Merus Announces Unique Mechanism of Action of MCLA-128 That Potently Blocks HER3 Signaling Published in Cancer Cell

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UTRECHT, The Netherlands, May 15, 2018 (GLOBE NEWSWIRE) -- Merus N.V. (Nasdaq:MRUS), a clinical-stage immuno-oncology company developing innovative bispecific antibody therapeutics (Biclonics®), today announced the unique mechanism of action (MOA) of MCLA-128, the Company's most-advanced Biclonics® candidate that binds to HER2 and HER3-expressing solid tumor cells and potently blocks signaling HRG/HER3 tumor-signaling pathway, was published in the May 2018 edition of Cancer Cell titled, "Unbiased Combinatorial Screening Identifies a Bispecific IgG1 that Potently Inhibits HER3 Signaling via HER2-Guided Ligand Blockade."

"This study demonstrates the power of empirical functional screening to unlock innovative biology unique to the bispecific antibody format," said Mark Throsby, Ph.D., Executive Vice President and Chief Scientific Officer of Merus. "The HRG/HER3 tumor-signaling pathway has been difficult to target effectively. Using unbiased combinatorial screening, we identified a bispecific antibody that employs a unique mechanism to selectively and potently block signaling down this pathway (Dock & Block™). The development candidate advanced from this work, MCLA-128, is being evaluated in multiple clinical studies where this pathway is believed to drive tumor growth and resistance to existing standard of care therapies. Our expectation is MCLA-128 will improve the treatment of cancer patients in a variety of indications."

PB4188, the research candidate described in the paper, was identified after screening a large panel of >500 bispecific antibodies in relevant functional assays. Using a structure function approach, Merus demonstrated that PB4188 employs a unique mechanism to inhibit the growth of tumors by docking to HER2 and blocking ligand interaction with HER3, thereby preventing stabilization of the HER2:HER3 heterodimer and sustained signaling. The activity of PB4188 was unaffected by increasing concentrations of HRG, the ligand for HER3 which mirrors the autocrine or paracrine signaling environment of the tumor, in contrast to monoclonal antibodies against the same targets, tested as single agents or in combination. These in vitro findings were verified in four independent and pathophysiologically relevant xenograft models, which showed dose dependency and correlation with relevant pharmacodynamic factors.

MCLA-128, the development candidate of PB4188, is currently being studied in a Phase 2 clinical trial in combination with current standards of care in two metastatic breast cancer (MBC) populations, including HER2-positive MBC patients and hormone receptor positive/HER2-low MBC patients. MCLA-128 is also being studied as a single agent in an ongoing Phase 1/2 trial in gastric, ovarian, endometrial and non-small cell lung cancer patients.

About Merus N.V.

Merus is a clinical-stage immuno-oncology company developing innovative full-length human bispecific antibody therapeutics, referred to as Biclonics®. Biclonics®, which are based on the full-length IgG format, 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. Merus' most advanced bispecific antibody candidate, MCLA-128, is being evaluated in a Phase 2 combination trial in two metastatic breast cancer populations. MCLA-128 is also being evaluated in a Phase 1/2 clinical trial in gastric, ovarian, endometrial and non-small cell lung cancers. Merus' second most advanced bispecific antibody candidate, MCLA-117, is being developed in a Phase 1 clinical trial in patients with acute myeloid leukemia. The Company also has a pipeline of proprietary bispecific antibody candidates in preclinical development, including MCLA-158, which is designed to bind to cancer stem cells and is being developed as a potential treatment for colorectal cancer and other solid tumors, as well as MCLA-145, which is designed to bind to PD-L1 and a non-disclosed second immunomodulatory target, which is being developed in collaboration with Incyte Corporation. For additional information, please visit Merus' website, www.merus.nl.

Forward Looking Statement

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 formulation of clinical development plans and clinical development of our bispecific antibody candidates, the design and treatment potential of our bispecific antibody candidates including MCLA-128, MCLA-117, MCLA-158 and MCLA-145, the ability of MCLA-128 to improve the treatment of cancer patients in a variety of indications, the treatment potential of the mechanism of action of MCLA-128, and the ability of Merus' functional screening to unlock innovative biology unique to the bispecific antibody format.

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 Biclonics® and bispecific 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; we may not identify suitable Biclonics® or bispecific antibody candidates under our collaboration with Incyte or Incyte may fail to perform adequately under our collaboration; 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 existing and 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 Annual Report on Form 20-F filed with the Securities and Exchange Commission, or SEC, on April 28, 2017, 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.

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