CD137 and PD-L1 bispecific antibody with context-dependent T cell activation

UTRECHT, Netherlands, April 01, 2019 (GLOBE NEWSWIRE) -- Merus N.V. (Nasdaq: MRUS) (“Merus”, “we”, “our” or the “Company”), a clinical-stage immuno-oncology company developing Biclonics®, innovative full-length human bispecific antibody therapeutics, and in collaboration with Incyte (Nasdaq: INCY), presented preclinical data from the MCLA-145 program at the American Association for Cancer Research (AACR) Annual Meeting 2019 in Atlanta, GA. Merus and Incyte presented two posters outlining preclinical data on MCLA-145, the Biclonics® program targeting CD137 and PD-L1, on Sunday, March 31.

“MCLA-145 data presented at AACR demonstrate potent triple action, designed to recruit and activate T cells through CD137 and prevent their exhaustion through inhibition of PD-1 for patients with solid tumors,” said Mark Throsby, EVP and Chief Scientific Officer of Merus. “Because the T cell activation is context-dependent, requiring PD-L1 expression in the tumor microenvironment, MCLA-145 has the potential to overcome known side effects of CD137 agonists currently in development.”

MCLA-145 Poster Presentations at AACR 2019:

I. An unbiased screen identifies a CD137xPD-L1 bispecific IgG1 antibody with unique T cell activation and binding properties

Abstract and Poster number: #541/5
Session: PO.IM02.16 - Therapeutic Antibodies 1

The poster outlines data demonstrating MCLA-145 binds to CD137 and PD-L1 with relative high affinity, and importantly, the activation of CD137 signaling specifically occurs in the presence of PD-L1 expressing cells through a ‘trans’ activation mechanism. MCLA-145 blocks the PD-1 checkpoint inhibition pathway resulting in T cell activation independent of CD137 agonist activity.

II. A bispecific Fc-silenced IgG1 antibody (MCLA-145) requires PD-L1 binding to activate CD137

Abstract and Poster number: #539/3
Session: PO.IM02.16 - Therapeutic Antibodies 1

The poster shows MCLA-145 induces CD137 signaling specifically in the presence of PD-L1 expressing cells, with signaling strength directly correlated to PD-L1 expression level. In preclinical studies, MCLA-145 was shown to induce cytokine secretion from T cells, to overcome the suppressive activity of M2 macrophages and Tregs, and to have antitumor activity associated with the recruitment of CD8+ T cells into the tumor microenvironment.

The clinical trial for MCLA-145 is expected to initiate in the second quarter of 2019. Copies of the posters are available on the Merus website in the events section, which can be accessed via the link here. Full abstracts of the presentations can be accessed on the AACR website at www.aacr.org.

About MCLA-145

Discovered through an unbiased functional screening of multiple immunomodulatory target combinations, MCLA-145 is a Biclonics® T-cell agonist that binds with high affinity and specificity to human PD-L1 and CD137 in preclinical models. The unique immunostimulatory profile of MCLA-145 derives from the ability to potently activate immune effector cells in the context of the tumor microenvironment while simultaneously blocking inhibitory signals in the same immune cell population. Merus is developing MCLA-145 as part of a collaboration entered into with Incyte Corporation in December 2016 to potentially develop and commercialize up to 11 bispecific and monospecific antibodies from the Merus Biclonics® platform. Under the terms of the collaboration, Merus will retain all rights to develop and commercialize MCLA-145, if approved, in the United States, while Incyte has rights to develop and commercialize MCLA-145, if approved, outside the United States.

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. For additional information on the company and programs, please visit Merus’ website, www.merus.nl.

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 for the design, activity and efficacy of MCLA-145 as described in preclinical studies, including, without limitation statements regarding the characteristics and immunostimulatory profile of MCLA-145, such as inducing CD137 to signal specifically in the presence of PD-L1 expressing cells, with signaling strength directly correlated to PD-L1 expression level, its capability to induce cytokine secretion from T cells, to overcome the suppressive activity of M2 macrophages and Tregs, and to have antitumor activity associated with the recruitment of CD8+ T cells into the tumor microenvironment and its capacity for CD137 signaling to specifically occur in the presence of PD-L1 expressing cells through a ‘trans’ activation mechanism and potential to block the PD-1 checkpoint inhibition pathway resulting in T cell activation independent of CD137 agonist activity inducement, and this profile having a potential of MCLA-145 to overcome known side effects of CD137 agonists; the development and or timing of MCLA-145, Biclonics® program; the continuing collaboration with Incyte on MCLA-145’s global development, and potential to develop and commercialize up to 11 bispecific and monospecific antibodies from the Merus Biclonics® platform; and whether any of the programs under the collaboration will be successful, including for
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 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 (the “SEC”) on April 30, 2018, 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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