MacroGenics Announces Lancet Oncology Publication of Margetuximab Data in Gastric Cancer

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Rockville, MD, July 09, 2020 (GLOBE NEWSWIRE) --

MacroGenics, Inc. (NASDAQ: MGNX), a clinical-stage biopharmaceutical company focused on discovering and developing innovative monoclonal antibody-based therapeutics for the treatment of cancer, today announced that *Lancet Oncology* has published results from a Phase 2 study of margetuximab plus pembrolizumab as a chemotherapy-free regimen for patients with advanced HER2-positive gastroesophageal adenocarcinoma (GEA) who have previously been treated with chemotherapy and trastuzumab. Margetuximab is an investigational, Fc-engineered, monoclonal antibody targeting HER2. Pembrolizumab is an anti-PD-1 monoclonal antibody.

“Current standard of care treatment for patients with metastatic gastroesophageal adenocarcinoma is heavily dependent on the use of cytotoxic chemotherapy,” said Stephen Eck, M.D., Ph.D., Senior Vice President, Clinical Development & Chief Medical Officer. “The published data suggest that a chemotherapy-free regimen combining the immune-enhancing properties of margetuximab with checkpoint blockade may improve upon clinical outcomes for certain first-line patients with metastatic HER2-positive gastroesophageal adenocarcinoma and provide a strong rationale for the ongoing Phase 2/3 MAHOGANY study.”

The Phase 2 study enrolled patients with gastric cancer (GC) or gastroesophageal junction (GEJ) cancer whose tumors were IHC3-positive or IHC2-positive/FISH-positive at diagnosis. Enrollment was regardless of PD-L1 expression status, which was subsequently determined from available archived tumor tissue.

Tolerability of margetuximab and pembrolizumab was acceptable in patients treated in this study. Grade 3 or higher treatment-related adverse events (TRAEs) were reported in 20% of patients, with anemia (4%) and infusion-related reactions (3%) being the most common. No treatment-related deaths were reported.

Patients who had received margetuximab at the recommended Phase 2 dose of 15 mg/kg every three weeks were evaluable for response. In this overall population, the objective response rate (ORR) was 18% (17/92 patients), including complete responses (CR) and partial responses (PR). The disease control rate (DCR), which includes CR, PR, and stable disease (SD), was 53% (49/92 patients). Median progression-free survival (PFS) was 2.7 months (95% CI 1.6–4.3) and median overall survival (OS) was 12.5 months (95% CI 9.1–14.1).

Activity of margetuximab and anti-PD-1 in this study was more pronounced in key biomarker-positive subgroups. The most pronounced benefit was observed in patients whose tumors had high HER2 expression at diagnosis (HER2 IHC3-positive) and were PD-L1-positive. In this double-positive subgroup, the ORR was 44% (11/25 patients) and the DCR was 72% (18/25 patients). Median PFS was 4.8 months (95% CI 1.6–13.9) and median OS was 20.5 months (95% CI 8.1–NR).

Patients with initial HER2-positive GEA may lose HER2 expression after trastuzumab-based therapy. In this second-line study, HER2 amplification was not detectable in circulating tumor DNA (ctDNA) in 42% of patients who were tested, suggesting loss of HER2 following prior trastuzumab and before treatment with margetuximab and pembrolizumab. The presence of HER2 amplification in ctDNA was associated with better response rates in this study. HER2amp-positive/HER2 IHC3-positive/PD-L1-positive ORR was 60% (9/15 patients) and DCR was 80% (12/15 patients).

Consistent with prior studies of margetuximab in other tumor types, correlative analyses of samples from GEA patients treated in the study showed an increase in anti-HER2 specific T-cell immunity, suggesting the potential for engagement of both innate and adaptive immune responses.

These data in second-line patients who were refractory to trastuzumab provide the rationale for the ongoing Phase 2/3 MAHOGANY clinical trial of margetuximab in combination with checkpoint blockade, with or without chemotherapy, as a potential first-line treatment for patients with HER2-positive GC or GEJ cancer (NCT04082364). The data published in *Lancet Oncology* are reported as of July 10, 2019 and were presented at the European Society for Medical Oncology (ESMO) Annual Congress in September 2019.

About Gastric and Gastroesophageal Junction Cancer

Cancer of the stomach (gastric cancer) or the gastroesophageal junction (where the esophagus joins the stomach) is collectively known as gastroesophageal adenocarcinoma. According to the American Cancer Society, approximately 27,600 new cases of gastric cancer will be diagnosed in the U.S in 2020 and more than 11,000 people will die from the disease. Both GC and GEJ cancer are often diagnosed at an advanced stage and therefore have very poor prognosis, with a 5-year survival of 5-20%. Chemotherapy is the standard of care for first-line therapy and may be combined with trastuzumab for the approximately 20% of patients whose tumors are HER2-positive.

About Margetuximab

Margetuximab is an Fc-engineered, monoclonal antibody that targets the HER2 oncoprotein. HER2 is expressed by tumor cells in breast,

gastroesophageal and other solid tumors. Margetuximab was designed to provide HER2 blockade and has similar HER2 binding and antiproliferative effects as trastuzumab. In addition, margetuximab has been engineered using MacroGenics' Fc Optimization technology to enhance the engagement of the immune system. A Biologics License Application (BLA) for margetuximab for the treatment of patients with metastatic HER2-positive breast cancer in combination with chemotherapy is under review by the FDA, with a Prescription Drug User Fee Act (PDUFA) goal date of December 18, 2020. A Phase 2/3 MAHOGANY clinical trial in of margetuximab in combination with checkpoint inhibition, with or without chemotherapy, as a potential first-line treatment for patients with HER2-positive GC or GEJ cancer (NCT04082364) is ongoing. Margetuximab has been granted an orphan drug designation by the FDA for the treatment of GC or GEJ cancer.

About MacroGenics, Inc.

MacroGenics is a clinical-stage biopharmaceutical company focused on discovering and developing innovative monoclonal antibody-based therapeutics for the treatment of cancer. The Company generates its pipeline of product candidates primarily from its proprietary suite of next-generation antibody-based technology platforms, which have applicability across broad therapeutic domains. The combination of MacroGenics' technology platforms and protein engineering expertise has allowed the Company to generate promising product candidates and enter into several strategic collaborations with global pharmaceutical and biotechnology companies. For more information, please see the Company's website at www.macrogenics.com. MacroGenics and the MacroGenics logo are trademarks or registered trademarks of MacroGenics, Inc.

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Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, future operations, clinical development of the Company's therapeutic candidates, milestone or opt-in payments from the Company's collaborators, the Company's anticipated milestones and future expectations and plans and prospects for the Company and other statements containing the words "subject to", "believe", "anticipate", "plan", "expect", "intend", "estimate", "project", "may", "will", "should", "would", "could", "can", the negatives thereof, variations thereon and similar expressions, or by discussions of strategy constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the uncertainties inherent in the initiation and enrollment of future clinical trials, expectations of expanding ongoing clinical trials, availability and timing of data from ongoing clinical trials, expectations for the timing and steps required in the regulatory review process, expectations for regulatory approvals, the impact of competitive products, our ability to enter into agreements with strategic partners and other matters that could affect the availability or commercial potential of the Company's product candidates, business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises such as the novel coronavirus (referred to as COVID-19), and other risks described in the Company's filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the Company's views only as of the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so, except as may be required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

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