July 28, 2015

European Medicines Agency Validates Two Parallel Type II Variation Applications to Extend the Opdivo (nivolumab) Indication in Europe

(PRINCETON, N.J., July 23, 2015) – Bristol-Myers Squibb Company (NYSE: BMY) announced that the European Medicines Agency (EMA) has validated two of the company's type II variation applications, which seek to extend the current indication for its Immuno-Oncology agent, Opdivo. Validation of the applications confirms that the submissions are complete and starts the EMA's centralized review process.

Through the collaboration agreement entered into in September 2011 between ONO and BMS, ONO granted BMS exclusive rights to develop and commercialize Opdivo in the rest of the world, except in Japan, Korea and Taiwan where ONO had retained all rights to develop and commercialize the compound. In July 2014, ONO and BMS signed a new collaboration agreement in which the companies agreed to jointly develop and commercialize Opdivo, ipilimumab and three early-stage immunotherapies in Japan, South Korea and Taiwan.

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. 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, Bladder 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 and Hodgkin Lymphoma.

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

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Bristol-Myers Squibb

European Medicines Agency Validates Two Parallel Type II Variation Applications to Extend the *Opdivo* (nivolumab) Indication in Europe

Variations include* Opdivo *in previously treated non-squamous, non-small cell lung cancer (NSCLC) and* Opdivo *in combination with* Yervoy (ipilimumab) *in advanced melanoma

(PRINCETON, N.J., July 23, 2015) – Bristol-Myers Squibb Company (NYSE: BMY) today announced that the European Medicines Agency (EMA) has validated two of the company's type II variation applications, which seek to extend the current indication for its Immuno-Oncology agent, *Opdivo*. Validation of the applications confirms that the submissions are complete and starts the EMA's centralized review process.

In lung cancer, the proposed new indication addresses the non-squamous NSCLC population -- *Opdivo* as monotherapy for the treatment of locally advanced or metastatic non-squamous NSCLC after prior chemotherapy in adults. In melanoma, the proposed new indication aims to extend the use of *Opdivo* monotherapy to its use in combination -- *Opdivo* in combination with *Yervoy* for the treatment of advanced (unresectable or metastatic) melanoma in adults.

"The starting of the EMA's centralized review process marks a significant milestone in our commitment to make *Opdivo* available for a broader range of appropriate patients with advanced melanoma and lung cancer in Europe," said Michael Giordano, M.D., senior vice president, head of Oncology Development, Bristol-Myers Squibb. "Today's announcement also is a step forward in realizing our vision to change survival expectations, transform the standard of cancer care, and the way patients live with cancer across multiple tumor types. We look forward to working with the EMA during its review process."

The type II variation submitted to the EMA in non-squamous NSCLC is supported by data from the landmark, global Phase 3 study, CheckMate -057, which evaluated the survival of patients with advanced non-squamous NSCLC who had progressed during or after one prior platinum doublet-based chemotherapy regimen. The type II variation application in advanced melanoma is based on data from two studies: CheckMate -067, a pivotal Phase 3 study that evaluated the *Opdivo*+*Yervoy* regimen or *Opdivo* monotherapy vs. *Yervoy* monotherapy in adults

with previously-untreated advanced melanoma, and the Phase 2 CheckMate -069, the first randomized trial evaluating the *Opdivo+Yervoy* regimen in patients with previously-untreated advanced melanoma, as well as supportive data from the Phase 1b CA209004 study in advanced melanoma.

About the Marketing Authorization Applications

Bristol-Myers Squibb submitted two separate Marketing Authorization Applications (MAA), one in advanced melanoma under the tradename *Opdivo* and one for squamous NSCLC under the tradename Nivolumab BMS in order to accelerate availability of nivolumab for health care professionals in both indications. The EMA has accepted Bristol-Myers Squibb's application to "reconcile" the MAAs into a single marketing authorization under the tradename *Opdivo*. The goal is to have the MAAs reconciled toward the end 2015.

About *Opdivo* and *Yervoy*

Cancer cells may exploit "regulatory" pathways, such as checkpoint pathways, to hide from the immune system and shield the tumor from immune attack. *Opdivo* and *Yervoy* are both monoclonal antibodies and immune checkpoint inhibitors that target separate, distinct checkpoint pathways. Inhibition of these immune checkpoint pathways results in enhanced T-cell function greater than the effects of either antibody alone.

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. In the U.S., the Food and Drug Administration (FDA) granted its first approval for *Opdivo* for the treatment of patients with unresectable or metastatic melanoma and disease progression following *Yervoy* and, if BRAF V600 mutation positive, a BRAF inhibitor. On March 4, 2015, *Opdivo* received its second FDA approval for the treatment of patients with advanced squamous non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. The European Commission (EC) announced approval of *Opdivo* on June 19, 2015, for the treatment of advanced (unresectable or metastatic) melanoma in adults, regardless of BRAF status, and on July 20, 2015, the EC announced it approved Nivolumab

BMS for the treatment of locally advanced or metastatic squamous NSCLC after prior chemotherapy.

On March 25, 2011, the FDA approved *Yervoy* 3 mg/kg monotherapy for patients with unresectable or metastatic melanoma. In July 2011, approval of *Yervoy* was granted in Europe by the European Commission for the treatment of advanced melanoma patients after prior treatment; the Marketing Authorization was extended in May 2013 to the untreated advanced melanoma population. *Yervoy* is now approved in more than 40 countries.

Bristol-Myers Squibb has a broad, global development program with over 8,000 patients enrolled in more than 50 trials evaluating nivolumab across multiple tumor types – as monotherapy or in combination with other therapies.

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.

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 agreement with Ono Pharmaceutical, Bristol-Myers Squibb expanded its territorial rights to develop and commercialize nivolumab 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 pharmaceutical 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 be approved for an additional indication in lung cancer in Europe, that the combination treatment of Opdivo and Yervoy will receive regulatory approval, or if approved, that it will become a commercially successful product. 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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