



## Petosemtamab granted Breakthrough Therapy designation by the U.S. FDA for 1L PD-L1 positive head and neck squamous cell carcinoma

February 18, 2025

### This marks the second BTD for petosemtamab in HNSCC

UTRECHT, The Netherlands and CAMBRIDGE, Mass., Feb. 18, 2025 (GLOBE NEWSWIRE) -- [Merus N.V.](#) (Nasdaq: MRUS), a clinical-stage oncology company developing innovative, full-length multispecific antibodies and antibody drug conjugates (Biclronics<sup>®</sup>, Triclronics<sup>®</sup> and ADClronics<sup>®</sup>), for cancer, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation (BTD) to petosemtamab in combination with pembrolizumab for the first-line treatment of adult patients with recurrent or metastatic programmed death-ligand 1 (PD-L1) positive head and neck squamous cell carcinoma (r/m HNSCC) with combined positive score (CPS)  $\geq 1$ .

This second BTD designation follows the initial receipt of BTD and Fast Track designation for petosemtamab for the treatment of patients with r/m HNSCC whose disease has progressed following treatment with platinum-based chemotherapy and an anti-programmed cell death protein 1 (anti-PD-1) antibody announced in May 2024 and August 2023, respectively.

BTD is supported by updated data from the ongoing phase 1/2 open-label, multicenter trial evaluating petosemtamab in combination with pembrolizumab in 1L HNSCC expressing PD-L1 (CPS $\geq 1$ ) (NCT03526835). Data for this cohort was initially presented at the American Society of Clinical Oncology<sup>®</sup> (ASCO<sup>®</sup>) Annual Meeting 2024, which demonstrated a 67% response rate among 24 evaluable patients. The oral presentation was detailed in our press release, [Merus' Petosemtamab in Combination with Pembrolizumab Interim Data Demonstrates Robust Response Rate and Favorable Safety Profile in 1L r/m HNSCC](#) (May 28, 2024). In the BTD application, Merus provided updated interim clinical data on efficacy, durability and safety of the cohort of petosemtamab with pembrolizumab in 1L PD-L1+ r/m HNSCC.

"We believe petosemtamab's second BTD continues to validate its potential to become a new standard of care for patients with r/m HNSCC and underscores our commitment to accelerate development of petosemtamab for these patients," said Fabian Zohren, M.D., Ph.D., Chief Medical Officer of Merus. "Importantly, this designation indicates the interim clinical data we shared with the FDA demonstrates petosemtamab's potential for substantial improvement over available therapies in the 1L PD-L1+ setting."

BTD is intended to expedite the development and review of a medicine to treat a serious or life-threatening condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on clinically significant endpoints over available therapies. BTD allows for more intensive FDA guidance on an efficient drug development program, an organizational commitment involving senior managers, and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review, and eligibility for rolling review and priority review. With this BTD, Merus plans to engage in these discussions with the FDA in an expedited manner as we move toward our goal of a potential Biologics License Application (BLA) submission.

#### About LiGeR-HN1

LiGeR-HN1, a phase 3 trial, will evaluate the safety and efficacy of petosemtamab in combination with pembrolizumab, compared to pembrolizumab in 1L PD-L1+ r/m HNSCC patients. The trial is open to adult patients eligible to receive pembrolizumab as 1L monotherapy with tumors expressing PD-L1, CPS  $\geq 1$ . The primary endpoints are overall response rate as assessed by BICR based on RECIST v1.1 and overall survival. Secondary endpoints are duration of response and progression free survival. Merus plans to enroll approximately 500 patients in the trial.

#### About LiGeR-HN2

LiGeR-HN2, a phase 3 trial, will evaluate the safety and efficacy of petosemtamab compared to investigator's choice of methotrexate, docetaxel, or cetuximab in 2/3L r/m HNSCC patients. The trial is open to adult patients that have progressed on or after anti-PD-1 therapy and platinum-containing therapy. The primary endpoints are overall response rate as assessed by BICR based on RECIST v1.1 and overall survival. Secondary endpoints are duration of response and progression free survival. Merus plans to enroll approximately 500 patients in the trial.

#### About Head and Neck Cancer

Head and neck squamous cell carcinoma (HNSCC) describes a group of cancers that develop in the squamous cells that line the mucosal surfaces of the mouth, throat, and larynx. These cancers begin when healthy cells change and grow in an unchecked manner, ultimately forming tumors. HNSCC is generally associated with tobacco consumption, alcohol use and/or HPV infections, depending on where they develop geographically. HNSCC is the sixth most common cancer worldwide and it is estimated that there were more than 930,000 new cases and over 465,000 deaths from HNSCC globally in 2020.<sup>1</sup> The incidence of HNSCC continues to rise and is anticipated to increase by 30% to more than 1 million new cases annually by 2030.<sup>2</sup> HNSCC is a serious and life-threatening disease with poor prognosis despite currently available standard of care therapies.

<sup>1</sup> Sung et al. *CA Cancer J Clin*, 71:209-49, 2021; <sup>2</sup> Johnson, D.E., Burtneess, B., Leemans, C.R. et al. *Head and neck squamous cell carcinoma*. *Nat Rev Dis Primers* 6(1):92, 2020

#### About Petosemtamab

Petosemtamab, or MCLA-158, is a Biclronics<sup>®</sup> low-fucose human full-length IgG1 antibody targeting the epidermal growth factor receptor (EGFR) and the leucine-rich repeat containing G-protein-coupled receptor 5 (LGR5). Petosemtamab is designed to exhibit three independent mechanisms of action including inhibition of EGFR-dependent signaling, LGR5 binding leading to EGFR internalization and degradation in cancer cells, and enhanced antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP) activity.

#### About Merus N.V.

[Merus](#) is a clinical-stage oncology company developing innovative full-length human bispecific and trispecific antibody therapeutics, referred to as [Multiclronics<sup>®</sup>](#). Multiclronics<sup>®</sup> are manufactured using industry standard processes and have been observed in preclinical and clinical studies to have

several of the same features of conventional human monoclonal antibodies, such as long half-life and low immunogenicity. For additional information, please visit [Merus' website](#), [Twitter](#) and [LinkedIn](#).

### Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation, the potential benefits of BTd for petosemtamab's development for the first-line treatment of adult patients with recurrent or metastatic programmed death-ligand 1 (PD-L1) positive head and neck squamous cell carcinoma (R/M HNSCC) with CPS  $\geq 1$ ; Merus' belief that petosemtamab's second BTd continues to validate its potential to become a new standard of care for patients with r/m HNSCC; Merus' commitment to accelerate development of petosemtamab for these patients; Merus' belief that this designation indicates the interim clinical data shared with the FDA demonstrates petosemtamab's potential for substantial improvement over available therapies in the 1L PD-L1+ setting; the potential for BTd to expedite the development and review of a medicine to treat a serious or life-threatening condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on clinically significant endpoints over available therapies; the potential of BTd to allow for more intensive FDA guidance on an efficient drug development program, an organizational commitment involving senior managers, and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review, and eligibility for rolling review and priority review; and Merus' plans to engage in these discussions with the FDA in an expedited manner as we move toward our goal of a potential Biologics License Application (BLA) submission. 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: 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, which would impact our ability to commercialize our product candidates and affect our ability to generate revenue; 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 delays in enrollment of patients, which could affect the receipt of necessary regulatory approvals; our reliance on third parties to conduct our clinical trials and the potential for those third parties to not perform satisfactorily; impacts of the volatility in the global economy, including global instability, including the ongoing conflicts in Europe and the Middle East; we may not identify suitable Biclomics<sup>®</sup> or bispecific antibody candidates under our collaborations or our collaborators may fail to perform adequately under our collaborations; 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 may be found invalid, unenforceable, circumvented by competitors and our patent applications may be found not to comply with the rules and regulations of patentability; we may fail to prevail in potential lawsuits for infringement of third-party intellectual property; and our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. 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 with the Securities and Exchange Commission, or SEC, on October 31, 2024, 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 press release. Any such forward-looking statements represent management's estimates as of the date of this press release. 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, except as required under applicable law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release. Multiclomics<sup>®</sup>, Biclomics<sup>®</sup>, Triclomics<sup>®</sup> and ADClomics<sup>®</sup> are registered trademarks of Merus N.V.

#### Investor and Media Inquiries:

Sherri Spear  
Merus N.V.  
SVP Investor Relations and Strategic Communications  
617-821-3246  
[s.spear@merus.nl](mailto:s.spear@merus.nl)

Kathleen Farren  
Merus N.V.  
Assoc. Director IR/Corp Comms  
617-230-4165  
[k.farren@merus.nl](mailto:k.farren@merus.nl)

Source: Merus N.V.