

January 15, 2015

**CheckMate -017, A Phase 3 Study of Opdivo (Nivolumab) Compared to Docetaxel in Patients with Second-Line Squamous Cell Non-small Cell Lung Cancer, Stopped Early**  
*Opdivo demonstrates superior overall survival in this Phase 3 trial*

(PRINCETON, NJ, January 11, 2015) – [Bristol-Myers Squibb Company](#) (NYSE:BMJ) (“BMS”) announced that an open-label, randomized Phase 3 study evaluating Opdivo versus docetaxel in previously treated patients with advanced, squamous cell non-small cell lung cancer (NSCLC) was stopped early because an assessment conducted by the independent Data Monitoring Committee (DMC) concluded that the study met its endpoint, demonstrating superior overall survival in patients receiving Opdivo compared to the control arm. The Company will share these data- which for the first time indicate a survival advantage with an anti-PD1 immune checkpoint inhibitor in lung cancer - with health authorities.

Opdivo is a human anti-human PD-1 monoclonal antibody generated under a research collaboration entered into in May 2005 between ONO PHARMACEUTICAL CO.,LTD. (“ONO”) and the US-based company Medarex, Inc. When Medarex, Inc. was acquired by BMS in 2009, it also granted BMS its rights to develop and commercialize the human anti-human PD-1 monoclonal antibody in North America. 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. On July 23, 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® (ipilimumab) and, if BRAF V600 mutation positive, a BRAF inhibitor in December 2014. Also, BMS has a robust clinical development program in a variety of tumor types overseas, including: Non-Small Cell Lung Cancer (NSCLC), 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 and Esophageal Cancer.

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

Contact

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## **CheckMate -017, A Phase 3 Study of Opdivo (Nivolumab) Compared to Docetaxel in Patients with Second-Line Squamous Cell Non-small Cell Lung Cancer, Stopped Early**

- *Opdivo demonstrates superior overall survival in this Phase 3 trial*

(PRINCETON, NJ, January 11, 2015) – [Bristol-Myers Squibb Company](#) (NYSE:BMJ) today announced that an open-label, randomized Phase 3 study evaluating *Opdivo* versus docetaxel in previously treated patients with advanced, squamous cell non-small cell lung cancer (NSCLC) was stopped early because an assessment conducted by the independent Data Monitoring Committee (DMC) concluded that the study met its endpoint, demonstrating superior overall survival in patients receiving *Opdivo* compared to the control arm. The company will share these data – which for the first time indicate a survival advantage with an anti-PD1 immune checkpoint inhibitor in lung cancer – with health authorities.

CheckMate -017 investigators are being informed of the decision to stop the comparative portion of the trial. Bristol-Myers Squibb is working to ensure that eligible patients will be informed of the opportunity to continue or start treatment with *Opdivo* in an open-label extension as part of the Company's commitment to providing patient access to *Opdivo*, and characterizing long-term survival. The company will complete a full evaluation of the final CheckMate -017 data and work with investigators on the future presentation and publication of the results.

### **About the Study**

CheckMate -017 is a Phase 3, open-label, randomized study of *Opdivo* versus docetaxel in previously treated patients with advanced or metastatic squamous cell NSCLC. The trial randomized 272 patients to receive either nivolumab 3 mg/kg intravenously every two weeks or docetaxel 75 mg/m<sup>2</sup> intravenously every three weeks. The primary endpoint is overall survival. Secondary endpoints include objective response rate and progression free survival.

### **About Lung Cancer**

Lung cancer is the leading cause of cancer deaths globally, resulting in more than 1.5 million deaths each year according the World Health Organization. NSCLC is one of the most common types of the disease and accounts for approximately 85 percent of cases. Survival rates vary depending on the stage and type of the cancer when it is diagnosed. Globally, the five-year survival rate for Stage I NSCLC is between 47 and 50 percent; for Stage IV NSCLC, the five-year

survival rate drops to two percent. Historically, the expected one-year survival rate for third-line squamous cell NSCLC patients is approximately 5.5% - 18%.

### **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 and complementary 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 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 7,000 patients have been enrolled worldwide.

In the U.S., *Opdivo* is 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.

## **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 574 patients with solid tumors, fatal immune-mediated pneumonitis occurred in 0.9% (5/574) of patients receiving OPDIVO; no cases occurred in Trial 1. 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. 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. 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. 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. 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. 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, the following clinically significant, immune-mediated adverse reactions occurred in less than 1% of OPDIVO-treated patients: pancreatitis, uveitis, demyelination, autoimmune neuropathy, adrenal insufficiency, and facial and abducens nerve paresis. 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, Guillian-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**

- 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.

### **Common Adverse Reactions**

The most common adverse reaction ( $\geq 20\%$ ) reported with OPDIVO was rash (21%).

Please see [US Full Prescribing Information](#) for OPDIVO.

### **About the Bristol-Myers Squibb and Ono Pharmaceutical Collaboration**

In 2011, through a collaboration agreement 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. Ono Pharmaceutical received manufacturing and marketing approval in Japan for *Opdivo* in July 2014 for the treatment of patients with unresectable melanoma, making *Opdivo* the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world.

**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](http://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 an additional indication in lung cancer or, if approved, that it will become commercially 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, 2013 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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