

October 5, 2015

**Bristol-Myers Squibb Receives Approval from the U.S. Food and Drug Administration
for the *Opdivo* (nivolumab) + *Yervoy* (ipilimumab) Regimen
in *BRAF* V600 Wild-Type Unresectable or Metastatic Melanoma**

(PRINCETON, NJ, October 1, 2015) – Bristol-Myers Squibb Company (NYSE: BMY) announced that the U.S. Food and Drug Administration (FDA) approved *Opdivo* (nivolumab) in combination with *Yervoy* (ipilimumab), for the treatment of patients with *BRAF* V600 wild-type unresectable or metastatic melanoma. Today's announcement marks the first and only FDA approval of a Regimen of two Immuno-Oncology agents in cancer. 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 confirmatory trials.

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, 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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Bristol-Myers Squibb Receives Approval from the U.S. Food and Drug Administration for the *Opdivo* (nivolumab) + *Yervoy* (ipilimumab) Regimen in *BRAF* V600 Wild-Type Unresectable or Metastatic Melanoma

- *First and only FDA-approved combination of two Immuno-Oncology agents¹*
- *Pivotal study CheckMate -069 demonstrates significantly superior responses and progression-free survival with the *Opdivo* + *Yervoy* Regimen vs. *Yervoy* alone¹*
- *Approval of the Regimen marks a new development, demonstrating the potential of targeting distinct and complementary immune system pathways, offering patients a novel combination treatment*

(PRINCETON, NJ, October 1, 2015) – [Bristol-Myers Squibb Company](#) (NYSE: BMY) today announced that the U.S. Food and Drug Administration (FDA) approved *Opdivo* (nivolumab) in combination with *Yervoy* (ipilimumab), for the treatment of patients with *BRAF* V600 wild-type unresectable or metastatic melanoma.¹ Today’s announcement marks the first and only FDA approval of a Regimen of two Immuno-Oncology agents in cancer. This indication is approved under accelerated approval based on tumor response rate and durability of response.¹ Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.¹

The approval is based on data from the pivotal study, CheckMate -069, which was the first to report outcomes of the *Opdivo* + *Yervoy* Regimen in previously untreated patients with unresectable or metastatic melanoma. Results from the trial demonstrated a statistically significant ($p < 0.001$) increase in confirmed objective response rate – the study’s primary endpoint – in patients with *BRAF* wild-type melanoma treated with the *Opdivo* + *Yervoy* Regimen [60% (95% CI: 48-71; $p < 0.001$)] compared to those treated with *Yervoy* monotherapy [11% (95% CI: 3-25)]. Complete responses were seen in 17% of patients. Partial responses were seen in 43% of the Regimen group and 11% of the *Yervoy* monotherapy group. The *Opdivo* + *Yervoy* Regimen demonstrated a 60% reduction in the risk of progression vs. *Yervoy* alone (HR=0.40; 95% CI: 0.22-0.71; $p < 0.002$). Median PFS was 8.9 months with the Regimen (95% CI: 7.0, NA) and 4.7 months with *Yervoy* alone (95% CI: 2.8-5.3).¹ This trial provides clinical rationale for targeting the immune system with two Immuno-Oncology agents in metastatic melanoma.

Opdivo is associated with immune-mediated: pneumonitis, colitis, hepatitis, endocrinopathies, nephritis and renal dysfunction, rash, other adverse reactions; infusion reactions; and embryofetal toxicity.¹ Please see the Important Safety Information section below, including Boxed WARNING for *Yervoy* regarding immune-mediated adverse reactions.

“Targeting the immune system in the treatment of cancer has been of interest to the oncology community for decades,⁴ and our first Immuno-Oncology agent, *Yervoy*, was approved in 2011 for metastatic melanoma. *Opdivo* reinforced the power of the immune system in the fight against cancer, and is quickly becoming a foundational component in how the oncology community treats this devastating disease,” said Giovanni Caforio, chief executive officer, Bristol-Myers Squibb. “Today’s approval of the *Opdivo* + *Yervoy* Regimen marks another first for our research in Immuno-Oncology and represents our unwavering commitment to continually redefine cancer care, and offer patients new treatment options with the goal of improved outcomes.”

About the *Opdivo* + *Yervoy* Regimen: Advancing Metastatic Melanoma Treatment

CheckMate -069 is a Phase 2, double-blind, randomized study which enrolled 140 patients with previously untreated unresectable or metastatic melanoma,¹ and included patients with both *BRAF* wild-type and *BRAF* mutation-positive melanoma.² The primary endpoint was objective response rate (ORR) in patients with *BRAF* wild-type tumors.¹ Additional efficacy outcome measures were investigator-assessed duration of response and progression-free survival (PFS) in patients with *BRAF* V600 wild-type melanoma. Randomization was stratified by *BRAF* mutation status.² The Regimen includes four cycles of the *Opdivo* + *Yervoy* combination followed by *Opdivo* monotherapy.¹ In the clinical study, patients in the *Opdivo* + *Yervoy* Regimen group received *Opdivo* 1mg/kg plus *Yervoy* 3mg/kg every 3 weeks for 4 doses during the combination phase, followed by *Opdivo* 3mg/kg every 2 weeks during the monotherapy phase. Treatment was continued until progression or unacceptable toxicity.¹ In the *Yervoy* monotherapy group, patients were treated with *Yervoy* 3mg/kg every 3 weeks for 4 doses with matched placebo.¹ Of the 95 patients randomized to receive the *Opdivo* + *Yervoy* Regimen, 50% were 65 years or older and 13% were 75 years or older.³ Fifty-nine percent of patients completed all 4 doses in the initial combination phase over a median of 9.1 weeks (range: 9.0 weeks to 26.3 weeks).¹

Among patients (n=109) with *BRAF* wild-type melanoma, the Regimen demonstrated a significantly superior response rate of 60% (95% CI: 48-71; p<0.001) vs. *Yervoy* alone, 11% (95% CI: 3-25).¹ Seventeen percent of patients experienced a complete response in the *BRAF* wild-type population.¹ Partial responses were seen in 43% of the Regimen group and 11% of the *Yervoy*

monotherapy group.¹ Seventy-nine percent (34/43) of patients had ongoing responses of at least 6 months at the time of analysis. Of these patients, 14 had a duration of response of at least 6 months but less than 9 months, and 20 patients had a duration of response of at least 9 months. The remaining 21% (9/43) of patients had a duration of response ranging from 3 to 7 months and have progressed after response, died, or received subsequent therapy.¹ Along with higher ORR and more complete responses, the *Opdivo* + *Yervoy* Regimen demonstrated a 60% reduction in the risk of progression among *BRAF* wild-type patients vs. *Yervoy* alone (HR=0.40, 95% CI: 0.22-0.71; p<0.002).¹ Median PFS was 8.9 months with the Regimen (95% CI: 7.0, NA) and 4.7 months with *Yervoy* alone (95% CI: 2.8-5.3).¹

“Historically, metastatic melanoma has been a difficult disease to treat.⁶ Now, a new treatment option based on the combination of two valued Immuno-Oncology agents demonstrates significant efficacy versus ipilimumab (*Yervoy*) in metastatic melanoma,”² said Jedd D. Wolchok, MD, PhD, Chief, Melanoma and Immunotherapeutics Service, Department of Medicine and Ludwig Center at Memorial Sloan Kettering Cancer Center. “Today’s approval represents a step forward for the melanoma community, providing hope for patients with metastatic melanoma.”

In CheckMate -069, serious adverse reactions (62% vs. 39%), adverse reactions leading to permanent discontinuation (43% vs. 11%) or dose delays (47% vs. 22%), and Grade 3 or 4 adverse reactions (69% vs. 43%) all occurred more frequently in patients receiving the *Opdivo* + *Yervoy* Regimen compared with those receiving *Yervoy* alone. In the *Opdivo* + *Yervoy* Regimen group, 27% (25/94) of patients did not complete all four cycles of the *Opdivo* + *Yervoy* Regimen. The first occurrence of a Grade 3 or 4 adverse reaction was during administration of the *Opdivo* + *Yervoy* Regimen in 56 patients (59%), while 9 patients (10%) experienced first occurrence of a Grade 3 or 4 adverse reaction during administration of *Opdivo* alone.

The most common adverse reactions leading to discontinuation of *Opdivo*, as compared to *Yervoy* alone, were colitis (16% vs. 2%), diarrhea not treated with corticosteroids (4% vs. 4%), increased ALT levels (4% vs. 0), pneumonitis (3% vs. 0), and AST increase (3% vs. 0). The most frequent serious adverse events with the *Opdivo* + *Yervoy* Regimen, as compared to *Yervoy* alone, were colitis (17% vs. 9%), diarrhea (9% vs. 7%), pyrexia (6% vs. 7%), and pneumonitis (5% vs. 0). The most common adverse reactions ($\geq 20\%$) reported in patients receiving the *Opdivo* + *Yervoy* Regimen 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%).

“We are currently witnessing a turning point in cancer history, based on the significant impact Immuno-Oncology is making in the lives of patients with metastatic melanoma. Today’s approval of the

first Regimen of two Immuno-Oncology agents, *Opdivo* and *Yervoy*, is an exciting moment for our community because it reinforces we are on a positive path forward, providing new approaches which translate into meaningful results for patients,” said Tim Turnham, Executive Director, Melanoma Research Foundation.

About the *Opdivo* + *Yervoy* Regimen

The scientific rationale for targeting the immune system via dual immune checkpoint inhibition in cancer has formed the basis of a novel approach to the treatment of metastatic melanoma.⁴

“At Bristol-Myers Squibb, we have been at the forefront of researching the potential of two different immune checkpoint pathways – CTLA-4 and PD-1 – in the treatment of cancer,” said Francis Cuss, MB BChir, FRCP, executive vice president and chief scientific officer, Bristol-Myers Squibb. “From initial pre-clinical research, to pivotal studies resulting in regulatory approval of *Yervoy* and *Opdivo* as monotherapies, to today’s FDA approval, we are proud to be leading the way in bringing a dual Immuno-Oncology Regimen to cancer patients for the first time.”

Cancer cells may exploit “regulatory” pathways, such as checkpoint pathways, to hide from the immune system and shield the tumor from immune attack.⁴ *Opdivo* and *Yervoy* are immune checkpoint inhibitors that target separate, distinct and complementary checkpoint pathways (PD-1 and CTLA-4).⁴ The mechanism of action involves dual immune checkpoint inhibition resulting in increased anti-tumor activity.⁵ *Yervoy* blockade of CTLA-4 has been shown to augment T-cell activation and proliferation,⁴ while *Opdivo* restores the active T-cell response directed at the tumor.⁴ This may affect healthy cells and result in immune-mediated adverse reactions, which can be severe and potentially fatal.⁴

Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that has received approval from the FDA in other indications, including metastatic squamous non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy.

Bristol-Myers Squibb has a broad, global development program to study the combination of *Opdivo* and *Yervoy* consisting of more than 14 trials in which more than 2,000 patients have been enrolled worldwide through September 2015.

About Metastatic Melanoma

Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment-producing cells (melanocytes) located in the skin.⁶ Metastatic melanoma is the deadliest form of the disease, and occurs when cancer spreads beyond the surface of the skin to other organs.⁶ The incidence

of melanoma has been increasing for at least 30 years.⁶ An estimated 73,870 melanoma cases will be diagnosed in the U.S. in 2015.⁶ Melanoma is mostly curable when treated in its early stages.⁶ However, in its late stages, 5-year and 10-year survival rates in the U.S. average 15-20% and 10-15%, respectively.⁶

About Bristol-Myers Squibb's Patient Support Programs

Bristol-Myers Squibb remains committed to helping patients access our medicines. For support and assistance, patients and physicians may call 1-855-OPDIVO-1. This number offers one-stop access to a range of support services for patients and healthcare professionals alike.

About Bristol-Myers Squibb's Access Support

Bristol-Myers Squibb is committed to helping patients access the *Opdivo* + *Yervoy* Regimen and offers BMS Access Support[®] to support patients and providers in gaining access. BMS Access Support, the Bristol-Myers Squibb Reimbursement Services program, is designed to support access to BMS medicines and expedite time to therapy through reimbursement support including Benefit Investigations, Prior Authorization Facilitation, Appeals Assistance, and assistance for patient out-of-pocket costs. BMS Access Support assists patients and providers throughout the treatment journey – whether it is at initial diagnosis or in support of transition from a clinical trial. More information about our reimbursement support services can be obtained by calling 1-800-861-0048 or by visiting www.bmsaccesssupport.com. For healthcare providers seeking specific reimbursement information, please visit the BMS Access Support Product section by visiting www.bmsaccesssupportopdivo.com.

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 0.7% (5/691) of patients receiving OPDIVO as a single agent; no cases occurred in Checkmate 063. In Checkmate 063, immune-mediated pneumonitis occurred in 6% (7/117) of patients receiving OPDIVO as a single agent including five Grade 3 and two Grade 2 cases. 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 063, diarrhea occurred in 21% (24/117) of patients receiving OPDIVO as a single agent. Grade 3 immune-mediated colitis occurred in 0.9% (1/117) of patients. 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 ≥ 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 063, the incidences of increased liver test values were AST (16%), alkaline phosphatase (14%), ALT (12%), and total bilirubin (2.7%) in patients receiving OPDIVO as a single agent. 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). 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 063,

hypothyroidism occurred in 4.3% (5/117) of patients receiving OPDIVO as a single agent. Hyperthyroidism occurred in 1.7% (2/117) of patients, including one Grade 2 case.

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 063, the incidence of elevated creatinine was 22%. Immune-mediated renal dysfunction (Grade 2) occurred in 0.9% (1/117) 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 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).

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. In Checkmate 063, the following clinically significant immune-mediated adverse reactions occurred in <2% of single-agent OPDIVO-treated patients: uveitis, pancreatitis, facial and abducens nerve paresis, demyelination, autoimmune neuropathy, motor dysfunction, and vasculitis. 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: diabetes mellitus, 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. In Checkmate 069, Grade 2 infusion reactions occurred in 3% (3/94) 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 063, serious adverse reactions occurred in 59% of patients receiving OPDIVO as a single agent. The most frequent serious adverse drug reactions reported in $\geq 2\%$ of patients were dyspnea, pneumonia, chronic obstructive pulmonary disease exacerbation, pneumonitis, hypercalcemia, pleural effusion, hemoptysis, and pain.

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 063, the most common adverse reactions ($\geq 20\%$) reported with OPDIVO as a single agent were fatigue (50%), dyspnea (38%), musculoskeletal pain (36%), decreased appetite (35%), cough (32%), nausea (29%), and constipation (24%). 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, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY.](#)

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

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 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 the Opdivo + Yervoy Regimen 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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¹ Opdivo U.S. Product Information. Last updated: September 30, 2015.

² New England Journal of Medicine. “Nivolumab and Ipilimumab versus Ipilimumab in Untreated Melanoma” Available at <http://www.nejm.org/doi/full/10.1056/NEJMoa1414428>. Accessed on September 23, 2015.

³ Bristol-Myers Squibb Data on File.

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⁵ Nature Reviews Cancer. “The Blockade of Immune Checkpoints in Cancer Immunotherapy.” Available at <http://www.nature.com/nrc/journal/v12/n4/full/nrc3239.html>. Accessed on September 24, 2015.

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