



News Release

FOR IMMEDIATE RELEASE

Media Contacts:

Laura Cava Northrop, International Breast Cancer Study Group
(617) 632-3973, press@ibcsg.org

Cecilia Waldvogel, Breast International Group
+41 79 478-0238, cecilia.waldvogel@BIGagainstbc.org

Claire Mulhearn, Merck
(908) 236-1118, claire.mulhearn@merck.com

**International Breast Cancer Study Group, Breast International Group and Merck
Announce Opening of International PANACEA Study of Patients with HER2+
Breast Cancer**

**Collaborative Trial is First to Investigate an Anti-PD-1 Therapy, Pembrolizumab,
Combined with Trastuzumab**

**Study to Explore Whether New Approach May Reverse Trastuzumab Resistance in
Cancer with Significant Unmet Need**

SAN ANTONIO, Dec. 10, 2014 – The International Breast Cancer Study Group (IBCSG), Breast International Group (BIG), and Merck, known as MSD outside the United States and Canada, today announced the opening of the PANACEA study, a global collaborative study exploring a new way to treat HER2+ breast cancer that has become resistant to the current standard of care. The PANACEA study will investigate the use of pembrolizumab (KEYTRUDA®) in combination with trastuzumab to evaluate whether the addition of an anti-PD-1 therapy can reverse trastuzumab resistance in patients with HER2+ breast cancer whose cancer has spread while on trastuzumab therapy.

Worldwide, breast cancer is the most common cancer among women.¹ About one in five patients with breast cancer have too much of a growth-promoting protein known as HER2/neu (or just HER2) on the surface of cancer cells. Breast cancers with too much of this protein tend to grow and spread more aggressively.

“PANACEA is the first phase 2 immunotherapy trial not only in HER2+ breast cancer, but in the entire breast cancer field,” said Sherene Loi, MD, PhD, study chair, division of cancer

medicine, Peter MacCallum Cancer Centre, Australia. “If successful, this may herald a new treatment approach in certain types of breast cancer.”

“Traditionally, breast cancer has not been thought as an ‘immunogenic’ solid tumor, which is why immunotherapies have been initially evaluated in melanoma and renal cancers,” said Fabrice André, MD, PhD, study co-chair, department of medical oncology, Institut Gustave Roussy, France. “However, a significant amount of preclinical and correlative clinical data suggest that HER2+ breast cancer could be amenable to immuno-therapeutic approaches. That’s what the many centers involved in this worldwide collaborative study will try to prove in the next couple of years.”

“Merck is committing its resources to advance the science of immuno-oncology, so we can better understand the role of the PD-1 and other immune pathways in the treatment of breast and other cancers,” said Alise Reicin, MD, vice president, global clinical development, oncology, Merck Research Laboratories. “This study will provide insight into the role of the PD-1/PD-L1 pathway in HER2+ breast cancer, and we are very pleased to be collaborating with IBCSG and BIG on the PANACEA study.”

About PANACEA Study

The trial, “Anti-PD-1 Monoclonal Antibody in Advanced, Trastuzumab-resistant, HER2+ Breast Cancer (PANACEA),” is a Phase 1b/2 study in patients with HER2+ breast cancer whose cancer has spread while on treatment with trastuzumab. Primary outcome measures of the study are recommended dose and efficacy and safety profile of pembrolizumab in combination with trastuzumab. Response will be assessed by RECIST 1.1 criteria. Secondary outcome measures include safety and tolerability, disease control, duration of response, time to progression, progression-free survival and overall survival.

The study is enrolling adult females with unresectable or metastatic breast adenocarcinoma with confirmed HER2-positivity. There are 10 sites participating in the study across Europe and Australia: Peter MacCallum Cancer Centre and Westmead Hospital in Australia; Medical University of Vienna in Austria; Jules Bordet Institute and CHU Sart Tilman in Belgium; Institut de Cancérologie de l’OUEST, Centre Léon Bérard and Institut Gustave Roussy in France; and Istituto Europeo di Oncologia Milano and Azienda USL4 Prato in Italy.

For more information on the PANACEA study, including how to enroll, please visit: <http://clinicaltrials.gov/ct2/show/NCT02129556?term=pembrolizumab+AND+breast&rank=1>.

About KEYTRUDA (pembrolizumab)

KEYTRUDA (pembrolizumab) is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. By binding to the PD-1 receptor and blocking the interaction with the receptor ligands, KEYTRUDA releases the PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response.

KEYTRUDA is indicated in the United States at a dose of 2 mg/kg every three weeks for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. This indication is 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

Pneumonitis occurred in 12 (2.9%) of 411 patients with advanced melanoma receiving KEYTRUDA (the approved indication in the United States), including Grade 2 or 3 cases in 8 (1.9%) and 1 (0.2%) patients, respectively. 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 for signs and symptoms of hypophysitis. 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.

Nephritis occurred in 3 (0.7%) patients receiving KEYTRUDA, 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.

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 hypothyroidism may be managed with replacement therapy without treatment interruption and without corticosteroids.

Other clinically important immune-mediated adverse reactions can occur. The following clinically significant, immune-mediated adverse reactions occurred in less than 1% of patients treated with KEYTRUDA: exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, hemolytic anemia, partial seizures arising in a patient with inflammatory foci in brain parenchyma, adrenal insufficiency, 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.

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.

For the treatment of advanced melanoma, KEYTRUDA was discontinued for adverse reactions in 6% of 89 patients who received the recommended dose of 2 mg/kg and 9% of 411

patients across all doses studied. Serious adverse reactions occurred in 36% of patients receiving KEYTRUDA. The most frequent serious adverse drug reactions reported in 2% or more of patients were renal failure, dyspnea, pneumonia, and cellulitis.

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

The recommended dose of KEYTRUDA is 2 mg/kg administered as an intravenous infusion over 30 minutes every three weeks until disease progression or unacceptable toxicity. 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.

About the International Breast Cancer Study Group (IBCSG)

The International Breast Cancer Study Group is a non-profit research organization dedicated to innovative clinical research designed to improve the prognosis of women with breast cancer. Formed in 1977 as the Ludwig Breast Cancer Study Group, IBCSG strives to conduct clinical trials at the highest level of knowledge in breast cancer medicine, trial methodology, data handling, and ethical conduct. Patients and investigators from six continents (Europe, Australia/New Zealand, Africa, Asia, North and South America) cooperate by participating in extensive clinical trials in breast cancer populations, guided by the highest scientific and ethical standards. IBCSG plays a key role in disseminating practice-changing trial results to the breast cancer community. For more information, visit www.ibcsq.org.

About Breast International Group (BIG)

The Breast International Group (BIG) is a non-profit organization for academic breast cancer research groups from around the world, based in Brussels, Belgium.

Founded by leading European opinion leaders in 1999, BIG now constitutes a network of 55 collaborative groups from Europe, Canada, Latin America, Asia and Australasia. These entities are tied to several thousand specialized hospitals and research centers worldwide. More than 30 clinical trials are run or are under development under the BIG umbrella at any one time. BIG also works closely with the US National Cancer Institute (NCI) and the North American Breast Cancer Groups (NABCG), so that together they act as a strong integrating force in the breast cancer research arena.

To make significant scientific advances in breast cancer research, reduce unnecessary duplication of effort, and optimally serve those affected by the disease, global collaboration is crucial. Therefore BIG facilitates breast cancer research at international level, by stimulating cooperation between its members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry.

www.BIGagainstbreastcancer.org

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside 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](#), [Facebook](#) and [YouTube](#).

Merck's Focus on Cancer

Our goal is to translate breakthrough science into biomedical innovations to help people with cancer worldwide. For Merck Oncology, helping people fight cancer is our passion, supporting accessibility to our cancer medicines is our commitment, and pursuing research in immuno-oncology is our focus to potentially bring new hope to people with cancer. For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

Forward-Looking Statement

This news release 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 Merck'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; Merck'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 Merck's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

Merck 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 Merck's 2013 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).

#

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

¹ GLOBOCAN. Breast Cancer: Estimated Incidence, Mortality and Prevalence Worldwide in 2012. Available at: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Accessibility verified on December 9, 2014.