MacroGenics Presents Results from the SOPHIA Study of Margetuximab in Patients with HER2-Positive Metastatic Breast Cancer at the San Antonio Breast Cancer Symposium

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Biologics License Application (BLA) submission to FDA expected before the end of 2019

Rockville, MD, Dec. 11, 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 presented updated results from the Phase 3 SOPHIA study comparing margetuximab plus chemotherapy versus trastuzumab plus chemotherapy in patients with HER2-positive metastatic breast cancer who have previously been treated with anti-HER2-targeted therapies. Margetuximab is an investigational, immune-enhancing monoclonal antibody derived from the Company's proprietary Fc-engineering technology platform. The data were presented today during an oral session at the San Antonio Breast Cancer Symposium (SABCS) by Dr. Hope Rugo, M.D., Director, Breast Oncology and Clinical Trials Education, University of California San Francisco Helen Diller Family Comprehensive Cancer Center.

"Patients with later stage HER2-positive metastatic breast cancer need access to new therapies. The updated SOPHIA study results presented today at the second interim survival analysis showed a trend in overall survival favoring margetuximab and are encouraging. Furthermore, margetuximab is the only HER2-targeted agent to show PFS superiority versus trastuzumab in a head-to-head Phase 3 clinical trial," said Dr. Rugo. "The SOPHIA study also includes a pre-specified analysis of CD16A genotype as a predictor of anti-HER2 antibody efficacy, which although exploratory, is the first such prospective clinical analysis and suggests differential benefit in this population."

Overall survival (OS) results favored margetuximab plus chemotherapy compared with trastuzumab and chemotherapy in the intention-to-treat (ITT) population; however, these data did not reach statistical significance at this second interim analysis as of a September 2019 cut-off after 270 events (median OS=21.6 months versus 19.8 months; hazard ratio [HR]=0.89; 95% CI: 0.69-1.13; P=0.326). The final pre-specified OS analysis is planned after 385 events have accrued, which is projected to occur in the second half of 2020. A pre-specified exploratory objective of the study was to evaluate the effect of CD16A (Fcγ receptor) allelic variation on margetuximab activity. Among the genetically defined subpopulation of patients carrying a CD16A 158F allele, who represent approximately 85% of the human (and SOPHIA study) population, the median OS at the second interim analysis was prolonged by 4.3 months in the margetuximab arm compared to the trastuzumab arm (23.7 months versus 19.4 months; HR=0.79; 95% CI: 0.61-1.04; nominal P=0.087). Among the approximately 15% of patients who were homozygous for the CD16A 158V allele, the trastuzumab arm performed better than the margetuximab arm.

As previously reported, margetuximab plus chemotherapy showed a statistically significant improvement in independently-assessed progression-free survival (PFS) compared to trastuzumab plus chemotherapy in this study as of an October 2018 cut-off after 256 events (median PFS=5.8 months versus 4.9 months; HR=0.76; 95% CI: 0.59-0.98; P=0.033). An updated investigator-assessed analysis as of a September 2019 cut-off showed consistent results after 430 PFS events (median PFS=5.7 months in the margetuximab arm versus 4.4 in the trastuzumab arm; HR=0.71; nominal P=0.0006). Similarly, at the time of this updated analysis, additional patients were evaluable for response in the ITT population. Investigator-assessed objective response rate (ORR) was 25.2% (95% CI: 20.1-30.9%) in the margetuximab arm compared to 13.7% (95% CI: 9.8–18.4%) in the trastuzumab (nominal P=0.0006). The clinical benefit rate (CBR, which includes CR+PR+SD>6 months, was 48.1% (95% CI: 42.0-54.3%) in the margetuximab arm versus 35.6% (95% CI: 29.9-41.6%) in the trastuzumab arm (nominal P=0.0025).

"MacroGenics is focused on developing novel antibody-based therapies for patients who face unmet medical needs. We believe that margetuximab, if approved by regulators, will address an important unmet need and could become a valuable treatment option for patients living with this devastating disease," said Scott Koenig, M.D., Ph.D., President and CEO of MacroGenics. "We are grateful for the patients who participated in this study, as well as their families, and look forward to submitting a BLA to the FDA, which we expect to occur before the end of the year."

Margetuximab plus chemotherapy has shown a safety profile generally comparable to that of trastuzumab plus chemotherapy in this study. As of the April 2019 cut-off for safety, Grade 3 or greater adverse events occurred in 142 (54%) patients on the margetuximab arm compared to 140 (53%) patients on the trastuzumab arm. Serious adverse events occurred in 43 (16%) patients on the margetuximab arm compared to 49 (18%) patients on the trastuzumab arm. Infusion-related reactions (IRR) were more common with margetuximab treatment than with trastuzumab (13% versus 3%) and were mostly Grade 1 or 2 and associated with the first dose. A substudy evaluating shorter, 30-minute infusions of margetuximab in Cycle 2 and beyond showed no effect on safety outcomes, as well as risk or severity of IRR. These data will be presented at the SABCS during Poster Session 1, today from 5:00 - 7:00 p.m. CT (P1-18-04: Gradishar, et al. "*Phase 3 SOPHIA study of margetuximab + chemotherapy vs trastuzumab + chemotherapy in patients with HER2+ metastatic breast cancer after prior anti-HER2 therapies: infusion time substudy results"*).

The presentations are available on the Events & Presentations page on MacroGenics' website at http://ir.macrogenics.com/events.cfm.

About the SOPHIA Study

The SOPHIA study (NCT02492711) is a randomized, open-label Phase 3 clinical trial evaluating margetuximab plus chemotherapy compared to trastuzumab plus chemotherapy in patients with HER2-positive metastatic breast cancer, who have previously been treated with anti-HER2-targeted therapies. All study patients had previously received trastuzumab and pertuzumab, and approximately 90% had previously received ado-trastuzumab emtansine, or T-DM1.

The study enrolled 536 patients who were randomized 1:1 to receive either margetuximab (n=266) given intravenously at 15 mg/kg every three weeks or trastuzumab (n=270) given intravenously at 6 mg/kg (or 8 mg/kg for loading dose) every three weeks in combination with one of four chemotherapy agents (capecitabine, eribulin, gemcitabine or vinorelbine) given at the standard dose. Intent-to-treat PFS analysis occurred after 265 PFS events.

Primary endpoints are sequentially-assessed PFS, determined by centrally-blinded radiological review, and OS. Key secondary endpoints are PFS by investigator assessment and ORR. Tertiary endpoints include ORR by investigator assessment and safety. PFS and ORR were assessed according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1).

About HER2-positive Breast Cancer

Human epidermal growth factor receptor 2 (HER2) is a protein found on the surface of some cancer cells that promotes growth and is associated with aggressive disease and poor prognosis. Approximately 15-20% of breast cancer cases are HER2-positive. Monoclonal antibodies targeting HER2 have greatly improved outcomes of patients with HER2-positive breast cancer and are now standard of care in both early-and late-stage disease. However, metastatic breast cancer remains an unmet need that eventually advances to the point where no currently approved HER2-targeting therapy continues to control the disease. Ongoing HER2 blockade is recommended for relapsed or refractory patients, but there is no approved therapy in the third line and beyond setting, or established standard of care after progression with trastuzumab, pertuzumab and ado-trastuzumab emtansine.

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, the Fc region of margetuximab has been engineered with MacroGenics' Fc Optimization technology to enhance the engagement of the immune system. Margetuximab is also being evaluated in combination with anti-PD-1 therapy for the treatment of patients with HER2-positive gastroesophageal cancer. The company has initiated the registration-directed Phase 2/3 MAHOGANY trial (NCT04082364).

About MacroGenics' Fc Optimization Technology

MacroGenics' Fc Optimization platform is designed to modulate an antibody's interaction with immune effector cells. The Fc region of certain antibodies binds activating and inhibitory receptors, referred to as FcγRs, on immune cells found within the innate immune system. Such interactions affect killing of cancer cells through antibody dependent cellular cytotoxicity (ADCC), among other Fc-dependent functions.

The activating CD16A FcγR occurs in two variants, or alleles, with high (158V) or low (158F) affinity for the Fc domain of IgG1. A majority (approximately 85%) of the population carries the 158F allele, either in the homozygous form or as heterozygous with 158V. Patients that carry the 158F allele have been reported to show diminished clinical responses to certain therapeutic antibodies, including trastuzumab.

MacroGenics' engineered Fc region binds with increased affinity to CD16A, including the 158F low-affinity allele and with reduced affinity to CD32B, the inhibitory FcγR. MacroGenics' engineered Fc mediates improved effector functions, such as ADCC.

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.

Anna Krassowska, Ph.D., Vice President, Investor Relations & Corporate Communications
Jim Karrels, Senior Vice President, CFO
1-301-251-5172, info@macrogenics.com

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