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MacroGenics Presents Phase 1 Data at ASCO Showing Signs of Clinical Benefit for Margetuximab in HER2 Expressing Tumors; Phase 2 Clinical Trial Underway to Evaluate Activity in Patients with Advanced Breast Cancer

ROCKVILLE, Md., June 3, 2013—MacroGenics, Inc. announced that results of the first-in-human study of margetuximab were reported during an oral abstract session today at the 2013 Annual Meeting of the American Society of Clinical Oncology (ASCO). Howard A. Burris, M.D., FACP, first author and Chief Medical Officer of Sarah Cannon Research Institute, presented "Phase 1 study of margetuximab (MGAH22), an Fc-modified chimeric monoclonal antibody (MAb), in patients with advanced solid tumors expressing the HER2 oncoprotein," during the Developmental Therapeutics - Immunotherapy Oral Abstract Session (http://abstracts2.asco.org/AbstView_132_115290.html). Margetuximab was found to be tolerated at all doses. In addition, anti-tumor activity was observed at all dose levels, including partial responses (PRs) and time-to-progression ≥ 5 months, even in patients who were heavily pre-treated (including anti-HER2 agents).

Study Results

This open-label, multi-dose, single-arm, multi-center Phase 1, dose-escalation study was conducted to define the toxicity profile, maximum tolerated dose, pharmacokinetics, immunogenicity, and potential anti-tumor activity of margetuximab in 34 patients with advanced HER2-positive breast cancer (2+ or 3+ by IHC) neoplasms, 23 of whom had breast cancer or gastroesophageal cancer.

Study results showed that margetuximab was well tolerated at all explored doses, including the highest dose tested, 6.0 mg/kg qw. Infusion reactions were well controlled with pre-medications. Margetuximab exhibited pharmacokinetics typical of human IgG1s.

At a dose of 0.1 mg/kg qw, one patient experienced time to progression of 9.2 months. In addition, three patients experienced confirmed partial responses (RECIST) – two with metastatic breast cancer (lasting 3.3 and 5.3 months) and one with cancer of the gastroesophageal junction (lasting 3.3 months). Four of 13 patients with gastroesophageal cancer experienced stable disease lasting a median of 3.6 months (range 1.5 - 5.3), with all but one previously failing anti-HER2 treatment.

The most common adverse events (AEs) were Grade 1-2 constitutional symptoms and infusion-related reactions. Additionally, related AEs ≥ Grade 3 were limited to a single infusion reaction, two episodes of brief lymphopenia confounded by steroids, and transient worsening anemia. No cardiac toxicities were observed.

Dr. Burris commented, “We were pleased to find that margetuximab was well tolerated by patients and showed promising activity in patients who have limited treatment options, such as those with breast cancer or gastroesophageal cancer and who previously have failed other HER2 therapies.”

MacroGenics has optimized the Fc region of margetuximab with the goal of increasing cancer cell killing with Antibody-Dependent Cell-mediated Cytotoxicity (ADCC). During the study, ADCC was measured ex-vivo in peripheral blood mononuclear cells (PBMCs) and showed enhanced activity of margetuximab v. trastuzumab.

"The results of our Phase 1 study are very encouraging and show the potential for margetuximab in the treatment of HER2-expressing tumors,” stated Scott Koenig, M.D., Ph.D., President and CEO of MacroGenics. “With the recent initiation of a Phase 2 clinical trial, we will explore whether margetuximab can improve clinical outcomes in a sub-population of breast cancer patients, particularly those with low HER2 expression. We also anticipate future studies of margetuximab in patients with other HER2-expressing tumors.”

About Breast Cancer and HER2

The HER2 oncoprotein is over-expressed and plays an important role in tumorigenesis, tumor aggressiveness, and outcome in breast cancer and other solid tumors. HER2 has proven to be an excellent target for cancer therapeutics, given the success of currently marketed HER2-directed therapies.

According to the National Cancer Institute, over 230,000 women in the U.S. are diagnosed with breast cancer annually. Of these women, only about 20% have tumors that are HER2 positive (IHC 3+, or HER2 gene-amplified). One development goal for margetuximab is to target a similarly large group of patients whose tumors exhibit HER2 expression that is less than 3+ and lack evidence of HER2 gene amplification and for whom current anti-HER2 therapies are not indicated. Another goal for margetuximab is to determine if the Fc modifications will improve clinical outcomes in patients with tumors that are currently treated with other HER2 therapies, which would be consistent with results seen in laboratory models.

Background on Margetuximab

Margetuximab (MGAH22), an Fc-modified monoclonal antibody, targets the HER2 oncoprotein, which is overexpressed on the surface of various cancer cells and plays an important role in tumorigenesis, tumor aggressiveness, and outcome in breast and other cancers. HER2 has proven to be an excellent target for cancer therapeutics as shown by the clinical success of trastuzumab in both breast and gastric cancer.

The benefits of trastuzumab in metastatic breast and gastric cancer accrue primarily to patients with the highest level of HER2 expression (HER2 3+ by immunohistochemistry) or those who have gene-amplified tumors. Thus, therapies are needed for patients whose tumors overexpress the HER2 oncoprotein at lower levels without gene amplification. Furthermore, the benefits of trastuzumab in metastatic breast cancer are primarily in patients who are homozygous for the high affinity allele of the Fcγ receptor, CD16A (FcγRIIIA). These patients represent only approximately 15% of the population.

MacroGenics has engineered margetuximab for increased binding to the low affinity allele of CD16A, thus offering potentially increased effectiveness in the approximately 85% of patients who carry this FcγR allele. In addition, this engineering work has been shown in pre-clinical studies to enhance killing of tumors expressing low levels of HER2. In prior research, margetuximab showed improved control of tumor growth in human tumor xenograft models in mice, as compared to that of anti-HER2 antibodies with a wild type Fc counterpart and in effector cell-dependent ADCC assays. This ADCC activity was independent of FcγR genotype. A development goal for margetuximab is to enable the treatment of a broader population of patients than those eligible for treatment with current HER2-targeted therapies.

About MacroGenics, Inc.

MacroGenics is a leader in the discovery and development of innovative medicines that utilize its next-generation antibody-based technologies. The company is advancing a pipeline of product candidates to treat patients with cancer and other serious, complex diseases. MacroGenics' products and platforms have attracted multiple partnerships with leading pharmaceutical companies around the globe. www.macrogenics.com

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