

Merus

Merus Bispecific Antibody MCLA-128 Shows Encouraging Early Clinical Activity in Patients with Cancers Harboring NRG1 Gene Fusions

October 27, 2019

Tumor shrinkage observed in three patients harboring NRG1 fusions (two pancreatic, one non-small cell lung cancer) presented by investigators at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

Of nine patients enrolled across the MCLA-128 Early Access Program and the eNRGy Clinical Trial, four of seven treated showed clinical activity, two are too early in treatment for first assessment

Company to host investor call to review presented data and provide an update on MCLA-128 program on Monday, October 28th at 8:00 a.m. ET

UTRECHT, The Netherlands, and BOSTON, Oct. 27, 2019 (GLOBE NEWSWIRE) -- Merus N.V. (Nasdaq: MRUS), a clinical-stage company developing innovative, full-length bispecific antibodies (Biclonics®), today announced initial clinical data for three patients with cancers harboring NRG1 fusions treated with MCLA-128 through an Early Access Program (EAP), and provided an overall update on the MCLA-128 clinical programs. Data on the three EAP patients were presented today by study investigators at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston, MA.

Investigators from Memorial Sloan Kettering Cancer Center (MSKCC) provided a summary and initial data concerning the treatment of three cancer patients harboring NRG1 fusions with MCLA-128 at 750 mg administered intravenously every other week. These patients' NRG1 gene fusions were identified using RNA-based sequencing. Assessments from this EAP program were conducted locally at MSKCC. All three patients exhibited tumor shrinkage, symptomatic improvement and durability up to their most recent assessment. All three patients currently remain on treatment.

- **Pancreatic Ductal Adenocarcinoma (PDAC) EAP patient 1:** imaging at 8 weeks showed a 44% reduction in tumor diameter, which further improved to a 54% reduction at the following confirmatory 5-month scan (partial response (PR) by RECIST v1.1). Positron Emission Tomography (PET) imaging showed no evidence of metabolically active tumor, and relevant serum biomarker (CA 19-9) showed improvement within the first 4 weeks. Also, within weeks of the first dose, the patient's symptoms, including fatigue and weight loss, improved. The patient remains on treatment after over 7 months of therapy.
- **PDAC EAP patient 2:** imaging at 7 weeks showed 22% reduction in tumor diameter and showed a 25% reduction at the following confirmatory 5-month scan (stable disease (SD) by RECIST v1.1); PET imaging showed no evidence of metabolically active tumor. The patient's tumor-related abdominal pain improved following treatment. The patient remains on treatment after over 7 months of therapy.
- **Non-small cell lung cancer (NSCLC) EAP patient 3:** imaging at 8 weeks showed a 33% reduction in tumor diameter which further improved to a 41% reduction at the following confirmatory 5-month scan (PR by RECIST v1.1) and improvement in brain metastases. Prior to MCLA-128 treatment, the patient progressed on six lines of therapy, including the tyrosine kinase inhibitor afatinib. The patient remains on treatment after approximately 5 months of therapy.

"These initial data are an important proof-of-concept demonstrating the promise of targeting NRG1 fusions with MCLA-128," said Alison Schram, MD, a medical oncologist in the Early Drug Development Service at MSKCC, and investigator for the three patients presented today. "It is notable that two of the patients described have pancreatic cancer, a disease with a poor prognosis and limited therapeutic options. MCLA-128's mechanism of action addresses the specific molecular abnormality in cancers harboring NRG1 fusions by binding to HER2 and blocking the interaction of the NRG1 fusion oncoprotein with HER3, and may make MCLA-128 uniquely suited to target this distinct oncogenic driver."

MCLA-128 continues to be well tolerated in the Phase 1/2 clinical trial, which is consistent with prior reports. As of January 2019, 117 patients treated with single-agent MCLA-128 with dosing regimens ranging from weekly to once every three weeks, reported mostly mild to moderate adverse events (AEs). The incidence of grade 3 and 4 AEs irrespective of causality was 37% and 3% respectively, with the incidence of suspected drug-related grade 3 AEs of about 4% and no suspected drug-related grade 4 events. One patient experienced a grade 5 hypersensitivity reaction. To date, the safety results for MCLA-128 in patients with cancers harboring NRG1 fusions has been consistent with what has been previously reported in the overall patient population treated with MCLA-128.

The materials presented at the AACR-NCI-EORTC conference, as well as additional pre-clinical and clinical data on MCLA-128, can be found on the Merus website, <https://merus.nl/publications/>.

Overall MCLA-128 Program Update

MCLA-128 is currently being evaluated in both an ongoing Phase 1/2 trial in patients harboring NRG1 fusions and a Phase 2 trial in patients with metastatic breast cancer. The Phase 1/2 eNRGy trial was amended June 2019 to focus on patients with solid tumors diagnosed as harboring an NRG1 fusion.

MCLA-128 NRG1 Experience to Date from the EAP and Phase 1/2 Clinical Trial (eNRGy trial) in Solid Tumors

As of October 27, 2019, nine patients identified with cancers harboring NRG1 fusions (three PDAC patients and six NSCLC patients) have been enrolled and treated with MCLA-128 across the EAP and eNRGy trial. Of the nine patients treated, six have had at least one evaluation and all patients had previously progressed through standard of care.

Two PDAC patients were treated under the EAP (each enrolled under single patient INDs) at MSKCC with data presented today showing tumor shrinkage and symptomatic improvement. These patients remain on treatment after over 7 months of therapy. A third EAP PDAC patient was enrolled under a single patient IND outside of MSKCC. This patient received two treatments with MCLA-128, at a four-week non-standard interval due to severity of the patient's illness, and was non-evaluable, passing away due to complications related to the underlying disease prior to a first tumor evaluation.

Of the six NSCLC patients, one patient with data presented today was treated under the EAP and exhibited a confirmed PR by RESIST 1.1 criteria and remains on treatment after approximately 5 months of therapy. The other five patients were enrolled in the MCLA-128 eNRGy clinical trial. Of these, one patient had stable disease for greater than 7 months but discontinued the trial due to poor adherence to the treatment protocol (unrelated to any AE or lack of efficacy); two patients had progressive disease and are no longer on the trial; and two patients have only recently started treatment and have not yet been assessed for response.

"In summary, we are very encouraged by the early responses observed in these several patients with cancers harboring NRG1 fusions treated with MCLA-128," said Ton Logtenberg, Ph.D., President and Chief Executive Officer of Merus. "We are focused on our plan to continue to identify and recruit patients that may be amenable to MCLA 128 therapy, and to execute on our recently amended clinical development strategy for the program. We expect to next report on interim NRG1 data at a medical conference by the end of 2020, when we may be able to better characterize the activity of MCLA-128 in a larger set of patients and with more mature data."

MCLA-128 Phase 2 Combination Trial Update in Metastatic Breast Cancer

Following enrollment completion, Merus does not have plans to advance into a Phase 3 clinical trial in metastatic breast cancer or gastric cancer in the absence of a collaborator and intends instead to refocus efforts on the MCLA-128 NRG1 eNRGy trial as well as its other clinical and late-stage preclinical pipeline programs.

In patients enrolled as of August 31, 2019, in the Phase 2 combination trial in metastatic breast cancer, Merus conducted an unplanned interim efficacy analysis with a data cut-off of October 23, 2019. For this analysis, Disease Control Rate¹ (DCR) and Overall Response Rate² (ORR) were estimated in both cohorts, "HER2+" and "ER+/HER2^{low}". Patients in the metastatic breast cancer trial were not evaluated for NRG1 fusions.

In the HER2+ cohort, 24 patients were treated with MCLA-128 and a combination of trastuzumab and vinorelbine, and the estimated DCR observed was 75%. The estimated ORR was 4% (confirmed), 17% (unconfirmed) including 3 PRs and 1 CR. All patients were previously treated with trastuzumab, pertuzumab, and an anti-HER2 antibody drug conjugate. The median number of prior lines of anti-HER2 therapy in the metastatic setting was three, and 71% of patients had visceral involvement.

In the ER+ cohort, 40 patients were treated with MCLA-128 and continuation of endocrine therapy on which they progressed prior to study entry, and the estimated DCR observed was 40%. The ORR was 0%. All patients were previously treated with CDK4/6 inhibitors. The median number of prior lines of endocrine therapy in the metastatic setting was two, and 85% of patients had visceral involvement.

Enrollment in the ER+ cohort is now closed, having reached the minimum target accrual of 40 patients. Merus plans to continue to enroll another approximately 10 patients in the HER2+ cohort to reach the target accrual.

Merus expects to present mature results, including the primary endpoint of clinical benefit rate at 24 weeks for both cohorts in this trial, at a medical conference in 2020.

¹ Disease Control Rate is defined as the proportion of patients at first scheduled assessment who have achieved complete response, partial response and or stable disease as the best overall response to therapy.

² Overall Response Rate is defined as the proportion of patients who have a partial or complete response as the best overall response to therapy.

Company Conference Call and Webcast Information

Merus N.V. will host a conference call and Q&A on Monday, October 28, 2019 at 8:00 a.m. ET to discuss the presented materials. To participate in the conference call, please dial (877) 260-1463 (domestic) or (706) 643-5907 (international) and refer to conference ID 7229788. You may also access the call via webcast [here](#). A replay will be available shortly after the conclusion of the call and archived on the company's website for a limited time.

About MCLA-128

MCLA-128 is an antibody-dependent cell-mediated cytotoxicity (ADCC) -enhanced Biclomics® that utilizes Merus Dock & Block® mechanism and inhibits the neuregulin/HER3 tumor-signaling pathway in solid tumors. MCLA-128 is believed to target the HER3 signaling pathway and to overcome the resistance of tumor cells to HER2-targeted therapies using two mechanisms: blocking growth and survival pathways to stop tumor expansion and recruitment and enhancement of immune effector cells to eliminate the tumor. Learn more about MCLA-128 Dock & Block® at <https://merus.nl/technology/>

About NRG1 Fusions

The NRG1 gene encodes for neuregulin (also known as heregulin), the ligand for HER3. Fusions between NRG1 and partner genes are rare genetic events occurring in patients with certain lung, pancreatic and other solid tumors, associated with activation of HER2/HER3 signaling and growth of cancer cells. Overall projections for NRG1 fusions occurrence are based on limited published information at present. Based on the current literature available, Merus estimates NRG1 fusions occur at a rate of approximately 0.3% – 3.0% in NSCLC, 0.5% - 1.5% in PDAC, and less than 1% in all other tumor types.

In preclinical studies, the mechanism by which the NRG1 fusion protein stimulates tumor growth has been observed to be especially sensitive to inhibition by the MCLA-128 Dock & Block® mechanism of binding (docking) to HER2 and blocking the interaction of HER3 with its ligand neuregulin or with the NRG1 fusion protein. In preclinical studies, Merus has observed that MCLA-128 is capable of potent inhibition of neuregulin-driven HER2/HER3 heterodimer formation and tumor growth in models harboring NRG1 fusions.

About the eNRGy clinical trial

The Merus eNRGy clinical trial is a global Phase 1/2 study of MCLA-128 monotherapy in patients with solid tumors harboring NRG1 fusions, enrolling three cohorts: NSCLC, PDAC, and all other tumor types. More information on NRG1 and MCLA-128 can be found on Merus' websites: NRG1.com or www.merus.nl. More information on the clinical trial generally may be found at clinicaltrials.gov. To learn more about the eNRGy trial, patients or clinicians may call the Merus NRG1 Physician and Patient Clinical Trial Hotline 1-833-NRG-1234.

About Merus NV

Merus is a clinical-stage immuno-oncology company developing innovative full-length human bispecific antibody therapeutics, referred to as Biclomics®. Biclomics® 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, www.merus.nl and <https://twitter.com/MerusNV>.

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 statements regarding clinical development plans for MCLA-128 including plans to not advance into a Phase 3 clinical trial in the absence of a collaborator and plan to obtain a collaborator, the timing of clinical trial results, estimated DCR and ORR in the Phase 2 trial of MCLA-128, enrollment plans for the HER2+ cohort and eNRGy clinical trial, MCLA-128's mechanism of action and potential to be uniquely suited to target the oncogenic driver of NRG1 fusions across multiple cancer subtypes, and projections and estimates regarding the occurrence of NRG1 fusions. 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 Biclronics® 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, including for the treatment of rare subpopulations such as NRG1 fusions, 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 Biclronics® or bispecific antibody candidates under our collaboration with Incyte or any of our other collaborators, or Incyte or any of our other collaborators may fail to perform adequately under our collaborations with them; 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 ("SEC"), on April 3, 2019, 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.

Biclronics® is a registered trademark of Merus N.V.

Investor and Media Inquiries:

Jillian Connell
Merus N.V.
Investor Relations and Corporate Communications
617-955-4716
j.connell@merus.nl

Source: Merus N.V.