MacroGenics Presents Margetuximab Data in Gastroesophageal Cancer at the ESMO 2019 Congress

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ROCKVILLE, MD, Sept. 30, 2019 (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 updated results from a Phase 2 study of margetuximab, an investigational, Fc-optimized monoclonal antibody targeting HER2, plus pembrolizumab, an anti-PD-1 monoclonal antibody, in a chemotherapy-free regimen that is designed to engage innate and adaptive immunity, for patients with advanced HER2-positive gastroesophageal adenocarcinoma (GEA) who have previously been treated with chemotherapy and trastuzumab in the metastatic setting. Data were presented at the European Society for Medical Oncology (ESMO) Annual Congress 2019.

"In the updated analysis from this Phase 2 study, we have observed a median overall survival of 20.5 months with response rates of 48% for patients with HER2 IHC3-positive and PD-L1-positive metastatic gastroesophageal adenocarcinoma treated with margetuximab and pembrolizumab in the second line setting, and with a safety profile that is similar to pembrolizumab monotherapy. Notably, a response rate of 47% with a median overall survival of 13.1 months has previously been reported for gastroesophogeal patients treated with first line standard of care, trastuzumab and chemotherapy," said Daniel V. Catenacci, M.D., The University of Chicago Medical Center, Chicago, IL. "Based on these observations, the combination of margetuximab and a checkpoint inhibitor could potentially provide a chemotherapy-free regimen for the treatment of HER2 IHC3-positive and PD-L1-positive GEA tumors or be used with chemotherapy in a broader HER2-positive population to improve the clinical activity of existing first line standard of care."

In the Phase 2 (NCT02689284) open-label, dose escalation and expansion study, 92 patients with HER2-positive (IHC3-positive or IHC2-positive/FISH-positive) GEA, including 61 patients with gastric cancer (GC) and 31 patients with gastroesophageal junction cancer (GEJ), were treated at the recommended phase 2 dose (RP2D) of 15 mg/kg margetuximab and 200 mg pembrolizumab, both administered every three weeks, and were included in the analysis. Patients in the study were enrolled irrespective of PD-L1 expression status. Loss of HER2 expression after treatment with trastuzumab has previously been reported in GEA patients, and was observed in some patients in the current study. Pembrolizumab is provided by Merck & Co. for this study, under a previously announced arrangement.

Data are reported as of July 10, 2019. As of this data cut-off date, the study was ongoing with eight patients remaining on therapy. Acceptable tolerability was observed in this study in patients treated with margetuximab and pembrolizumab. Grade 3 or higher treatment-related adverse events (TRAE) occurred in 19.6% of patients.

Response rates, median progression-free survival (PFS) and overall survival (OS) observed in the ongoing study are summarized in the following table:

	Gastroesophageal Adenocarcinoma (GEA = GC + GEJ)				Gastric Cancer (GC)			
	ORR	DCR	Median PFS (months)	Median OS (months)	ORR	DCR	Median PFS (months)	Median OS (months)
All Patients	20*/92 (21.7%)	50/92 (54.4%)	2.7	12.5	18*/61 (29.5%)	40/61 (65.6%)	4.1	13.9
HER2 IHC3+	20*/71 (28.2%)	45/71 (63.4%)	4.3	13.9	18*/55 (32.7%)	38/55 (69.1%)	4.7	14.6
HER2 IHC3+/PD-L1+	12/25 (48.0%)	19/25 (76.0%)	4.8	20.5	12/23 (52.2%)	19/23 (82.6%)	5.5	20.5

*Three unconfirmed; ORR=objective response rate (CR+PR); DCR=disease control rate (CR+PR+SD)

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.

"These data provide strong rationale for combining the innate and adaptive immune enhancing properties of margetuximab with checkpoint blockade in patients with HER2-positive gastroesophageal adenocarcinoma," said Scott Koenig, M.D., Ph.D., President and CEO of MacroGenics. "We plan to initiate the Phase 2/3 MAHOGANY study to evaluate margetuximab in combination with a checkpoint inhibitor, with or without chemotherapy, in front-line GEA patients. One module is designed to test the chemotherapy-free regimen in patients whose tumors are both HER2 IHC3-positive and PD-L1-positive. Another module is designed to test margetuximab plus checkpoint inhibitors in combination with chemotherapy in patients with HER2-positive tumors regardless of PD-L1 expression status and is planned to be conducted globally in collaboration with Zai Labs, our partner in

Greater China."

Margetuximab Presentations at ESMO

• Abstract #2812: Catenacci, et al. "Margetuximab (M) + pembrolizumab (P) for treatment of patients (pts) with HER2+ gastroesophageal adenocarcinoma (GEA) post-trastuzumab (T): Survival analysis" – Poster Discussion 1188

• Abstract #2794: Park, et al. "Determinants of response of HER2+ gastric cancer (GC) vs gastroesophageal junction adenocarcinoma (GEJ) to margetuximab (M) plus pembrolizumab (P) post trastuzumab (T)" – Poster Discussion 1189

• Abstract #2547: Rutella, et al. "Evaluation of tumor microenvironment identifies immune correlates of response to combination immunotherapy with margetuximab (M) and pembrolizumab (P) in HER2+ gastroesophageal adenocarcinoma (GEA)" – Poster 123

These posters will be available for download from the Events & Presentations page on MacroGenics' website at http://ir.macrogenics.com/events.cfm.

About Margetuximab

Margetuximab is an investigational 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 with MacroGenics' Fc Optimization technology to enhance the engagement of the immune system and affect killing of cancer cells through antibody dependent cellular cytotoxicity (ADCC). Beyond GEA, margetuximab is also being evaluated in combination with chemotherapy in the Phase 3 SOPHIA study for the treatment of patients with metastatic HER2-positive breast cancer who have previously been treated with anti-HER2-targeted therapies.

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 regulatory approvals, other matters that could affect the availability or commercial potential of the Company's product candidates 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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