

October 30, 2015

**Bristol-Myers Squibb's Opdivo (nivolumab)  
Recipient of Prix Galien USA 2015 Award for Best Biotechnology Product**

(PRINCETON, NJ, October 28, 2015) – Bristol-Myers Squibb Company (NYSE:BMJ) announced that it received the Prix Galien USA 2015 Award for Best Biotechnology Product for Opdivo (nivolumab), the Company's PD-1 immune checkpoint inhibitor.

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.

Contact  
ONO PHARMACEUTICAL CO., LTD.  
Corporate Communications  
[public\\_relations@ono.co.jp](mailto:public_relations@ono.co.jp)



**Bristol-Myers Squibb's *Opdivo* (nivolumab) Recipient of Prix Galien USA 2015 Award for Best Biotechnology Product**

***Bristol-Myers Squibb team honored for its innovative approach to the scientific discovery and development of its PD-1 immune checkpoint inhibitor, Opdivo, in the treatment of advanced melanoma and squamous non-small cell lung cancer***

***Represents the second award from Prix Galien USA given to Bristol-Myers Squibb's Immuno-Oncology portfolio; Yervoy (ipilimumab) received Best Biotechnology Product in 2012***

(PRINCETON, NJ, October 28, 2015) – [Bristol-Myers Squibb Company](#) (NYSE:BMJ) today announced that it received the Prix Galien USA 2015 Award for Best Biotechnology Product for *Opdivo* (nivolumab), the Company's PD-1 immune checkpoint inhibitor. Bristol-Myers Squibb was recognized for its innovative discovery and development of *Opdivo* in approved indications for previously treated metastatic squamous non-small cell lung cancer (NSCLC), and in unresectable or metastatic melanoma and disease progression following *Yervoy* (ipilimumab) and, if *BRAF* V600 mutation positive, a *BRAF* inhibitor, for which it received accelerated approval based on tumor response rate and durability of response. Since the submission for the Best Biotechnology Award, *Opdivo* has also been approved by the U.S. Food and Drug Administration (FDA) in the combination of *Opdivo* + *Yervoy*, the first FDA-approved regimen of two Immuno-Oncology agents, in *BRAF* V600 wild-type unresectable or metastatic melanoma, as well as for the treatment of patients with metastatic non-squamous NSCLC with progression on or after platinum-based chemotherapy.

The announcement was made during the ninth annual Prix Galien USA Awards Ceremony held on October 27, 2015 in New York City. The Prix Galien USA Award, which is selected by a preeminent scientific committee that includes several Nobel Laureates, honors outstanding achievements in improving the human condition through the development of innovative therapies. This is the second honor received by Bristol-Myers Squibb in the Best Biotechnology Product category, making it the only company to receive this award for two Immuno-Oncology agents. In 2012, *Yervoy* received the award, following its initial approval for unresectable or metastatic melanoma. Building on this pioneering science, the Company continues to research the potential of Immuno-Oncology to extend survival in some of the hardest-to-treat cancers.

“We are pleased to be acknowledged for our Company's scientific contributions to this historic time in cancer research, when the science of Immuno-Oncology is helping to change expectations in cancer care,” said Francis Cuss, MB BChir, FRCP, executive vice president and chief scientific officer,

Bristol-Myers Squibb. “Receiving the Prix Galien USA 2015 Award for Best Biotechnology Product underscores our efforts with the *Opdivo* early- and late-stage clinical program in patients with some of the hardest-to-treat cancers, like advanced melanoma and squamous non-small cell lung 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 8,000 patients have been enrolled worldwide.

*Opdivo* was 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.

In the U.S., *Opdivo* is indicated for patients with unresectable or metastatic melanoma and disease progression following *Yervoy* (ipilimumab) and, if *BRAF* V600 mutation positive, a *BRAF* inhibitor. *Opdivo* is also approved for use in combination with *Yervoy*, for the treatment of patients with *BRAF* V600 wild-type unresectable or metastatic melanoma. These indications are approved under accelerated approval based on tumor response rate and durability of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials. *Opdivo* is also indicated in the U.S. for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving *Opdivo*.

### **IMPORTANT SAFETY INFORMATION**

#### **WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS**

**YERVOY can result in severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of YERVOY.**

**Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy and evaluate clinical chemistries including liver function tests (LFTs) and thyroid function tests at baseline and before each dose.**

**Permanently discontinue YERVOY and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions.**

**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; Grade 3 (n=1) and Grade 2 (n=5). In Checkmate 057, immune-mediated pneumonitis, including interstitial lung disease, occurred in 3.4% (10/287) of patients receiving OPDIVO as a single agent: Grade 3 (n=5), Grade 2 (n=2), and Grade 1 (n=3). Across the clinical trial experience in 188 patients with melanoma who received OPDIVO in combination with YERVOY, in Checkmate 069 (n=94) and an additional dose-finding study (n=94), fatal immune-mediated pneumonitis occurred in 0.5% (1/188) of patients. In Checkmate 069, there were six additional patients who died without resolution of abnormal respiratory findings. Monitor patients for signs with radiographic imaging and symptoms of pneumonitis. Administer corticosteroids for Grade 2 or greater pneumonitis. Permanently discontinue for Grade 3 or 4 and withhold until resolution for Grade 2. In Checkmate 069, pneumonitis, including interstitial lung disease, occurred in 10% (9/94) of patients receiving OPDIVO in combination with YERVOY and 2.2% (1/46) of patients receiving YERVOY. Immune-mediated pneumonitis occurred in 6% (6/94) of patients receiving OPDIVO in combination with YERVOY: Grade 5 (n=1), Grade 3 (n=2) and Grade 2 (n=3).

**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. As a single agent, withhold OPDIVO for Grade 2 or 3 and permanently discontinue for Grade 4 or recurrent colitis upon restarting OPDIVO. In combination with YERVOY, withhold OPDIVO for Grade 2 and permanently discontinue for Grade 3 or 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; Grade 3 (n=5) and Grade 2 (n=1). In Checkmate 057, diarrhea or colitis occurred in 17% (50/287) of patients receiving OPDIVO as a single agent. Immune-mediated colitis occurred in 2.4% (7/287) of patients: Grade 3 (n=3), Grade 2 (n=2), and Grade 1 (n=2). In Checkmate 069, diarrhea or colitis occurred in 57% (54/94) of patients receiving OPDIVO in combination with YERVOY and 46% (21/46) of patients receiving YERVOY. Immune-mediated colitis occurred in 33% (31/94) of patients receiving OPDIVO in combination with YERVOY: Grade 4 (n=1), Grade 3 (n=16), Grade 2 (n=9), and Grade 1 (n=5).

In a separate YERVOY Phase 3 study, severe, life-threatening, or fatal (diarrhea of  $\geq 7$  stools above baseline, fever, ileus, peritoneal signs; Grade 3-5) immune-mediated enterocolitis occurred in 34 (7%) patients. Across all YERVOY-treated patients in that study (n=511), 5 (1%) developed intestinal

perforation, 4 (0.8%) died as a result of complications, and 26 (5%) were hospitalized for severe enterocolitis.

### **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 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; Grade 3 (n=2) and Grade 2 (n=1). In Checkmate 057, one patient (0.3%) developed immune-mediated hepatitis. In Checkmate 069, immune-mediated hepatitis occurred in 15% (14/94) of patients receiving OPDIVO in combination with YERVOY: Grade 4 (n=3), Grade 3 (n=9), and Grade 2 (n=2).

In a separate YERVOY Phase 3 study, severe, life-threatening, or fatal hepatotoxicity (AST or ALT elevations >5x the ULN or total bilirubin elevations >3x the ULN; Grade 3-5) occurred in 8 (2%) patients, with fatal hepatic failure in 0.2% and hospitalization in 0.4%.

### **Immune-Mediated Dermatitis**

In a separate YERVOY Phase 3 study, severe, life-threatening, or fatal immune-mediated dermatitis (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full thickness dermal ulceration, or necrotic, bullous, or hemorrhagic manifestations; Grade 3-5) occurred in 13 (2.5%) patients. 1 (0.2%) patient died as a result of toxic epidermal necrolysis. 1 additional patient required hospitalization for severe dermatitis.

### **Immune-Mediated Neuropathies**

In a separate YERVOY Phase 3 study, 1 case of fatal Guillain-Barré syndrome and 1 case of severe (Grade 3) peripheral motor neuropathy were reported.

### **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 for Grade 2 or 3 and permanently discontinue for Grade 4 hypophysitis. Administer corticosteroids for Grade 3 or 4 adrenal insufficiency. Withhold 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.

In Checkmate 069, hypophysitis occurred in 13% (12/94) of patients receiving OPDIVO in combination with YERVOY: Grade 3 (n=2) and Grade 2 (n=10). Adrenal insufficiency occurred in 1% (n=555) of

patients receiving OPDIVO as a single agent. In Checkmate 069, adrenal insufficiency occurred in 9% (8/94) of patients receiving OPDIVO in combination with YERVOY: Grade 3 (n=3), Grade 2 (n=4), and Grade 1 (n=1). In Checkmate 069, hypothyroidism occurred in 19% (18/94) of patients receiving OPDIVO in combination with YERVOY. All were Grade 1 or 2 in severity except for one patient who experienced Grade 3 autoimmune thyroiditis. Grade 1 hyperthyroidism occurred in 2.1% (2/94) of patients receiving OPDIVO in combination with YERVOY. 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 as a single agent. Grade 1 or 2 hyperthyroidism occurred in 1.4% (4/287) of patients.

In a separate YERVOY Phase 3 study, severe to life-threatening immune-mediated endocrinopathies (requiring hospitalization, urgent medical intervention, or interfering with activities of daily living; Grade 3-4) occurred in 9 (1.8%) patients. All 9 patients had hypopituitarism, and some had additional concomitant endocrinopathies such as adrenal insufficiency, hypogonadism, and hypothyroidism. 6 of the 9 patients were hospitalized for severe endocrinopathies.

### **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 and administer corticosteroids; if worsening or no improvement occurs, permanently discontinue. Administer corticosteroids for Grade 4 serum creatinine elevation and permanently discontinue. 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 receiving OPDIVO as a single agent. In Checkmate 069, Grade 2 or higher immune-mediated nephritis or renal dysfunction occurred in 2.1% (2/94) of patients. One patient died without resolution of renal dysfunction.

### **Immune-Mediated Rash**

Immune-mediated rash can occur with OPDIVO treatment. Monitor patients for rash. Administer corticosteroids for Grade 3 or 4 rash. Withhold for Grade 3 and permanently discontinue for Grade 4. In Checkmate 037 (n=268), the incidence of rash was 21%; the incidence of Grade 3 or 4 rash was 0.4%. In Checkmate 057, immune-mediated rash occurred in 6% (17/287) of patients receiving OPDIVO as a single agent including four Grade 3 cases. In Checkmate 069, immune-mediated rash occurred in 37% (35/94) of patients receiving OPDIVO in combination with YERVOY: Grade 3 (n=6), Grade 2 (n=10), and Grade 1 (n=19).

## **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 YERVOY, <1% of patients were identified as having encephalitis. In Checkmate 057, fatal limbic encephalitis occurred in one patient (0.3%) receiving OPDIVO as a single agent.

## **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 administered as a single agent 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. In Checkmate 069, the following additional immune-mediated adverse reactions occurred in 1% of patients treated with OPDIVO in combination with YERVOY: Guillain-Barré syndrome and hypopituitarism. Across clinical trials of OPDIVO in combination with YERVOY, the following additional clinically significant, immune-mediated adverse reactions were identified: uveitis, sarcoidosis, duodenitis, pancreatitis, and gastritis.

## **Infusion Reactions**

Severe infusion reactions have been reported in <1% of patients in clinical trials of OPDIVO as a single agent. In Checkmate 057, Grade 2 infusion reactions occurred in 1% (3/287) of patients receiving OPDIVO as a single agent. In Checkmate 069, Grade 2 infusion reactions occurred in 3% (3/94) of patients receiving OPDIVO in combination with YERVOY. 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 as a single agent. The most frequent serious adverse reactions reported in  $\geq 2\%$  of patients were pneumonia, pulmonary embolism, dyspnea, pleural effusion, and respiratory failure. In Checkmate 069, serious adverse reactions occurred in 62% of patients receiving OPDIVO; the most frequent serious adverse events with OPDIVO in combination with YERVOY, as compared to YERVOY alone, were colitis (17% vs 9%), diarrhea (9% vs 7%), pyrexia (6% vs 7%), and pneumonitis (5% vs 0).

## **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 as a single agent were fatigue (49%), musculoskeletal pain (36%), cough (30%), decreased appetite (29%), and constipation (23%). In Checkmate 069, the most common adverse reactions ( $\geq 20\%$ ) reported in patients receiving OPDIVO in combination with YERVOY vs YERVOY alone were rash (67% vs 57%), pruritus (37% vs 26%), headache (24% vs 20%), vomiting (23% vs 15%), and colitis (22% vs 11%).

In a separate YERVOY Phase 3 study, the most common adverse reactions ( $\geq 5\%$ ) in patients who received YERVOY at 3 mg/kg were fatigue (41%), diarrhea (32%), pruritus (31%), rash (29%), and colitis (8%).

Please see U.S. Full Prescribing Information for [OPDIVO](#) and [YERVOY](#), including **Boxed WARNING** for YERVOY **regarding immune-mediated adverse reactions**.

## **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.

## **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. 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.*

###

**Contacts:**

**Media:** Carrie Fernandez, 215-859-2605, [carrie.fernandez@bms.com](mailto:carrie.fernandez@bms.com)

**Investors:** Ranya Dajani, 609-252-5330, [ranya.dajani@bms.com](mailto:ranya.dajani@bms.com)  
Bill Szablewski, 609-252-5864, [william.szablewski@bms.com](mailto:william.szablewski@bms.com)