Kyowa Hakko Kirin and Bristol-Myers Squibb Announce Immuno-Oncology Clinical Collaboration Studying Mogamulizumab and *Opdivo* (nivolumab) in Advanced Solid Tumors in the U.S.

(NEW YORK and TOKYO, July 29, 2015) - Kyowa Hakko Kirin Co., Ltd. (Tokyo: 4151,"Kyowa Hakko Kirin") and Bristol-Myers Squibb Company (NYSE: BMY, "Bristol-Myers Squibb") today announced that the companies have entered into a clinical trial collaboration agreement to conduct a Phase 1/2 combination study with mogamulizumab, an anti-CCR4 antibody and *Opdivo* (nivolumab), a PD-1 immune checkpoint inhibitor. The study, which will be conducted in the U.S., will focus on evaluating the safety, tolerability and anti-tumor activity of combining mogamulizumab and *Opdivo* as a potential treatment option for patients with advanced or metastatic solid tumors. Prior to this agreement, Kyowa Hakko Kirin, Bristol-Myers Squibb and Ono Pharmaceutical Co., Ltd. (Tokyo: 4528) entered into a clinical trial collaboration agreement to study the combination of mogamulizumab and *Opdivo* in Japan.

Mogamulizumab and *Opdivo* are part of a new class of cancer treatments known as immunotherapies, which are designed to harness the body's own immune system in fighting cancer by targeting distinct regulatory components of the immune system.

"We are pleased to conduct a combination study with Bristol-Myers Squibb not only in Japan but also in the U.S.," said Yoichi Sato, Director of the Board Managing Executive Officer, Vice President, Head of Research and Development Division of Kyowa Hakko Kirin. "We believe that the planned combination of these two immunotherapies has the potential to deliver better outcomes in patients with advanced cancers than existing treatments."

"Today's agreement builds on our initial collaboration with Kyowa Hakko Kirin in Japan, which includes our partner Ono Pharmaceutical Co., Ltd., and is the latest example of our continued commitment to evaluating the potential of combination immuno-oncology regimens for patients with metastatic cancer," stated Michael Giordano, senior vice president, Head of Development, Oncology, Bristol-Myers Squibb.

The study will be conducted by Kyowa Hakko Kirin. Additional details of the collaboration were not disclosed.

About Mogamulizumab

Mogamulizumab (Brand name: POTELIGEO®) is a novel, humanized mAb directed against CC chemokine receptor type 4 (CCR4). Engineered by Kyowa Hakko Kirin's unique POTELLIGENT® Technology, the antibody is designed to kill its target cells through potent antibody-dependent cellular cytotoxicity. Mogamulizumab was launched in Japan in May 2012 for the treatment of patients with relapsed or refractory CCR4-positive adult T-cell leukemia-lymphoma (ATL). The drug was approved for indication expansion and was granted marketing authorization in Japan for the treatment of patients with relapsed or refractory CCR4-positive, peripheral T-cell lymphoma (PTCL) and cutaneous T-cell lymphoma (CTCL) in March 2014, and with chemotherapy-native CCR4-positive ATL in December 2014. Clinical trials with mogamulizumab are ongoing in the US, EU and other countries.

About *Opdivo*

Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that has received approval from the U.S. Food and Drug Administration (FDA) as a monotherapy in two cancer indications. On March 5, 2015, *Opdivo* received FDA approval for the treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy.

In the U.S., *Opdivo* is also indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following *Yervoy* (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. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. *Opdivo* became the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world on July 4, 2014 when Ono Pharmaceutical Co. announced that it received manufacturing and marketing approval in Japan for the treatment of patients with unresectable melanoma. Bristol-Myers Squibb has a broad, global development program to study *Opdivo* in multiple tumor types consisting of more than 50 trials – as monotherapy or in combination with other therapies – in which more than 7,000 patients have been enrolled worldwide.

IMPORTANT SAFETY INFORMATION

Immune-Mediated Pneumonitis

- Severe pneumonitis or interstitial lung disease, including fatal cases, occurred with OPDIVO treatment. Across the clinical trial experience in 691 patients with solid tumors, fatal immune-mediated pneumonitis occurred in 0.7% (5/691) of patients receiving OPDIVO; no cases occurred in Trial 1 or Trial 3. In Trial 1, pneumonitis, including interstitial lung disease, occurred in 3.4% (9/268) of patients receiving OPDIVO and none of the 102 patients receiving chemotherapy. Immune-mediated pneumonitis occurred in 2.2% (6/268) of patients receiving OPDIVO; one with Grade 3 and five with Grade 2. In Trial 3, immune-mediated pneumonitis occurred in 6% (7/117) of patients receiving OPDIVO, including, five Grade 3 and two Grade 2 cases. Monitor patients for signs and symptoms of pneumonitis. Administer corticosteroids for Grade 2 or greater pneumonitis. Permanently discontinue OPDIVO for Grade 3 or 4 and withhold OPDIVO until resolution for Grade 2.

Immune-Mediated Colitis

- In Trial 1, diarrhea or colitis occurred in 21% (57/268) of patients receiving OPDIVO and 18% (18/102) of patients receiving chemotherapy. Immune-mediated colitis occurred in 2.2% (6/268) of patients receiving OPDIVO; five with Grade 3 and one with Grade 2. In Trial 3, diarrhea occurred in 21% (24/117) of patients receiving OPDIVO. Grade 3 immune-mediated colitis occurred in 0.9% (1/117) of patients. Monitor patients for immune-mediated colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO for Grade 2 or 3. Permanently discontinue OPDIVO for Grade 4 colitis or recurrent colitis upon restarting OPDIVO.

Immune-Mediated Hepatitis

- In Trial 1, there was an increased incidence of liver test abnormalities in the OPDIVO-treated group as compared to the chemotherapy-treated group, with increases in AST (28% vs 12%), alkaline phosphatase (22% vs 13%), ALT (16% vs 5%), and total bilirubin (9% vs 0). Immune-mediated hepatitis occurred in 1.1% (3/268) of patients receiving OPDIVO; two with Grade 3 and one with Grade 2. In Trial 3, the incidences of increased liver test values were AST (16%), alkaline phosphatase (14%), ALT (12%), and total bilirubin (2.7%). Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater transaminase elevations. Withhold OPDIVO for Grade 2 and permanently discontinue OPDIVO for Grade 3 or 4 immune-mediated hepatitis.

Immune-Mediated Nephritis and Renal Dysfunction

- In Trial 1, there was an increased incidence of elevated creatinine in the OPDIVO-treated group as compared to the chemotherapy-treated group (13% vs 9%). Grade 2 or 3 immune-mediated nephritis or renal dysfunction occurred in 0.7% (2/268) of patients. In Trial 3, the incidence of elevated creatinine was 22%. Immune-mediated renal dysfunction (Grade 2) occurred in 0.9% (1/117) of patients. Monitor patients for elevated serum creatinine prior to and periodically during treatment. For Grade 2 or 3 serum creatinine elevation, withhold OPDIVO and administer corticosteroids; if worsening or no improvement occurs, permanently discontinue OPDIVO. Administer corticosteroids for Grade 4 serum creatinine elevation and permanently discontinue OPDIVO.

Immune-Mediated Hypothyroidism and Hyperthyroidism

- In Trial 1, Grade 1 or 2 hypothyroidism occurred in 8% (21/268) of patients receiving OPDIVO and none of the 102 patients receiving chemotherapy. Grade 1 or 2 hyperthyroidism occurred in 3% (8/268) of patients receiving OPDIVO and 1% (1/102) of patients receiving chemotherapy. In Trial 3, hypothyroidism occurred in 4.3% (5/117) of patients receiving OPDIVO. Hyperthyroidism occurred in 1.7% (2/117) of patients, including one Grade 2 case. Monitor thyroid function prior to and periodically during treatment. Administer hormone replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism.

Other Immune-Mediated Adverse Reactions

- In Trial 1 and 3 (n=385), the following clinically significant immune-mediated adverse reactions occurred in <2% of OPDIVO-treated patients: adrenal insufficiency, uveitis, pancreatitis, facial and abducens nerve paresis, demyeliniation, autoimmune neuropathy, motor dysfunction, and vasculitis. Across clinical trials of OPDIVO administered at doses 3 mg/kg and 10 mg/kg, additional clinically significant, immune-mediated adverse reactions were identified: hypophysitis, diabetic ketoacidosis, hypopituitarism, Guillain-Barré syndrome, and myasthenic syndrome. Based on the severity of adverse reaction, withhold OPDIVO, administer high-dose corticosteroids, and, if appropriate, initiate hormone- replacement therapy.

Embryofetal Toxicity

- Based on its mechanism of action, OPDIVO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with OPDIVO and for at least 5 months after the last dose of OPDIVO.

Lactation

- It is not known whether OPDIVO is present in human milk. Because many drugs, including antibodies, are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from OPDIVO, advise women to discontinue breastfeeding during treatment.

Serious Adverse Reactions

- In Trial 1, serious adverse reactions occurred in 41% of patients receiving OPDIVO. Grade 3 and 4 adverse reactions occurred in 42% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse drug reactions reported in 2% to <5% of patients receiving OPDIVO were abdominal pain, hyponatremia, increased aspartate aminotransferase, and increased lipase.
- In Trial 3, serious adverse reactions occurred in 59% of patients receiving OPDIVO. The most frequent serious adverse drug reactions reported in ≥2% of patients were dyspnea, pneumonia, chronic obstructive pulmonary disease exacerbation, pneumonitis, hypercalcemia, pleural effusion, hemoptysis, and pain.

Common Adverse Reactions

- The most common adverse reactions (≥20%) reported with OPDIVO in Trial 1 were rash (21%) and in Trial 3 were fatigue (50%), dyspnea (38%), musculoskeletal pain (36%), decreased appetite (35%), cough (32%), nausea (29%), and constipation (24%).

Please see U.S. Full Prescribing Information for OPDIVO here.

About Kyowa Hakko Kirin

Kyowa Hakko Kirin is a leading biopharmaceutical company in Japan focusing on its core business area of oncology, nephrology and immunology/allergy. Kyowa Hakko Kirin leverages antibody-related leading-edge technologies to discover and develop innovative new drugs aiming to become a global specialty pharmaceutical company which contributes to the health and well-being of people around the world. For more information, visit http://www.kyowa-kirin.com.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit www.bms.com or follow us on Twitter at http://twitter.com/bmsnews.

Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that the study combining mogamulizumab and Opdivo will be successful. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2014 in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

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