MacroGenics Announces Positive Results from Phase 3 SOPHIA Study of Margetuximab in Patients with HER2-Positive Metastatic Breast Cancer

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Study meets first sequential primary endpoint of progression-free survival (PFS) in head-to-head with current standard of care (trastuzumab and chemotherapy)

Oral abstract will be presented at American Society of Clinical Oncology (ASCO) Annual Meeting on June 4, 2019 at 9:45 a.m. CT (Abstract #1000)

ROCKVILLE, MD, May 15, 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 additional details of the results from the Phase 3 SOPHIA study of margetuximab 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 Optimization technology platform.

The study met its first sequential primary endpoint of progression-free survival (PFS). The median PFS of patients treated with margetuximab and chemotherapy was 5.8 months compared to 4.9 months in patients treated with trastuzumab and chemotherapy (hazard ratio [HR]=0.76; 95% CI: 0.59-0.98; P=0.033). Among the approximately 85% of patients carrying the CD16A 158F allele, a pre-specified exploratory subpopulation in the study, PFS was prolonged by 1.8 months in the margetuximab arm compared to the trastuzumab arm (6.9 months versus 5.1 months; HR=0.68; 95% CI: 0.52-0.90; P=0.005). The objective response rate (ORR), a secondary outcome measure in the SOPHIA study, was 22% in the margetuximab arm (95% CI: 17.3-27.7%) compared to 16% in the trastuzumab arm (95% CI: 11.8-21.0%). The data cut-off date for the primary PFS analysis of the study was October 10, 2018.

At the time of the primary PFS analysis, overall survival (OS) data based on 158 events were immature. The median OS at that time was prolonged by 1.7 months in patients treated with margetuximab and chemotherapy compared to patients treated with trastuzumab and chemotherapy. For the exploratory subpopulation of patients carrying the CD16A 158F allele, the median OS was prolonged by 6.8 months in the margetuximab arm compared to the trastuzumab arm. The Company anticipates conducting a second pre-specified interim OS analysis based on 270 events in the second half of this year. The final pre-specified OS analysis is planned after 385 events have accrued, and is projected to be completed in 2020.

"The activity observed to date in SOPHIA is promising. Of note, this is the first randomized Phase 3 study that was designed to examine the potential benefit of Fc modification and the role of Fc-gamma receptor genotypes on anti-HER2 antibody efficacy. For overall survival, we anticipate the preliminary positive trend in favor of margetuximab to continue, although subsequent results could fluctuate as additional events accrue," saidScott Koenig, M.D., Ph.D., President and CEO of MacroGenics. "At ASCO, we will also present data from our Phase 1 study that show HER2-specific T-cell and antibody responses in margetuximab-treated patients. These data are consistent with the hypothesis that margetuximab facilitates the cooperation of both innate and adaptive immune responses, an emerging paradigm in immuno-oncology."

"With no FDA-approved therapies after progression on trastuzumab, pertuzumab, and ado-trastuzumab emtansine, patients with HER2-positive metastatic breast cancer continue to need new treatment options. If approved, based on SOPHIA data, I believe that margetuximab could become a valuable treatment option for these patients," said Hope S. Rugo, M.D., Director, Breast Oncology and Clinical Trials Education, University of California San Francisco Comprehensive Cancer Center. "I look forward to presenting results from SOPHIA at ASCO."

Margetuximab with chemotherapy had an acceptable safety profile, generally comparable overall to that of trastuzumab and chemotherapy. Grade 3 or greater adverse events occurred in 138 (52%) patients on the margetuximab arm compared to 128 (48%) patients on the trastuzumab arm. Serious adverse events occurred in 39 (15%) patients on the margetuximab arm compared to 46 (17%) patients on the trastuzumab arm. Infusion-related reactions were more common with margetuximab treatment than with trastuzumab (13% versus 4%) and were mostly Grade 1 or 2 and associated with the first dose.

MacroGenics recently held a pre-BLA meeting regarding margetuximab with the U.S. Food and Drug Administration (FDA). The company plans to submit a Biologics License Application (BLA) to the FDA in the second half of 2019.

Margetuximab Presentations at ASCO

The SOPHIA study presentation at the ASCO Annual Meeting will be during the Oral Abstract Session: Breast Cancer – Metastatic on Tuesday, June 4, 2019, at 9:45 a.m. CT (Abstract #1000).

A separate abstract, "High frequency of HER2-specific immunity observed in patients (pts) with HER2+ cancers treated with margetuximab (M), an Fc-enhanced anti-HER2 monoclonal antibody (mAb)," will be presented during ASCO's Poster Session: Breast Cancer – Metastatic on Sunday, June 2, 2019 at 8:00 - 11:00 a.m. CT (Poster Board #111; Abstract #1030).

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. To be eligible for the study, patients must have received at least two prior lines of anti-HER2-directed therapy in the metastatic setting, or in the case of having received (neo)adjuvant pertuzumab, at least one prior line of anti-HER2-directed therapy in the metastatic setting; and who have received at least one and no more than three prior lines of therapy overall in the metastatic setting. All study patients had previously received trastuzumab (HERCEPTIN®) and pertuzumab (PERJETA®), and approximately 90% had previously received ado-trastuzumab emtansine (KADCYLA®).

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. Patients were stratified by the number of metastatic sites (?2 or >2), number of lines of prior therapy for metastatic disease (?2 or >2) and choice of chemotherapy. Intent-to-treat 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. 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 (mAbs) 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, 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 with a registration-directed Phase 2/3 trial planned.

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 Fc?Rs, 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 Fc?R 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' optimized Fc region binds with increased affinity to CD16A, including the 158F low-affinity allele, and, unique to MacroGenics' technology, with reduced affinity to CD32B, the inhibitory Fc?R. MacroGenics' optimized Fc mediates improved effector functions, such as ADCC. To date, MacroGenics has successfully incorporated its proprietary Fc Optimization technology in margetuximab, as well as enoblituzumab, an anti-B7-H3 monoclonal antibody currently in development in combination with anti-PD-1 therapy for cancer treatment.

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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