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European Medicines Agency Validates Bristol-Myers Squibb's Type II Variation Application for *Opdivo* (nivolumab) in Previously Treated Advanced Renal Cell Carcinoma

(PRINCETON, NJ, November 5, 2015) – Bristol-Myers Squibb Company (NYSE: BMY) announced that the European Medicines Agency (EMA) validated a type II variation application, which seeks to extend the current indication for Opdivo to include the treatment of adult patients with advanced renal cell carcinoma (RCC) after prior therapy. Validation of the application confirms the submission is complete and begins the EMA's centralized review process.

In USA, Opdivo was approved under accelerated approval for the treatment of unresectable or metastatic melanoma and disease progression following Yervoy and, if BRAF V600 mutation positive, a BRAF inhibitor in December 2014 and approved for the treatment of metastatic squamous NSCLC with progression on or after platinum-based chemotherapy in March 2015. Also, Opdivo in combination with Yervoy for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma received the approval in October 2015. Opdivo received expanded FDA approval in previously-treated metastatic non-small cell lung cancer in the same month. In EU, Opdivo was approved for the treatment of advanced (unresectable or metastatic) melanoma in adults regardless of BRAF status in June 2015. European Commission approved Nivolumab BMS for the treatment of locally advanced or metastatic squamous NSCLC after prior chemotherapy in July 2015.

Also, BMS has a robust clinical development program in a variety of tumor types overseas, including: Renal Cell Carcinoma (RCC), Head and Neck Cancer, Blood Cancer, Glioblastoma, Colorectal Cancer, Pancreatic Cancer, Gastric Cancer, Hepatocellular Carcinoma, Triple-Negative Breast Cancer, Small-Cell Lung Cancer, Urothelial Cancer. In Japan, ONO launched it for the treatment of unresectable melanoma in September 2014. Also, ONO is conducting clinical development programs including RCC, NSCLC, Head and Neck Cancer, Gastric Cancer, Esophageal Cancer, Hepatocellular Carcinoma, Hodgkin Lymphoma, Urothelial Cancer and Glioblastoma.

Attached from the following page is the press release made by BMS for your information.

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European Medicines Agency Validates Bristol-Myers Squibb’s Type II Variation Application for *Opdivo* (nivolumab) in Previously Treated Advanced Renal Cell Carcinoma

Overall survival results from CheckMate -025, a landmark Phase 3 study comparing Opdivo versus everolimus, in this patient population, serves as basis for application

(PRINCETON, NJ, November 5, 2015) – [Bristol-Myers Squibb Company](#) (NYSE: BMY) today announced that the European Medicines Agency (EMA) validated a type II variation application, which seeks to extend the current indication for *Opdivo* to include the treatment of adult patients with advanced renal cell carcinoma (RCC) after prior therapy. Validation of the application confirms the submission is complete and begins the EMA’s centralized review process.

Michael Giordano, M.D., senior vice president, head of Development, Oncology, Bristol-Myers Squibb, commented, “Europe has one of the highest incidence rates of renal cell carcinoma, and a significant percentage of these patients are diagnosed at an advanced stage of the disease. The validation of our application by the EMA is an important step in the regulatory review process in the European Union, and we will continue to work with the utmost speed to bring *Opdivo* to patients with this cancer.”

The type II variation submitted is based on data from CheckMate -025, a Phase 3 study that evaluated, as the primary endpoint, the overall survival of *Opdivo* versus everolimus, a current standard of care, in advanced or metastatic clear-cell RCC after prior anti-angiogenic treatment. Results from CheckMate -025 were recently presented at the 2015 European Cancer Congress, and published in *The New England Journal of Medicine*.

About Renal Cell Carcinoma

Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults, accounting for more than 100,000 deaths worldwide each year. Clear-cell RCC is the most prevalent type of RCC and constitutes 80% to 90% of all cases. RCC is approximately twice as common in men as it is in women, with the highest rates of the disease found in North America and Europe. Globally, the five-year survival rate for those diagnosed with advanced kidney cancer is 12.1%.

About *Opdivo*

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 8,000 patients have been enrolled worldwide. *Opdivo* is the first PD-1 immune

checkpoint inhibitor to receive regulatory approval anywhere in the world in July 2014, and currently has regulatory approval in more than 37 countries including the United States, Japan, and in the European Union.

IMPORTANT SAFETY INFORMATION

Immune-Mediated Pneumonitis

Immune-mediated pneumonitis or interstitial lung disease, including fatal cases, occurred with OPDIVO treatment. Across the clinical trial experience with solid tumors, fatal immune-mediated pneumonitis occurred in 0.5% (5/978) of patients receiving OPDIVO as a single agent. In Checkmate 037, 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 Checkmate 057, immune-mediated pneumonitis, including interstitial lung disease, occurred in 3.4% (10/287) of patients receiving OPDIVO including five Grade 3, two Grade 2, and three Grade 1 cases. Monitor patients for signs with radiographic imaging and symptoms of pneumonitis. Administer corticosteroids for Grade 2 or greater pneumonitis. Permanently discontinue OPDIVO for Grade 3 or 4 and withhold until resolution for Grade 2.

Immune-Mediated Colitis

Immune-mediated colitis can occur with OPDIVO treatment. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO for Grade 2 or 3 and permanently discontinue for Grade 4 or recurrent colitis upon restarting OPDIVO. In Checkmate 037, 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 Checkmate 057, diarrhea or colitis occurred in 17% (50/287) of patients receiving OPDIVO. Immune-mediated colitis occurred in 2.4% (7/287) of patients including three Grade 3, two Grade 2, and two Grade 1 cases.

Immune-Mediated Hepatitis

Immune-mediated hepatitis can occur with OPDIVO treatment. 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 for Grade 3 or 4 immune-mediated hepatitis. In Checkmate 037, 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 Checkmate 057, one patient (0.3%) developed immune-mediated hepatitis.

Immune-Mediated Endocrinopathies

Hypophysitis, adrenal insufficiency, and thyroid disorders can occur with OPDIVO treatment. Monitor patients for signs and symptoms of hypophysitis, signs and symptoms of adrenal insufficiency during and after treatment, and thyroid function prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater hypophysitis. Withhold OPDIVO for Grade 2 or 3 and permanently discontinue for Grade 4 hypophysitis. Administer corticosteroids for Grade 3 or 4 adrenal insufficiency. Withhold OPDIVO for Grade 2 and permanently discontinue for Grade 3 or 4 adrenal insufficiency. Administer hormone replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism. Adrenal insufficiency occurred in 1% (n=555) of patients receiving OPDIVO as a single agent. In Checkmate 037, 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 Checkmate 057, Grade 1 or 2 hypothyroidism, including thyroiditis, occurred in 7% (20/287) and elevated TSH occurred in 17% of patients receiving OPDIVO. Grade 1 or 2 hyperthyroidism occurred in 1.4% (4/287) of patients.

Immune-Mediated Nephritis and Renal Dysfunction

Immune-mediated nephritis can occur with OPDIVO treatment. Monitor patients for elevated serum creatinine prior to and periodically during treatment. For Grade 2 or 3 increased serum creatinine, 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. In Checkmate 037, 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 Checkmate 057, Grade 2 immune-mediated renal dysfunction occurred in 0.3% (1/287) of patients.

Immune-Mediated Rash

Immune-mediated rash can occur with OPDIVO treatment. Monitor patients for rash. Administer corticosteroids for Grade 3 or 4 rash. Withhold OPDIVO for Grade 3 and permanently discontinue for Grade 4 rash. . In Checkmate 057, immune-mediated rash occurred in 6% (17/287) of patients receiving OPDIVO including 4 Grade 3 cases.

Immune-Mediated Encephalitis

Immune-mediated encephalitis can occur with OPDIVO treatment. Withhold OPDIVO in patients with new-onset moderate to severe neurologic signs or symptoms and evaluate to rule out other causes. If other etiologies are ruled out, administer corticosteroids and permanently discontinue OPDIVO for immune-mediated encephalitis. Across clinical trials of 8490 patients receiving OPDIVO as a single agent or in combination with ipilimumab, <1% of patients were identified as having encephalitis. In Checkmate 057, fatal limbic encephalitis occurred in one patient (0.3%) receiving OPDIVO.

Other Immune-Mediated Adverse Reactions

Based on the severity of adverse reaction, permanently discontinue or withhold treatment, administer high-dose corticosteroids, and, if appropriate, initiate hormone- replacement therapy. The following clinically significant immune-mediated adverse reactions occurred in <2% (n=555) of single-agent OPDIVO-treated patients: uveitis, pancreatitis, abducens nerve paresis, demyelination, polymyalgia rheumatica, and autoimmune neuropathy,. Across clinical trials of OPDIVO as a single agent administered at doses 3 mg/kg and 10 mg/kg, additional clinically significant, immune-mediated adverse reactions were identified: facial nerve paralysis, motor dysfunction, vasculitis, diabetic ketoacidosis, and myasthenic syndrome.

Infusion Reactions

Severe infusion reactions have been reported in <1% of patients in clinical trials of OPDIVO. In Checkmate 057, Grade 2 infusion reactions occurred in 1% (3/287) of patients receiving OPDIVO. Discontinue OPDIVO in patients with severe or life-threatening infusion reactions. Interrupt or slow the rate of infusion in patients with mild or moderate infusion reactions.

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-containing regimen 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-containing regimen, advise women to discontinue breastfeeding during treatment.

Serious Adverse Reactions

In Checkmate 037, 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 Checkmate 057, serious adverse reactions occurred in 47% of patients receiving OPDIVO. The most frequent serious adverse reactions reported in $\geq 2\%$ of patients were pneumonia, pulmonary embolism, dyspnea, pleural effusion, and respiratory failure.

Common Adverse Reactions

In Checkmate 037, the most common adverse reaction ($\geq 20\%$) reported with OPDIVO was rash (21%).

In Checkmate 057, the most common adverse reactions ($\geq 20\%$) reported with OPDIVO were fatigue (49%), musculoskeletal pain (36%), cough (30%), decreased appetite (29%), and constipation (23%).

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

Immuno-Oncology at Bristol-Myers Squibb

Surgery, radiation, cytotoxic or targeted therapies have represented the mainstay of cancer treatment over the last several decades, but long-term survival and a positive quality of life have remained elusive for many patients with advanced disease.

To address this unmet medical need, Bristol-Myers Squibb is leading research in an innovative field of cancer research and treatment known as Immuno-Oncology, which involves agents whose primary mechanism is to work directly with the body's immune system to fight cancer. The company is exploring a variety of compounds and immunotherapeutic approaches for patients with different types of cancer, including researching the potential of combining Immuno-Oncology agents that target different pathways in the treatment of cancer.

Bristol-Myers Squibb is committed to advancing the science of Immuno-Oncology, with the goal of changing survival expectations and the way patients live with cancer.

About the Bristol-Myers Squibb and Ono Pharmaceutical Collaboration

In 2011, through a collaboration with Ono Pharmaceutical Co., Bristol-Myers Squibb expanded its territorial rights to develop and commercialize *Opdivo* globally except in Japan, South Korea and Taiwan, where Ono had retained all rights to the compound at the time. On July 23, 2014, Bristol-Myers Squibb and Ono Pharmaceutical further expanded the companies' strategic collaboration agreement to

jointly develop and commercialize multiple immunotherapies – as single agents and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.

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 about Bristol-Myers Squibb, 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 Opdivo will receive regulatory approval for the additional indication described in this release. 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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