Merus Announces FDA Approval of BIZENGRI® (zenocutuzumab-zbco) for NRG1+ Pancreatic Adenocarcinoma and NRG1+ Non–Small Cell Lung Cancer (NSCLC) Based on Safety and Efficacy Data From the eNRGy Study

December 4, 2024

- BIZENGRI® is the first and only therapy approved by the FDA specifically for pancreatic adenocarcinoma and NSCLC that harbor *NRG1* gene fusions and are advanced unresectable or metastatic[1]
- Merus and Partner Therapeutics announced a license agreement for U.S. commercialization

UTRECHT, The Netherlands and CAMBRIDGE, Mass., Dec. 04, 2024 (GLOBE NEWSWIRE) -- Merus N.V. (Nasdaq: MRUS) [Merus, the Company, we, or our], a clinical-stage oncology company developing innovative, full-length, multispecific antibodies (Biclonics® and Triclonics®), announced today that the U.S. Food and Drug Administration (FDA) approved BIZENGRI® (zenocutuzumab-zbco), the first and only treatment indicated for adults with pancreatic adenocarcinoma or non–small cell lung cancer (NSCLC) that are advanced unresectable or metastatic and harbor a neuregulin 1 (*NRG1*) gene fusion who have disease progression on or after prior systemic therapy. These indications are approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). BIZENGRI® has a Boxed WARNING for Embryo-Fetal Toxicity and warnings for infusion-related reactions (IRRs), hypersensitivity and anaphylactic reactions, interstitial lung disease (ILD)/pneumonitis, and left ventricular dysfunction.[1] See Important Safety Information below.

We believe this approval fills an important need for patients with *NRG1*+ cancer who have not previously had treatment options approved to specifically target this driver. BIZENGRI® (zenocutuzumab-zbco) 20 mg/mL Injection for Intravenous Use is expected to be available to patients in the coming weeks.

“The FDA approval of BIZENGRI® marks an important milestone for patients with pancreatic adenocarcinoma or NSCLC that is advanced unresectable or metastatic and harbors the *NRG1* gene fusion. I have seen firsthand how treatment with BIZENGRI® can deliver clinically meaningful outcomes for patients,” said Alison Schram, MD, an attending medical oncologist in the Early Drug Development Service at Memorial Sloan Kettering Cancer Center and a principal investigator for the ongoing eNRGy trial. “I am extraordinarily grateful for the patients and families who participated in the trial.”

“BIZENGRI® is Merus’s first approved medicine based on our highly innovative and proprietary Biclonics® technology platform and offers significant promise for patients with *NRG1*+ pancreatic adenocarcinoma and *NRG1*+ NSCLC,” said Shannon Campbell, Chief Commercial Officer of Merus. “This approval is a testament to both our technology and strong execution as we continue to develop our multispecific platforms and pipeline, including our lead asset petosemtamab.”

The approval of BIZENGRI® is based on data from the eNRGy trial, a multicenter, open-label clinical trial that enrolled patients with *NRG1*+ pancreatic adenocarcinoma or *NRG1*+ NSCLC that is advanced unresectable or metastatic and had disease progression on or after prior systemic therapy. In patients with *NRG1*+ pancreatic adenocarcinoma (n=30), BIZENGRI® demonstrated an ORR of 40% (95% CI, 23%-59%). DOR in *NRG1*+ pancreatic adenocarcinoma ranged from 3.7 months to 16.6 months. In the same trial, patients with *NRG1*+ NSCLC (n=64) who were treated with BIZENGRI® demonstrated an ORR of 33% (95% CI, 22%-46%). The median DOR in *NRG1*+ NSCLC was 7.4 months (95% CI, 4.0-16.6). Response rates were measured using the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as assessed by blinded independent central review (BICR). In the pooled safety population (N=175), the most common (≥10%) adverse reactions were diarrhea, musculoskeletal pain, fatigue, nausea, infusion-related reactions (IRR), dyspnea, rash, constipation, vomiting, abdominal pain, and edema. The most common Grade 3 or 4 laboratory abnormalities (≥2%) were increased gamma-glutamyltransferase, decreased hemoglobin, decreased sodium, decreased platelets, increased aspartate aminotransferase, increased alanine aminotransferase, increased alkaline phosphatase, decreased magnesium, decreased phosphate, increased activated partial thromboplastin time, and increased bilirubin.

“The Personalized Medicine Coalition applauds the approval of BIZENGRI®, a new targeted therapy for *NRG1*+ pancreatic adenocarcinoma and *NRG1*+ NSCLC that are advanced unresectable or metastatic,” said Edward Abrahams, President of the Washington-based education and advocacy organization. “In keeping with the growing number of personalized medicines on the market today, BIZENGRI® offers the only approved *NRG1*+ therapy for patients with these difficult-to-treat cancers.”

The company plans to help appropriate patients gain access to BIZENGRI® by providing resources and support based on each patient's needs and situation. PTx Assist™ is available to help guide patients through treatment, from providing educational information to helping to understand insurance coverage and identifying potential financial assistance options. For more information, patients and providers can call 1-844-637-8777, Monday through Friday, from 8:00 a.m. to 8:00 p.m. ET.

Please see full Prescribing Information, including Boxed WARNING, at www.BIZENGRI.com/pi.

About BIZENGRI®

BIZENGRI® is a bispecific antibody that binds to the extracellular domains of *HER2* and *HER3* expressed on the surface of cells, including tumor cells, inhibiting *HER2:HER3* dimerization and preventing *NRG1* binding to *HER3*. BIZENGRI® decreased cell proliferation and signaling through the phosphoinositide 3-kinase-AKT-mammalian target of rapamycin pathway. In addition, BIZENGRI® mediates antibody-dependent cellular cytotoxicity.

BIZENGRI® showed antitumor activity in mouse models of *NRG1+* lung and pancreatic cancers.[1]

About the eNRGy Trial

The eNRGy trial (Clinicaltrials.gov NCT02912949) is a multicenter, open-label clinical trial that includes patients with advanced unresectable or metastatic *NRG1+* pancreatic adenocarcinoma or *NRG1+* NSCLC who have disease progression on or after prior systemic therapy. There were 30 patients in the *NRG1+* pancreatic adenocarcinoma group and 64 patients in the *NRG1+* NSCLC group. The main outcome measures were ORR and DOR, as determined by BICR according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.[1]

In the *NRG1+* pancreatic adenocarcinoma group, the median age was 49 years (range, 21-72 years); 43% were female; 87% were White, 7% were Asian, and 3.3% were Black or African American. All patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and all patients had metastatic disease. Patients received a median of 2 prior systemic therapies (range, 0-5); 97% had prior systemic therapy with prior chemotherapy.[1]

In the *NRG1+* NSCLC group, the median age was 64 years (range, 32-86 years); 64% were female, 33% were White, 56% were Asian, and 3.4% were Black or African American. ECOG performance status was 0 or 1 in 97% of patients or 2 in 3% of patients, and 98% of patients had metastatic disease. Patients received a median of 2 prior systemic therapies (range, 1-6).[1]

IMPORTANT SAFETY INFORMATION

BOXED WARNING: EMBRYO-FETAL TOXICITY

Embryo-Fetal Toxicity: Exposure to BIZENGRI® during pregnancy can cause embryo-fetal harm. Advise patients of this risk and the need for effective contraception.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions/Hypersensitivity/Anaphylactic Reactions

BIZENGRI® can cause serious and life-threatening infusion-related reactions (IRRs), hypersensitivity and anaphylactic reactions. Signs and symptoms of IRR may include chills, nausea, fever, and cough.

In the eNRGy study, 13% of patients experienced IRRs, all were Grade 1 or 2; 91% occurred during the first infusion.

Administer BIZENGRI® in a setting with emergency resuscitation equipment and staff who are trained to monitor for IRRs and to administer emergency medications. Monitor patients closely for signs and symptoms of infusion reactions during infusion and for at least 1 hour following completion of first BIZENGRI® infusion and as clinically indicated. Interrupt BIZENGRI® infusion in patients with ≤ Grade 3 IRRs and administer symptomatic treatment as needed. Resume infusion at a reduced rate after resolution of symptoms. Immediately stop the infusion and permanently discontinue BIZENGRI® for Grade 4 or life-threatening IRR or hypersensitivity/anaphylaxis reactions.

Interstitial Lung Disease/Pneumonitis

BIZENGRI® can cause serious and life-threatening interstitial lung disease (ILD)/pneumonitis. In the eNRGy study, ILD/pneumonitis occurred in 2 (1.1%) patients treated with BIZENGRI®. Grade 2 ILD/pneumonitis (Grade 2) resulting in permanent discontinuation of BIZENGRI® occurred in 1 (0.6%) patient. Monitor for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold BIZENGRI® in patients with suspected ILD/pneumonitis and administer corticosteroids as clinically indicated. Permanently discontinue BIZENGRI® if ILD/pneumonitis ≥ Grade 2 is confirmed.

Left Ventricular Dysfunction

BIZENGRI® can cause left ventricular dysfunction.

Left ventricular ejection fraction (LVEF) decrease has been observed with anti-HER2 therapies, including BIZENGRI®. Treatment with BIZENGRI® has not been studied in patients with a history of clinically significant cardiac disease or LVEF less than 50% prior to initiation of treatment.

In the eNRGy study, Grade 2 LVEF decrease (40%-50%; 10 - 19% drop from baseline) occurred in 2% of evaluable patients. Cardiac failure without LVEF decrease occurred in 1.7% of patients, including 1 (0.6%) fatal event.

Before initiating BIZENGRI®, evaluate LVEF and monitor at regular intervals during treatment as clinically indicated. For LVEF of less than 45% or less than 50% with absolute decrease from baseline of 10% or greater which is confirmed, or in patients with symptomatic congestive heart failure (CHF), permanently discontinue BIZENGRI®.

Embryo-Fetal Toxicity

Based on its mechanism of action, BIZENGRI® can cause fetal harm when administered to a pregnant woman. No animal reproduction studies were conducted with BIZENGRI®. In postmarketing reports, use of a HER2-directed antibody during pregnancy resulted in cases of oligohydramnios manifesting as fatal pulmonary hypoplasia, skeletal abnormalities, and neonatal death. In animal models, studies have demonstrated that inhibition of HER2 and/or HER3 results in impaired embryo-fetal development, including effects on cardiac, vascular and neuronal development, and embryolethality. Advise patients of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to the initiation of BIZENGRI®. Advise females of reproductive potential to use effective contraception during treatment with BIZENGRI® and for 2 months after the last dose.

ADVERSE REACTIONS

***NRG1* Gene Fusion Positive Unresectable or Metastatic Pancreatic Adenocarcinoma**

Serious adverse reactions occurred in 23% of patients with NRG1 Gene Fusion Positive Pancreatic Adenocarcinoma who received BIZENGRI®.

There were 2 fatal adverse reactions, one due to COVID-19 and one due to respiratory failure.

In patients with NRG1 Gene Fusion Positive Pancreatic Adenocarcinoma who received BIZENGRI® the most common (≥20%) adverse reactions, including laboratory abnormalities, were increased alanine aminotransferase (51%), diarrhea (36%), increased aspartate aminotransferase (31%), increased bilirubin (31%), decreased phosphate (31%), increased alkaline phosphatase (28%), decreased sodium (28%) musculoskeletal pain (28%), decreased albumin (26%), decreased potassium (26%), decreased platelets (26%), decreased magnesium (24%), increased gamma-glutamyl transpeptidase (23%), decreased hemoglobin (23%), vomiting (23%), nausea (23%), decreased leukocytes (21%), and fatigue (21%).

***NRG1* Gene Fusion Positive Unresectable or Metastatic NSCLC**

Serious adverse reactions occurred in 25% of patients with NRG1 Gene Fusion Positive NSCLC who received BIZENGRI®. Serious adverse reactions in ≥ 2% of patients included pneumonia (n=4) dyspnea and fatigue (n=2 each). Fatal adverse reactions occurred in 3 (3%) patients and included respiratory failure (n=2), and cardiac failure (n=1). Permanent discontinuation of BIZENGRI® due to an adverse reaction occurred in 3% of patients. Adverse reactions resulting in permanent discontinuation of BIZENGRI® included dyspnea, pneumonitis and sepsis (n=1 each).

In patients with NRG1 Gene Fusion Positive NSCLC who received BIZENGRI®, the most common (>20%) Adverse Reactions, including laboratory abnormalities, were decreased hemoglobin (35%), increased alanine aminotransferase (30%), decreased magnesium (28%), increased alkaline phosphatase (27%), decreased phosphate (26%) diarrhea (25%), musculoskeletal pain (23%), increased gamma-glutamyl transpeptidase (23%), increased aspartate aminotransferase (22%), and decreased potassium (21%).

Please see full Prescribing Information, including Boxed WARNING, at BIZENGRI.com/pi.

About Merus N.V.

Merus is a clinical stage oncology company developing innovative full-length human bispecific and trispecific antibody therapeutics, referred to as Multiclonics®. Multiclonics® 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 https://merus.nl 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, statements regarding product development and the potential benefits and treatment impact of BIZENGRI® (zenocutuzumab-zbco); our belief that this approval fills an important need for patients with *NRG1+* cancer who have not previously had treatment options approved to specifically target this driver; the expectation of BIZENGRI® to be available to patients in the coming weeks; the promise BIZENGRI® holds for patients with *NRG1+* pancreatic adenocarcinoma and NSCLC; its implication to our technology and execution as we continue to develop our multispecific platforms and pipeline, including our lead asset petosemtamab; and our expectation to provide patients with access to BIZENGRI®, as well as offering helpful resources and support based on each patient's needs and situation. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Merus. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. 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 issues associated with 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; 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 Biclonics® 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.

Reference: 1. BIZENGRI. Prescribing information. Merus N.V.; 2024.

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Source: Merus N.V.