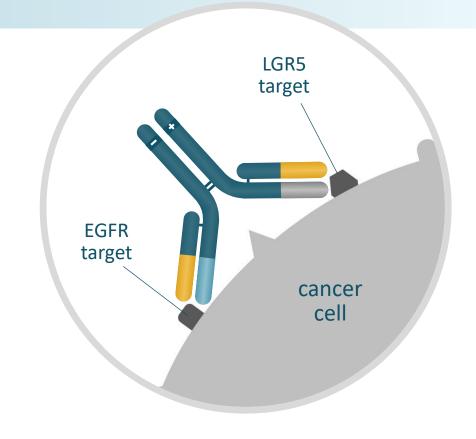
<sup>&</sup>lt;sup>1</sup> See PR News Releases - Merus

# Potential first and best in class EGFR x LGR5 Biclonics® antibody<sup>1</sup>

# **Petosemtamab**

MCLA-158 EGFR x LGR5 bispecific

- Targets EGFR and LGR5, a cancer-stem cell antigen; modifications to enhance antibody-dependent cell-mediated cytotoxicity (ADCC)
- Granted Fast Track Designation (FTD) and Breakthrough Therapy Designation (BTD) for monotherapy in 2L+ recurrent or metastatic HNSCC<sup>2</sup>
- Meaningful clinical activity as monotherapy in 2L+ HNSCC<sup>3</sup> and in combination with pembrolizumab in 1L PDL1+ HNSCC<sup>4</sup>
- Phase 3 trials: 1L PD-L1+ (LiGeR-HN1) and 2/3L (LiGeR-HN2) HNSCC enrolling
- Cohorts in 2L mCRC in combination with standard chemotherapy and 3L+ monotherapy enrolling; 1L cohort in combination with standard chemotherapy planned

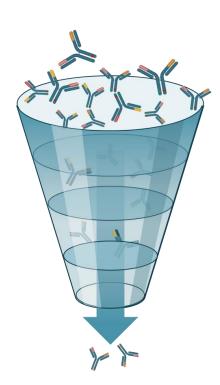




# **Petosemtamab**

# **Discovery & Mechanism of Action**

### DISCOVERY



### **Biclonics® Screen**

• >500 bispecifics: RTK x WNT

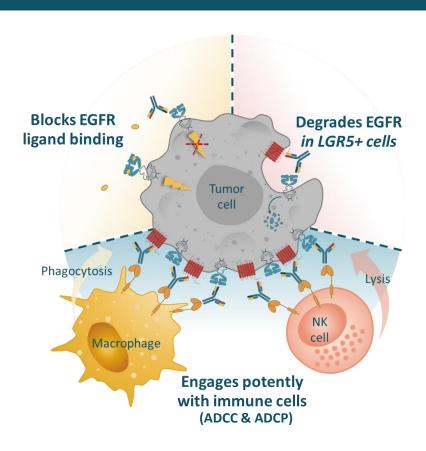
### **Growth Inhibition Score**

- Tumor vs Normal Organoid size, complexity
- Tumor growth inhibition

# EGFR x LGR5

Petosemtamab

### MECHANISM OF ACTION



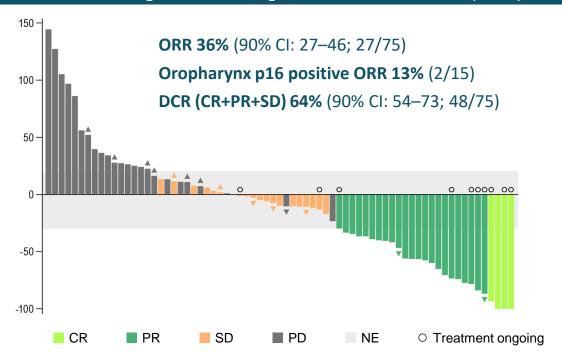
Herpers et al, Nature Cancer, 3, 418–36, 2022



# **Petosemtamab Monotherapy in 2L+ HNSCC**

# Confirmed overall response rate (ORR) 36%1

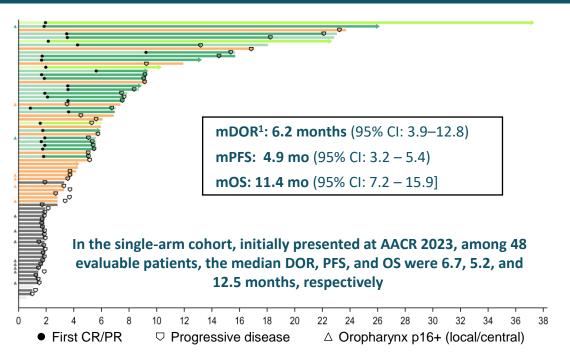
### Best Percent Change in Sum of Target Lesions From Baseline (N=75)<sup>2</sup>



### **Trial Design**

- Drug: Petosemtamab 1500 mg IV, Q2W, 28-day cycle
- Primary endpoint: ORR using RECIST v1.1 per investigator
- Data cutoff date: July 5, 2024

### Time to Response and Duration of Therapy (N=75)



### Safety

• Observed to be well-tolerated with a manageable safety profile



# Petosemtamab Safety and Pharmacokinetics in 2L+ HNSCC<sup>1</sup>

# Petosemtamab 1500 mg Q2W, safety-evaluable population (N=82)

### AEs irrespective of causality (>20% of patients)

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Preferred Term	1500 mg Q2W N=82			
Freienca ieini	All grades, n (%)	Grade ≥3, n (%)		
At least one TEAE	82 (100)	48 (59)		
Dermatitis acneiform	34 (41)	3 (4)		
Blood magnesium decreased	32 (39)	7 (9)		
Rash	24 (29)	0		
Fatigue	22 (27)	1 (1)		
Nausea	21 (26)	0		
Hypotension	20 (24)	4 (5)		
Pruritus	20 (24)	1 (1)		

### Infusion-related reactions (>10% of patients)

Preferred Term	Prior administration regimen N=49		Updated administration regimen N=33	
riciciica iciiii	All grades, n (%)	Grade 3-4, n (%)	All grades, n (%)	Grade 3, n (%)
At least one TEAE of IRR	33 (67)	12 (24)	15 (45)	3 (9)
Infusion-related reaction	12 (24)	7 (14)	7 (21)	2 (6)
Hypotension	10 (20)	4 (8)	4 (12)	0
Flushing	8 (16)	2 (4)	2 (6)	1 (3)
Nausea	6 (12)	0	2 (6)	0
Dyspnea	5 (10)	1 (2)	0	0
Erythema	5 (10)	0	0	0

# Safety

- IRRs were generally only seen on day 1 of cycle 1; the IRR mitigation strategy reduced the severity and frequency of IRRs
- Based on interim clinical data, skin toxicity such as rash and gastrointestinal side effects appear less frequent and less severe than observed for other EGFR directed antibody therapies

### **Pharmacokinetics**

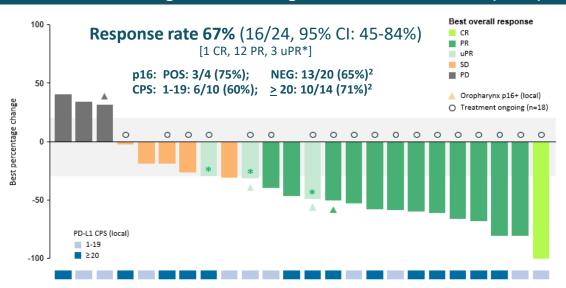
- Geometric mean steady state C<sub>trough</sub> was 68% higher with 1500 mg Q2W vs. 1100 mg Q2W
  - No positive exposure—safety (Grade ≥3 TEAE) relationship was observed
- 1500 mg Q2W was projected to achieve superior target engagement (i.e. ≥98%) for EGFR compared with 1100 mg Q2W dose



# Petosemtamab with Pembrolizumab in 1L HNSCC

# Response rate [confirmed + unconfirmed\*] 67%

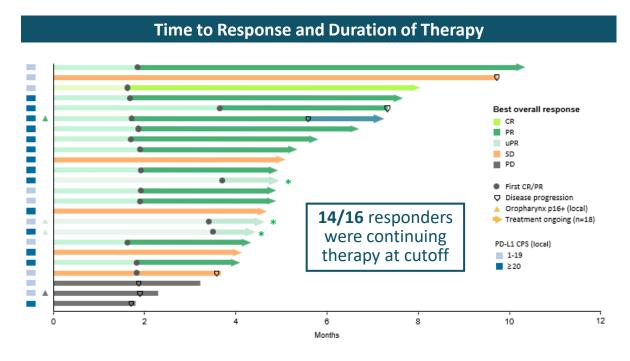
### Best Percent Change in Sum of Target Lesions From Baseline (N=24)



\*All 3 uPR were confirmed as PR after data cutoff date

### **Trial Design**

- Drug: Petosemtamab 1500 mg IV, Q2W (28-day cycle) with pembrolizumab 400 mg IV Q6W
- Primary endpoint: ORR using RECIST v1.1 per investigator
- Data cutoff date: March 6, 2024
- Enrollment/Safety population: 45 pts; Efficacy population<sup>2</sup>: 24 pts



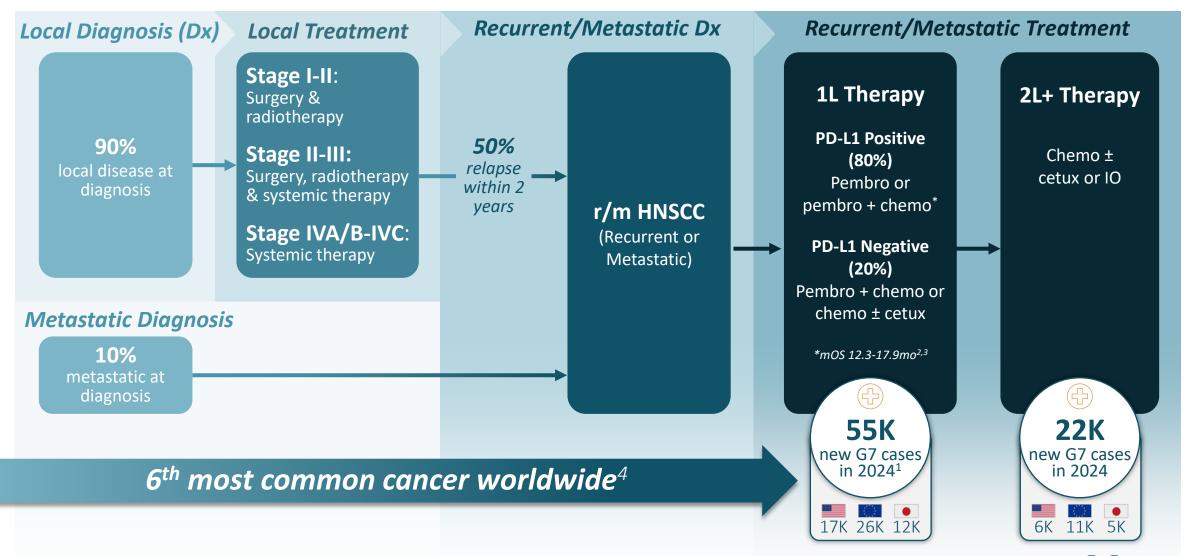
### Safety

- Favorable safety profile, no significant overlapping toxicities
- IRRs (composite term) in in 38% of patients, with 7% Grade 3; no Grade 4 or 5, mainly occurred during first infusion and were resolved
- Rechallenge after an IRR was successful in all patients rechallenged



# **HNSCC Patient Journey**

# Recurrent/metastatic head and neck cancer 1L and 2L+ treatment paradigm



# Potential market opportunity in colorectal cancer

COLORECTAL CANCER (CRC) PATIENTS

# **2022** Global Estimates<sup>1</sup>



930K deaths per year

# **2040 Global Projections**<sup>2</sup>



1.6M deaths per year (up 73%)

# **Phase 2 Trial Enrolling**

 Petosemtamab in combination with 5-fluorouracil (5-FU), leucovorin, and irinotecan (FOLFIRI) as 2L treatment of RAS/RAF wild-type metastatic CRC

### mCRC Cohorts Planned

- 1L in combination with standard chemotherapy
- 3L+ petosemtamab monotherapy

<sup>&</sup>lt;sup>1</sup> Bray, et al (2024) CA Cancer J Clin. <sup>2</sup> Morgan, et al (2022) Gut

# NOW APPROVED: First and only therapy for NRG1+ pancreatic adenocarcinoma and NRG1+ NSCLC

# **Bizengri**®

MCLA-128 or zenocutuzumab HER2 x HER3 bispecific

### **NRG1** fusions

- Translocations of the Neuregulin-1 (NRG1) gene, also called Heregulin, the ligand for the HER3 receptor. Rare events in solid tumors reported to typically occur in the absence of other cancer driver mutations<sup>1</sup>
- Reported as associated with poor prognosis<sup>1</sup>, lower response rates to standard therapy<sup>2</sup>, and shorter overall survival in lung cancer<sup>1,3</sup>

### Zeno

- Biclonics® antibody binds to HER2 and blocks HER3
- Approved under accelerated approval by U.S. FDA for NRG1+ pancreatic adenocarcinoma and NRG1+ NSCLC<sup>4</sup>



Please see full Prescribing Information, including Boxed WARNING, at

www.BIZENGRI.com/pi

<sup>&</sup>lt;sup>4</sup> For full description of approval see prior release <u>https://ir.merus.nl/news-releases</u>



<sup>&</sup>lt;sup>1</sup> Chang et al., Clin Cancer Research 2021,

<sup>&</sup>lt;sup>2</sup> Drilon et al., J Clin Oncol 2021,

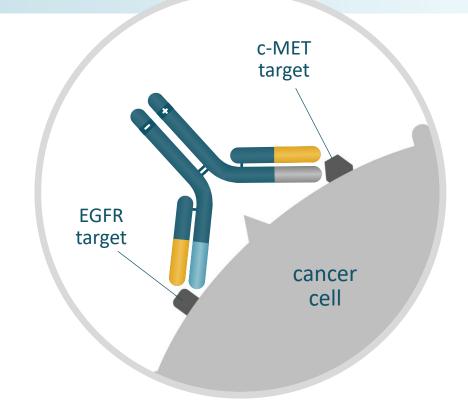
<sup>&</sup>lt;sup>3</sup> Shin et al., Oncotarget 2016,

# 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, observed preclinically to have greater potency than amivantamab in certain high-affinity (FcγRIII 158V) or low-affinity (FcγRIII 158F) variant effector cells<sup>1</sup>
- Clinically active in 1L and 2L+ EGFR mutant NSCLC<sup>2</sup> and Exon 14 Skipping Mutations (METex14) NSCLC<sup>3</sup>
- MCLA-129 in combination with chemotherapy in 2L+ EGFRm NSCLC enrolling





# MCLA-129 Monotherapy in METex14 NSCLC<sup>1</sup>

# Best % change in target lesions from baseline by RECIST v1.1 per investigator

# **Trial Design**

• Drug: MCLA-129 1500 mg IV Q2W

 Primary endpoint: ORR using RECIST v1.1 per investigator assessment

• Data cutoff date: February 6, 2024

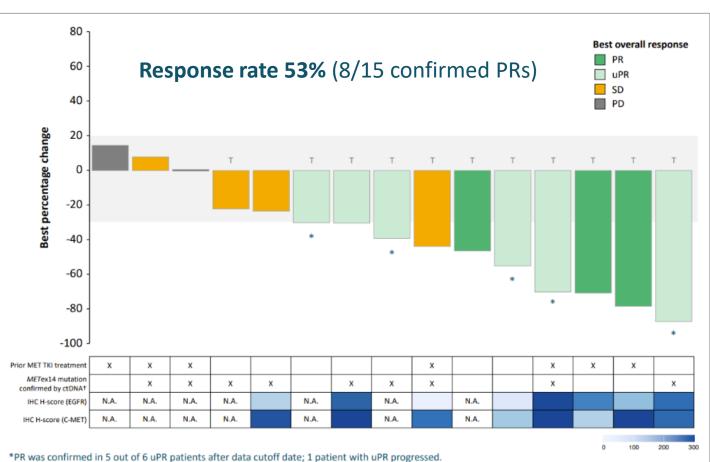
 Enrollment/Safety population: 22 patients with previously treated METex14 NSCLC

• Efficacy population<sup>2</sup>: 15 pts

# Safety

- IRRs (composite term) in 86% (18% ≥ grade(G) 3)
- Treatment discontinuations in 4 pts (18%)
- Treatment related interstitial lung disease in 1 pt (G2)
- Venous thromboembolic events in 2 pts; 1 G3 possibly treatment related, 1 G2 not treatment related

	TKI-naïve (n=8)	Prior MET TKI (n=7)
ORR, n (%)	5 (63)	3 (43)



<sup>\*</sup>PR was confirmed in 5 out of 6 uPR patients after data cutoff date; 1 patient with uPR progressed.

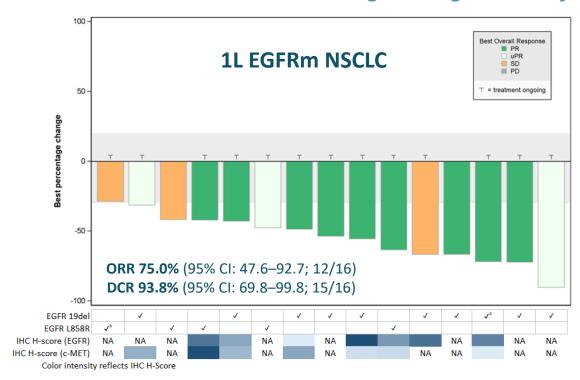
\*METex14 status was documented by site at screening; ctDNA alterations were evaluated by Guardant360\* next-generation sequencing.

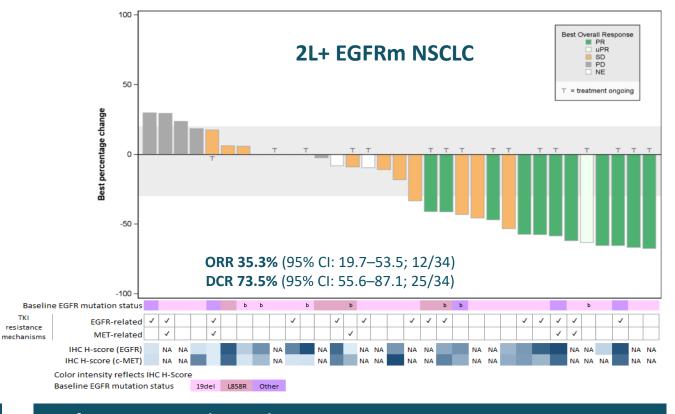
ctDNA, circulating tumor DNA; EGFR, epidermal growth factor receptor; IHC, immunohistochemistry; METex14, MET exon 14 skipping mutations; N.A., not applicable; PD, progressive disease; PR, partial response; SD, stable disease; T, treatment ongoing; TKI, tyrosine kinase inhibitor; uPR, unconfirmed partial response.



# MCLA-129 in Combination with Osimertinib in NSCLC<sup>1</sup>

Best % change in target lesions from baseline by RECIST v1.1 per investigator





### **Trial Design**

- Drug: MCLA-129 1500 mg IV Q2W & osimertinib 80 mg QD
- Primary endpoint: ORR using RECIST v1.1 per investigator assessment
- Data cutoff date: August 10, 2023
- Enrollment/Safety population: 60 EGFRm NSCLC pts; 16 1L/44 2L+
- Efficacy population<sup>2</sup>: 16 pts in 1L; 34 pts in 2L+

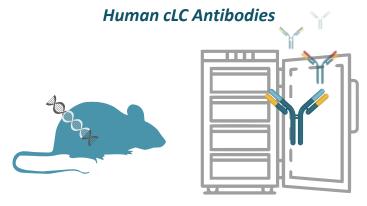
### Safety across 1L and 2L+ Cohorts

- IRRs (composite term) in 87% (12% ≥ grade(G) 3)
- Treatment discontinuations in 14 pts (23%)
- Treatment related interstitial lung disease/pneumonitis in 13 pts (22%): four G1, two G2, four G3, and three G5
- Venous thromboembolic events in 23%; 5% treatment related



# **Our Platform – Unique Capabilities in Multispecific Antibodies**

# **Generate**



# **Patented Mouse Technology**

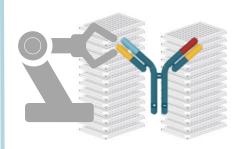
"Merus Mouse" (MeMo®) to generate diverse, high quality common light chain (cLC) antibody panels

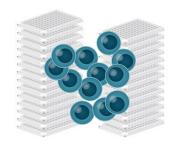
# **Established** *Inventory*

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 molecular and cellular assays

# Identify

**Best Candidates** 



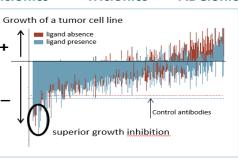




**Biclonics®** 

Triclonics®

**ADClonics®** 



Develop unique, best candidates from thousands of different molecules with potential to achieve meaningful clinical activity in patients



# Merus' Proprietary Biclonics® and Triclonics® Antibody Platform

Leveraging the success of monoclonal antibody therapies

### KEY FEATURES OF PLATFORM

# **Letting the Biology Drive Success**

- High throughput screens to select from thousands of molecules
- Biology drives the selection of the 'best' molecules
- Established methods for process development and manufacturing

# **Fully Human IgG**

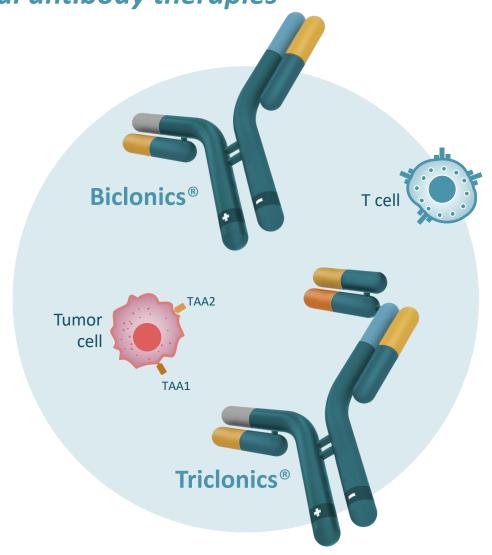
- Low immunogenicity risk and durable, consistent half-life
- Potential for ADCC enhancement and Fc domain silencing

# Novel, Innovative Tri-specific Format (Triclonics®)

- Allows for 3 specificities without the need to engineer each individual Fab
- Preferential tumor cell binding with two tumor antigens (TAA1 and TAA2)
- Potent T-cell activation in presence of tumor cells

# **Robust Intellectual Property**

• Pioneering patent estate covering platform technologies





# **Merus Overview**

# Petosemtamab: Blockbuster Potential in Multiple Oncology Indications

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