



October 22, 2015

MacroGenics and Merck to Collaborate on Immuno-Oncology Study Evaluating Margetuximab in Combination with KEYTRUDA(R) (pembrolizumab) for Advanced Gastric Cancer

Clinical trial to evaluate MacroGenics' Fc-optimized anti-HER2 antibody with Merck's anti-PD-1 therapy in patients with advanced HER2-positive gastric cancer

ROCKVILLE, MD and KENILWORTH, NJ, Oct. 22, 2015 (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, autoimmune disorders and infectious diseases, and Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced a collaboration to evaluate the combination of MacroGenics' anti-HER2 product candidate, margetuximab, with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in a Phase 1b/2 clinical trial in patients with advanced gastric cancer.

Margetuximab is an Fc-optimized monoclonal antibody that targets the human epidermal growth factor receptor 2, or HER2, which is an antigen critical for the growth of many types of tumors, including breast and gastroesophageal cancers. KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2.

"The combination of our proprietary Fc-optimized anti-HER2 antibody, with expected enhanced immune-mediated killing properties, and the anti-PD-1 antibody KEYTRUDA, is intended to exploit potentially complementary biology," said Scott Koenig, M.D., Ph.D., President and CEO of MacroGenics. "Treatment options for patients with advanced HER2-positive gastric cancer are extremely limited. The combination of mechanisms engaged by margetuximab and KEYTRUDA could provide an important alternative for patients who do not respond to currently available regimens."

"Today, there is a great opportunity and need to bring forward new scientific breakthroughs for the treatment of gastric cancer," said Dr. Eric Rubin, vice president and therapeutic area head, oncology early-stage development, Merck Research Laboratories. "Evaluating the potential of combination therapies through strategic collaborations in difficult-to-treat tumor types continues to be an important part of our immuno-oncology clinical development program for KEYTRUDA."

The Phase 1b/2 multicenter, open-label clinical trial will be conducted in two parts. The Phase 1b portion is designed to determine the safety and tolerability of margetuximab in combination with KEYTRUDA in patients with advanced gastric cancer, while the Phase 2 portion will evaluate the anti-tumor activity of margetuximab in combination with KEYTRUDA in patients with advanced HER2-positive gastric cancer. Trial startup activities are underway and MacroGenics expects to begin enrolling patients by the first quarter of 2016. The agreement includes a provision where the parties may extend the collaboration to include a potential Phase 3 clinical trial.

The agreement is between MacroGenics and Merck, through a subsidiary. Additional details were not disclosed.

About Gastric Cancer

Gastric cancer, also called stomach cancer, is a type of cancer that begins in the stomach. Most gastric cancers are adenocarcinomas, which develop from the cells of the innermost lining (mucosa) of the stomach. Among others, risk factors for gastric cancer include gender, age, ethnicity, geography and bacterial infection with *Helicobacter pylori*. More than 70 percent of gastric cancer cases occur in developing countries, with half of all cases occurring in Eastern Asia (predominately China). Worldwide, gastric cancer is the fifth most common type of cancer and the third leading cause of cancer death.

About Margetuximab

Margetuximab is an Fc-optimized monoclonal antibody that targets the human epidermal growth factor receptor 2, or HER2, an antigen critical for the growth of many types of tumors, including breast and gastroesophageal cancers. Using its Fc-optimization platform, MacroGenics has designed the Fc region of margetuximab to enhance the killing of tumor cells through an Fc-dependent mechanism, including antibody dependent cell-mediated cytotoxicity, or ADCC. MacroGenics has initiated dosing of patients in SOPHIA, a Phase 3 pivotal study evaluating margetuximab plus chemotherapy against trastuzumab plus chemotherapy in third-line HER2-positive metastatic breast cancer patients. The purpose of the SOPHIA study is to determine whether patients treated with margetuximab plus chemotherapy have longer progression-free and overall survival than patients treated with trastuzumab plus chemotherapy. For more information about this trial, please visit www.sophiastudy.com or www.clinicaltrials.gov.

About KEYTRUDA® (pembrolizumab) Injection 100 mg

KEYTRUDA is a humanized monoclonal antibody that works by increasing the ability of the body's immune system to help detect and fight tumor cells. KEYTRUDA blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, and may affect both tumor cells and healthy cells. KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. KEYTRUDA is also indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 as determined by an FDA-approved test with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA. These indications are approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Selected Important Safety Information for KEYTRUDA in Melanoma Trial

Pneumonitis occurred in 12 (2.9%) of 411 patients, including Grade 2 or 3 cases in 8 (1.9%) and 1 (0.2%) patients, respectively, receiving KEYTRUDA. Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected pneumonitis with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 pneumonitis.

Colitis (including microscopic colitis) occurred in 4 (1%) of 411 patients, including Grade 2 or 3 cases in 1 (0.2%) and 2 (0.5%) patients, respectively, receiving KEYTRUDA. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

Hepatitis (including autoimmune hepatitis) occurred in 2 (0.5%) of 411 patients, including a Grade 4 case in 1 (0.2%) patient, receiving KEYTRUDA. Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

Hypophysitis occurred in 2 (0.5%) of 411 patients, including a Grade 2 case in 1 and a Grade 4 case in 1 (0.2% each) patient, receiving KEYTRUDA. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids for Grade 2 or greater hypophysitis. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3; and permanently discontinue KEYTRUDA for Grade 4 hypophysitis.

Hyperthyroidism occurred in 5 (1.2%) of 411 patients, including Grade 2 or 3 cases in 2 (0.5%) and 1 (0.2%) patients, respectively, receiving KEYTRUDA. Hypothyroidism occurred in 34 (8.3%) of 411 patients, including a Grade 3 case in 1 (0.2%) patient, receiving KEYTRUDA. Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer corticosteroids for Grade 3 or greater hyperthyroidism. Withhold KEYTRUDA for Grade 3; permanently discontinue KEYTRUDA for Grade 4 hyperthyroidism. Isolated hyperthyroidism may be managed with replacement therapy without treatment interruption and without corticosteroids.

Type 1 diabetes mellitus, including diabetic ketoacidosis, has occurred in patients receiving KEYTRUDA. Monitor patients for hyperglycemia and other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA in cases of severe hyperglycemia until metabolic control is achieved.

Nephritis occurred in 3 (0.7%) patients, consisting of one case of Grade 2 autoimmune nephritis (0.2%) and two cases of interstitial nephritis with renal failure (0.5%), one Grade 3 and one Grade 4. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

Other clinically important immune-mediated adverse reactions can occur. The following clinically significant immune-mediated adverse reactions occurred in patients treated with KEYTRUDA: exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, hemolytic anemia, partial seizures arising in a patient with inflammatory foci in brain parenchyma, severe dermatitis including bullous pemphigoid, myasthenic syndrome, optic neuritis, and rhabdomyolysis.

For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold KEYTRUDA and administer corticosteroids. Upon improvement of the adverse reaction to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Restart KEYTRUDA if the adverse reaction remains at Grade 1 or less. Permanently discontinue KEYTRUDA for any severe or Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

Infusion-related reactions, including severe and life-threatening reactions, have occurred in patients receiving KEYTRUDA. Monitor patients for signs and symptoms of infusion-related reactions including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For severe or life-threatening reactions, stop infusion and permanently discontinue KEYTRUDA.

Based on its mechanism of action, KEYTRUDA may cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

KEYTRUDA was discontinued for adverse reactions in 9% of 411 patients. Adverse reactions, reported in at least two patients, that led to discontinuation of KEYTRUDA were: pneumonitis, renal failure, and pain. Serious adverse reactions occurred in 36% of patients. The most frequent serious adverse reactions, reported in 2% or more of patients, were renal failure, dyspnea, pneumonia, and cellulitis.

The most common adverse reactions (reported in at least 20% of patients) were fatigue (47%), cough (30%), nausea (30%), pruritus (30%), rash (29%), decreased appetite (26%), constipation (21%), arthralgia (20%), and diarrhea (20%).

No formal pharmacokinetic drug interaction studies have been conducted with KEYTRUDA.

It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA.

Safety and effectiveness of KEYTRUDA have not been established in pediatric patients.

Selected Safety Information for KEYTRUDA (pembrolizumab) in NSCLC Trial

Pneumonitis occurred in 19 (3.5%) of 550 patients, including Grade 2 (1.1%), 3 (1.3%), 4 (0.4%), or 5 (0.2%) pneumonitis in patients receiving KEYTRUDA. Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected pneumonitis with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

Colitis occurred in 4 (0.7%) of 550 patients, including Grade 2 (0.2%) or 3 (0.4%) colitis in patients receiving KEYTRUDA. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

Hepatitis occurred in patients receiving KEYTRUDA (pembrolizumab). Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

Hypophysitis occurred in 1 (0.2%) of 550 patients, which was Grade 3 in severity. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids and hormone replacement as indicated. Withhold KEYTRUDA for Grade 2 and withhold or discontinue for Grade 3 or 4 hypophysitis.

Hyperthyroidism occurred in 10 (1.8%) of 550 patients, including Grade 2 (0.7%) or 3 (0.3%). Hypothyroidism occurred in 38 (6.9%) of 550 patients, including Grade 2 (5.5%) or 3 (0.2%). Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer replacement hormones for hypothyroidism and manage hyperthyroidism with thionamides and beta-blockers as appropriate. Withhold or discontinue KEYTRUDA for Grade 3 or Grade 4 hyperthyroidism.

Type 1 diabetes mellitus, including diabetic ketoacidosis, has occurred in patients receiving KEYTRUDA. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer anti-hyperglycemics in patients with severe hyperglycemia.

Nephritis occurred in patients receiving KEYTRUDA. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold KEYTRUDA and administer corticosteroids. Upon improvement of the adverse reaction to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Resume KEYTRUDA when the adverse reaction remains at Grade 1 or less following steroid taper. Permanently discontinue KEYTRUDA for any severe or Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

The following clinically significant, immune-mediated adverse reactions occurred in patients treated with KEYTRUDA: rash, vasculitis, hemolytic anemia, serum sickness, myasthenia gravis, bullous pemphigoid, and Guillain-Barre syndrome.

Infusion-related reactions, including severe and life-threatening reactions, have occurred in patients receiving KEYTRUDA. Monitor patients for signs and symptoms of infusion-related reactions including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For severe or life-threatening reactions, stop infusion and permanently discontinue KEYTRUDA.

Based on its mechanism of action, KEYTRUDA (pembrolizumab) can cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

KEYTRUDA was discontinued due to adverse reactions in 14% of patients. Serious adverse reactions occurred in 38% of patients. The most frequent serious adverse reactions reported in 2% or more of patients were pleural effusion, pneumonia, dyspnea, pulmonary embolism, and pneumonitis.

The most common adverse reactions (reported in at least 20% of patients) were fatigue (44%), decreased appetite (25%), dyspnea (23%), and cough (29%).

No formal pharmacokinetic drug interaction studies have been conducted with KEYTRUDA. It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA and for 4 months after the final dose.

Safety and effectiveness of KEYTRUDA have not been established in pediatric patients.

About MacroGenics

MacroGenics is a clinical-stage biopharmaceutical company focused on discovering and developing innovative monoclonal antibody-based therapeutics for the treatment of cancer, as well as autoimmune disorders and infectious diseases. The company generates its pipeline of product candidates from its proprietary suite of next-generation antibody-based technology platforms. 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. The MacroGenics logo is a registered trademark of MacroGenics, Inc.

Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck Oncology, helping people fight cancer is our passion and supporting accessibility to our cancer medicines is our commitment. Our focus is on pursuing research in immuno-oncology and we are accelerating every step in the journey - from lab to clinic - to potentially bring new hope to people with cancer. For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside of the United States and Canada. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on [Twitter](https://twitter.com/merck), [Facebook](https://www.facebook.com/merck) and [YouTube](https://www.youtube.com/merck).

Forward-Looking Statement of MacroGenics

Any statements in this press release about future expectations, plans and prospects for MacroGenics, including statements about MacroGenics' strategy, future operations, clinical development of MacroGenics' therapeutic candidates, milestone or opt-in payments from MacroGenics' collaborators, MacroGenics' anticipated milestones and future expectations and plans and prospects for MacroGenics and other statements containing the words "anticipate," "believes," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. 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 MacroGenics' product candidates and other risk factors described in MacroGenics' filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent MacroGenics' views as of the date hereof. MacroGenics anticipates that subsequent events and developments will cause MacroGenics' views to change. However, while MacroGenics may elect to update these forward-looking statements at some point in the future, MacroGenics specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing MacroGenics' views as of any date subsequent to the date hereof.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, NJ, USA

This news release of Merck & Co., Inc., Kenilworth, NJ, USA (the "Company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the Company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include, but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and healthcare legislation in the United States and internationally; global trends toward healthcare cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the Company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the Company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the Company's 2014 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

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Please see Prescribing Information for KEYTRUDA (pembrolizumab) at http://www.merck.com/product/usa/pi_circulars/k/kevtruda/kevtruda_pi.pdf and the Medication Guide for KEYTRUDA at http://www.merck.com/product/usa/pi_circulars/k/kevtruda/kevtruda_mg.pdf

Source: MacroGenics, Inc.

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