

October 11, 2016

**Results From CheckMate-275 Validate Further Study of Opdivo (nivolumab)
in Patients With Advanced Form of Bladder Cancer**

(PRINCETON, NJ, October 8, 2016) – Bristol-Myers Squibb Company (NYSE: BMY) announced results from the CheckMate -275 trial, in which Opdivo had a confirmed objective response rate (ORR), the primary endpoint, of 19.6% (95% CI 15.0 – 24.9) in platinum-refractory patients with metastatic urothelial carcinoma. Responses were observed in both PD-L1 expressors and non-expressors. The confirmed ORR in patients expressing PD-L1 $\geq 1\%$ was 23.8% (95% CI 16.5–32.3) and 16.1% (95% CI 10.5–23.1) in patients expressing PD-L1 $< 1\%$. In patients expressing PD-L1 $\geq 5\%$, the confirmed ORR was 28.4% (95% CI 18.9–39.5) and 15.8% (95% CI 10.8-21.8) in patients expressing PD-L1 $< 5\%$. The median duration of response was not reached in the overall population with a minimum follow-up of six months, and responses were ongoing in 77% of patients. The safety profile of Opdivo in this study was consistent with the safety profile of Opdivo in other tumor types.

Bristol-Myers Squibb (BMS) has a robust clinical development program in Opdivo monotherapy and in combination therapy with other therapeutic drugs in a variety of tumor types overseas, including Glioblastoma, Small Cell Lung Cancer, Urothelial Cancer, Hepatocellular Carcinoma, Esophageal Cancer, Colorectal Cancer, Gastric Cancer, Blood Cancer, etc.

In Japan, Ono Pharmaceutical Co., Ltd. (ONO) launched Opdivo for the treatment of unresectable melanoma in September 2014. ONO received an approval for additional indication of unresectable, advanced or recurrent non-small cell lung cancer in December 2015 and unresectable or metastatic renal cell cancer in August 2016. In addition, ONO has submitted supplemental applications for additional indications of Hodgkin Lymphoma and Head and Neck Cancer, and is conducting clinical development program including Gastric Cancer, Esophageal Cancer, Small Cell Lung Cancer, Hepatocellular Carcinoma, Glioblastoma, Ovarian Cancer, Urothelial Cancer, Malignant Pleural Mesothelioma, Biliary Tract Cancer, etc.

In Japan, ONO and BMS (and BMS Japan subsidiary BMSKK) have formed a strategic partnership that includes co-development, co-commercialization, and co-promotion of multiple immunotherapies for patients with cancer.

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

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Results From CheckMate-275 Validate Further Study of *Opdivo* (nivolumab) in Patients With Advanced Form of Bladder Cancer

- *Confirmed overall response rate of 19.6% in all previously treated patients who received Opdivo*
- *Durable responses observed in PD-L1 expressors and non-expressors*
- *The safety profile of Opdivo in this study was consistent with previously reported studies*

(PRINCETON, NJ, October 8, 2016) – [Bristol-Myers Squibb Company](#) (NYSE: BMY) announced today results from the CheckMate -275 trial, in which *Opdivo* had a confirmed objective response rate (ORR), the primary endpoint, of 19.6% (95% CI 15.0 – 24.9) in platinum-refractory patients with metastatic urothelial carcinoma. Responses were observed in both PD-L1 expressors and non-expressors. The confirmed ORR in patients expressing PD-L1 $\geq 1\%$ was 23.8% (95% CI 16.5–32.3) and 16.1% (95% CI 10.5–23.1) in patients expressing PD-L1 $< 1\%$. In patients expressing PD-L1 $\geq 5\%$, the confirmed ORR was 28.4% (95% CI 18.9–39.5) and 15.8% (95% CI 10.8–21.8) in patients expressing PD-L1 $< 5\%$. The median duration of response was not reached in the overall population with a minimum follow-up of six months, and responses were ongoing in 77% of patients. The safety profile of *Opdivo* in this study was consistent with the safety profile of *Opdivo* in other tumor types.

These data will be presented today, October 8, at the 2016 European Society for Medical Oncology (ESMO) Congress during an oral proffered paper session from 9:15 – 9:30 a.m. CEST (Abstract #LBA31_PR).

“The prognosis for patients with metastatic urothelial carcinoma progressing despite platinum-based chemotherapy is poor, and treatment options have historically been quite limited,” said Matthew Galsky, M.D., professor of medicine and director of Genitourinary Medical Oncology, The Tisch Cancer Institute at Icahn School of Medicine at Mount Sinai. “In the CheckMate -275 study, we observe that with *Opdivo*, patients who responded experienced rapid and durable responses, including patients with PD-L1 expressing and non-expressing tumors. These results are encouraging and provide new information to the scientific community on the potential of *Opdivo* as a treatment option for this type of advanced bladder cancer.”

Urothelial carcinoma, a common type of bladder cancer, accounts for approximately 90% of cases. The majority of bladder cancers are diagnosed at an early stage, but approximately 78% of patients will experience a recurrence within five years.

Vicki Goodman, M.D., development lead, Melanoma and Genitourinary Cancers, Bristol-Myers Squibb, commented, “There is a significant unmet need for new treatment approaches for progressive metastatic urothelial carcinoma. The results from CheckMate -275 show treatment with *Opdivo* resulted in durable and clinically meaningful objective response of 19.6% in all-treated patients. Based on these findings, we believe *Opdivo* has the potential to become an important new treatment option for patients with platinum-refractory advanced bladder cancer.”

About CheckMate -275

CheckMate -275 is a Phase 2, single-arm clinical trial evaluating the safety and efficacy of *Opdivo* in 270 patients with metastatic or unresectable urothelial cancer who have progressed or recurred following treatment with a platinum-based agent in the metastatic setting or within one year after neoadjuvant/adjuvant platinum therapy. The trial enrolled patients regardless of PD-L1 expression. The primary endpoint was confirmed objective response rate (ORR) based on assessments by the blinded independent review committee in all treated patients and in patients with tumor PD-L1 expression $\geq 1\%$ and $\geq 5\%$. Key secondary endpoints included progression-free survival (PFS), overall survival (OS), safety and quality of life. Patients received *Opdivo* 3 mg/kg administered intravenously every two weeks and were assessed for response beginning eight weeks from randomization and continuing every eight weeks for 48 weeks, then every 12 weeks until progression or discontinuation.

The confirmed ORR was 19.6% (95% CI: 15.0 – 24.9) for all treated patients. About half of the overall patient population (46%) had a PD-L1 expression of $\geq 1\%$, and approximately 30% had a PD-L1 expression of $\geq 5\%$. Higher responses observed among patients with PD-L1 expression $\geq 1\%$ (23.8%; 95% CI: 16.5 – 32.3) and $\geq 5\%$ (28.4%; 95% CI: 18.9 – 39.5). Responses to *Opdivo* were also observed in patients with PD-L1 $< 1\%$ (16.1%; 95% CI: 10.5 – 23.1) and $< 5\%$ (15.8%; 95% CI 10.8 – 21.8)

Among the 52 patients who responded to treatment, the median time to a response was 1.9 months (1.6 – 5.9 months). Median duration of response was not reached, with an ongoing response among 77% of the responders at the time of the analysis.

The median PFS was 2.0 months in all treated patients (95% CI: 1.87 – 2.63), 1.87 months for patients with PD-L1 <1% (95% CI: 1.77 – 2.04), and 3.55 months in patients with PD-L1 ≥1% (95% CI: 1.94 – 3.71). The median OS was 8.74 months in all treated patients (95% CI: 6.05 – N.A.), 5.95 months in patients with PD-L1 <1% (95% CI: 4.30 – 8.08), and 11.3 months in patients with PD-L1 expression ≥1% (95% CI: 8.74 – N.A.). In addition, quality of life is maintained for patients remaining on study over 41 weeks on two quality of life measures – the EORTC (European Organisation for Research and Treatment of Cancer) QLQ-C30 and the EQ-5D Visual Analog Scale.

The safety profile of *Opdivo* in CheckMate -275 was consistent with the safety profile of *Opdivo* in other tumor types. Among the 270 patients who received *Opdivo*, 64.4% experienced a treatment-related adverse event (AE) of any grade, with grade 3 or 4 in 17.8%. The most frequently reported treatment-related AEs of any grade included fatigue (16.7%), pruritis (9.3%), diarrhea (8.9%), decreased appetite (8.1%), hypothyroidism (7.8%), nausea (7.0%), asthenia (5.9%), rash (5.9%) and pyrexia (5.6%). The most frequent treatment-related grade 3-4 AEs were fatigue (1.9%), diarrhea (1.9%), asthenia (1.5%) and rash (1.1%). Overall, 4.8% of patients discontinued therapy due to treatment-related AEs of any grade, and 3.0% discontinued therapy due to grade 3-4 treatment-related AEs.

Bristol-Myers Squibb: At the Forefront of Immuno-Oncology Science & Innovation

At Bristol-Myers Squibb, patients are at the center of everything we do. Our vision for the future of cancer care is focused on researching and developing transformational Immuno-Oncology (I-O) medicines that will raise survival expectations in hard-to-treat cancers and will change the way patients live with cancer.

We are leading the scientific understanding of I-O through our extensive portfolio of investigational and approved agents – including the first combination of two I-O agents in metastatic melanoma – and our differentiated clinical development program, which is studying broad patient populations across more than 20 types of cancers with 11 clinical-stage molecules designed to target different immune system pathways. Our deep expertise and innovative clinical trial designs uniquely position us to advance the science of combinations across multiple tumors and potentially deliver the next wave of I-O combination regimens with a sense of urgency. We also continue to pioneer research that will help facilitate a deeper understanding of the role of immune biomarkers and inform which patients will benefit most from I-O therapies.

We understand making the promise of I-O a reality for the many patients who may benefit from these therapies requires not only innovation on our part but also close collaboration with leading experts in the field. Our partnerships with academia, government, advocacy and biotech companies support our collective goal of providing new treatment options to advance the standards of clinical practice.

About Opdivo

Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to uniquely harness the body's own immune system to help restore anti-tumor immune response. By harnessing the body's own immune system to fight cancer, *Opdivo* has become an important treatment option across multiple cancers.

Opdivo's leading global development program is based on Bristol-Myers Squibb's scientific expertise in the field of Immuno-Oncology and includes a broad range of clinical trials across all phases, including Phase 3, in a variety of tumor types. To date, the *Opdivo* clinical development program has enrolled more than 25,000 patients. The *Opdivo* trials have contributed to gaining a deeper understanding of the potential role of biomarkers in patient care, particularly regarding how patients may benefit from *Opdivo* across the continuum of PD-L1 expression.

In July 2014, *Opdivo* was the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world. *Opdivo* is currently approved in more than 57 countries, including the United States, the European Union and Japan. In October 2015, the company's *Opdivo* and *Yervoy* combination regimen was the first Immuno-Oncology combination to receive regulatory approval for the treatment of metastatic melanoma and is currently approved in more than 47 countries, including the United States and the European Union.

U.S. FDA-APPROVED INDICATIONS FOR OPDIVO®

OPDIVO® (nivolumab) as a single agent is indicated for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma.

OPDIVO® (nivolumab) as a single agent is indicated for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this

indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

OPDIVO[®] (nivolumab), in combination with YERVOY[®] (ipilimumab), is indicated for the treatment of patients with unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

OPDIVO[®] (nivolumab) is indicated 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.

OPDIVO[®] (nivolumab) is indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

OPDIVO[®] (nivolumab) is indicated for the treatment of patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Please refer to the end of the Important Safety Information for a brief description of the patient populations studied in the CheckMate trials.

IMPORTANT SAFETY INFORMATION

WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS

YERVOY can result in severe and fatal immune-mediated adverse reactions. 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), adrenocorticotrophic hormone (ACTH) level, 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, including fatal cases, occurred with OPDIVO treatment. Across the clinical trial experience with solid tumors, fatal immune-mediated pneumonitis occurred with OPDIVO. In addition, in CheckMate 069, there were six 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 and 067, immune-mediated pneumonitis occurred in 6% (25/407) of patients receiving OPDIVO with YERVOY: Fatal (n=1), Grade 3 (n=6), Grade 2 (n=17), and Grade 1 (n=1). In CheckMate 037, 066, and 067, immune-mediated pneumonitis occurred in 1.8% (14/787) of patients receiving OPDIVO: Grade 3 (n=2) and Grade 2 (n=12). In CheckMate 057, immune-mediated pneumonitis, including interstitial lung disease, occurred in 3.4% (10/287) of patients: Grade 3 (n=5), Grade 2 (n=2), and Grade 1 (n=3). In CheckMate 025, pneumonitis, including interstitial lung disease, occurred in 5% (21/406) of patients receiving OPDIVO and 18% (73/397) of patients receiving everolimus. Immune-mediated pneumonitis occurred in 4.4% (18/406) of patients receiving OPDIVO: Grade 4 (n=1), Grade 3 (n=4), Grade 2 (n=12), and Grade 1 (n=1). In CheckMate 205 and 039, pneumonitis, including interstitial lung disease, occurred in 4.9% (13/263) of patients receiving OPDIVO. Immune-mediated pneumonitis occurred in 3.4% (9/263) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 2 (n=8).

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. When administered with YERVOY, withhold OPDIVO for Grade 2 and permanently discontinue for Grade 3 or 4 or recurrent colitis upon restarting OPDIVO. In CheckMate 069 and 067, diarrhea or colitis occurred in 56% (228/407) of patients receiving OPDIVO with YERVOY. Immune-mediated colitis occurred in 26% (107/407) of patients: Grade 4 (n=2), Grade 3 (n=60), Grade 2 (n=32), and Grade 1 (n=13). In CheckMate 037, 066, and 067, diarrhea or colitis occurred in 31% (242/787) of patients receiving OPDIVO. Immune-mediated colitis occurred in 4.1% (32/787) of patients: Grade 3 (n=20), Grade 2 (n=10), and Grade 1 (n=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: Grade 3 (n=3), Grade 2 (n=2), and Grade 1 (n=2). In CheckMate 025, diarrhea or colitis occurred in 25% (100/406) of patients receiving OPDIVO and 32% (126/397) of patients receiving everolimus. Immune-mediated diarrhea or colitis occurred in 3.2% (13/406) of patients receiving OPDIVO: Grade 3 (n=5), Grade 2 (n=7), and Grade 1 (n=1). In CheckMate 205 and 039, diarrhea or colitis occurred in 30% (80/263) of patients receiving OPDIVO. Immune-mediated diarrhea (Grade 3) occurred in 1.1% (3/263) of patients.

In a separate Phase 3 study of YERVOY 3 mg/kg, 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 069 and 067, immune-mediated hepatitis occurred in 13% (51/407) of patients receiving OPDIVO with YERVOY: Grade 4 (n=8), Grade 3 (n=37), Grade 2 (n=5), and Grade 1 (n=1). In CheckMate 037, 066, and 067, immune-mediated hepatitis occurred in 2.3% (18/787) of patients

receiving OPDIVO: Grade 4 (n=3), Grade 3 (n=11), and Grade 2 (n=4). In CheckMate 057, one patient (0.3%) developed immune-mediated hepatitis. In CheckMate 025, there was an increased incidence of liver test abnormalities compared to baseline in AST (33% vs 39%), alkaline phosphatase (32% vs 32%), ALT (22% vs 31%), and total bilirubin (9% vs 3.5%) in the OPDIVO and everolimus arms, respectively. Immune-mediated hepatitis requiring systemic immunosuppression occurred in 1.5% (6/406) of patients receiving OPDIVO: Grade 3 (n=5) and Grade 2 (n=1). In CheckMate 205 and 039, hepatitis occurred in 11% (30/263) of patients receiving OPDIVO. Immune-mediated hepatitis occurred in 3.4% (9/263): Grade 3 (n=7) and Grade 2 (n=2).

In a separate Phase 3 study of YERVOY 3 mg/kg, 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 Phase 3 study of YERVOY 3 mg/kg, 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 Phase 3 study of YERVOY 3 mg/kg, 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, thyroid disorders, and type 1 diabetes mellitus can occur with OPDIVO treatment. Monitor patients for signs and symptoms of hypophysitis, signs and symptoms of adrenal insufficiency during and after treatment, thyroid function prior to and periodically during treatment, and hyperglycemia. 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. Administer insulin for type 1 diabetes. Withhold OPDIVO for Grade 3 and permanently discontinue for Grade 4 hyperglycemia.

In CheckMate 069 and 067, hypophysitis occurred in 9% (36/407) of patients receiving OPDIVO with YERVOY: Grade 3 (n=8), Grade 2 (n=25), and Grade 1 (n=3). In CheckMate 037, 066, and 067, hypophysitis occurred in 0.9% (7/787) of patients receiving OPDIVO: Grade 3 (n=2), Grade 2 (n=3), and Grade 1 (n=2). In CheckMate 025, hypophysitis occurred in 0.5% (2/406) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 1 (n=1). In CheckMate 069 and 067, adrenal insufficiency occurred in 5% (21/407) of patients receiving OPDIVO with YERVOY: Grade 4 (n=1), Grade 3 (n=7), Grade 2 (n=11), and Grade 1 (n=2). In CheckMate 037, 066, and 067, adrenal insufficiency occurred in 1% (8/787) of patients receiving OPDIVO: Grade 3 (n=2), Grade 2 (n=5), and Grade 1 (n=1). In CheckMate 057, 0.3% (1/287) of OPDIVO-treated patients developed adrenal insufficiency. In CheckMate 025, adrenal insufficiency occurred in 2.0% (8/406) of patients receiving OPDIVO: Grade 3 (n=3), Grade 2 (n=4), and Grade 1 (n=1). In CheckMate 205 and 039, adrenal insufficiency (Grade 2) occurred in 0.4% (1/263) of patients receiving OPDIVO. In CheckMate 069 and 067, hypothyroidism or thyroiditis occurred in 22% (89/407) of patients receiving OPDIVO with YERVOY: Grade 3 (n=6), Grade 2 (n=47), and Grade 1 (n=36). Hyperthyroidism occurred in 8% (34/407) of patients: Grade 3 (n=4), Grade 2 (n=17), and Grade 1 (n=13). In CheckMate 037, 066, and 067, hypothyroidism or thyroiditis occurred in 9% (73/787) of patients receiving OPDIVO: Grade 3 (n=1), Grade 2 (n=37), Grade 1 (n=35). Hyperthyroidism occurred in 4.4% (35/787) of patients receiving OPDIVO: Grade 3 (n=1), Grade 2 (n=12), and Grade 1 (n=22). In CheckMate 057, Grade 1 or 2 hypothyroidism, including thyroiditis, occurred in 7% (20/287) and elevated thyroid stimulating hormone occurred in 17% of patients receiving OPDIVO. Grade 1 or 2 hyperthyroidism occurred in 1.4% (4/287) of patients. In CheckMate 025, thyroid disease occurred in 11% (43/406) of patients receiving OPDIVO, including one Grade 3 event, and in 3.0% (12/397) of patients receiving everolimus. Hypothyroidism/thyroiditis occurred in 8% (33/406) of patients receiving OPDIVO: Grade 3 (n=2), Grade 2 (n=17), and Grade 1 (n=14). Hyperthyroidism occurred in 2.5% (10/406) of patients receiving OPDIVO: Grade 2 (n=5) and Grade 1 (n=5). In CheckMate 205 and 039, hypothyroidism/thyroiditis occurred in 12% (32/263) of patients receiving OPDIVO: Grade 2 (n=18) and Grade 1: (n=14). Hyperthyroidism occurred in 1.5% (4/263) of patients receiving OPDIVO: Grade 2: (n=3) and Grade 1 (n=1). In CheckMate 069

and 067, diabetes mellitus or diabetic ketoacidosis occurred in 1.5% (6/407) of patients: Grade 4 (n=3), Grade 3 (n=1), Grade 2 (n=1), and Grade 1 (n=1). In CheckMate 037, 066, and 067, diabetes mellitus or diabetic ketoacidosis occurred in 0.8% (6/787) of patients receiving OPDIVO: Grade 3 (n=2), Grade 2 (n=3), and Grade 1 (n=1). In CheckMate 025, hyperglycemic adverse events occurred in 9% (37/406) patients. Diabetes mellitus or diabetic ketoacidosis occurred in 1.5% (6/406) of patients receiving OPDIVO: Grade 3 (n=3), Grade 2 (n=2), and Grade 1 (n=1). In CheckMate 205 and 039, diabetes mellitus occurred in 0.8% (2/263) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 1 (n=1).

In a separate Phase 3 study of YERVOY 3 mg/kg, 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 069 and 067, immune-mediated nephritis and renal dysfunction occurred in 2.2% (9/407) of patients: Grade 4 (n=4), Grade 3 (n=3), and Grade 2 (n=2). In CheckMate 037, 066, and 067, nephritis and renal dysfunction of any grade occurred in 5% (40/787) of patients receiving OPDIVO. Immune-mediated nephritis and renal dysfunction occurred in 0.8% (6/787) of patients: Grade 3 (n=4) and Grade 2 (n=2). In CheckMate 057, Grade 2 immune-mediated renal dysfunction occurred in 0.3% (1/287) of patients receiving OPDIVO. In CheckMate 025, renal injury occurred in 7% (27/406) of patients receiving OPDIVO and 3.0% (12/397) of patients receiving everolimus. Immune-mediated nephritis and renal dysfunction occurred in 3.2% (13/406) of patients receiving OPDIVO: Grade 5 (n=1), Grade 4 (n=1), Grade 3 (n=5), and Grade 2 (n=6). In CheckMate 205 and 039, nephritis and renal dysfunction occurred in 4.9% (13/263) of patients treated with OPDIVO. This included one reported case (0.3%) of Grade 3 autoimmune nephritis.

Immune-Mediated Rash

Immune-mediated rash can occur with OPDIVO treatment. Severe rash (including rare cases of fatal toxic epidermal necrolysis) occurred in the clinical program of OPDIVO. 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 and 067, immune-mediated rash occurred in 22.6% (92/407) of patients receiving OPDIVO with YERVOY: Grade 3 (n=15), Grade 2 (n=31), and Grade 1 (n=46). In CheckMate 037, 066, and 067, immune-mediated rash occurred in 9% (72/787) of patients receiving OPDIVO: Grade 3 (n=7), Grade 2 (n=15), and Grade 1 (n=50). In CheckMate 057, immune-mediated rash occurred in 6% (17/287) of patients receiving OPDIVO including four Grade 3 cases. In CheckMate 025, rash occurred in 28% (112/406) of patients receiving OPDIVO and 36% (143/397) of patients receiving everolimus. Immune-mediated rash, defined as a rash treated with systemic or topical corticosteroids, occurred in 7% (30/406) of patients receiving OPDIVO: Grade 3 (n=4), Grade 2 (n=7), and Grade 1 (n=19). In CheckMate 205 and 039, rash occurred in 22% (58/263) of patients receiving OPDIVO. Immune-mediated rash occurred in 7% (18/263) of patients on OPDIVO: Grade 3 (n=4), Grade 2 (n=3), and Grade 1 (n=11).

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. In CheckMate 067, encephalitis was identified in one patient (0.2%) receiving OPDIVO with YERVOY. In CheckMate 057, fatal limbic encephalitis occurred in one patient (0.3%) receiving OPDIVO. In CheckMate 205 and 039, encephalitis occurred in 0.8% (2/263) of patients after allogeneic HSCT after 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. In < 1.0% of patients receiving OPDIVO, the following clinically significant, immune-mediated adverse reactions occurred: uveitis, iritis, pancreatitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome, hypopituitarism, systemic inflammatory response syndrome, gastritis,

duodenitis, and sarcoidosis. Across clinical trials of OPDIVO as a single agent administered at doses of 3 mg/kg and 10 mg/kg, additional clinically significant, immune-mediated adverse reactions were identified: motor dysfunction, vasculitis, and myasthenic syndrome.

Infusion Reactions

Severe infusion reactions have been reported in <1.0% of patients in clinical trials of OPDIVO. Discontinue OPDIVO in patients with Grade 3 or 4 infusion reactions. Interrupt or slow the rate of infusion in patients with Grade 1 or 2. In CheckMate 069 and 067, infusion-related reactions occurred in 2.5% (10/407) of patients receiving OPDIVO with YERVOY: Grade 2 (n=6) and Grade 1 (n=4). In CheckMate 037, 066, and 067, Grade 2 infusion related reactions occurred in 2.7% (21/787) of patients receiving OPDIVO: Grade 3 (n=2), Grade 2 (n=8), and Grade 1 (n=11). In CheckMate 057, Grade 2 infusion reactions requiring corticosteroids occurred in 1.0% (3/287) of patients receiving OPDIVO. In CheckMate 025, hypersensitivity/infusion-related reactions occurred in 6% (25/406) of patients receiving OPDIVO and 1.0% (4/397) of patients receiving everolimus. In CheckMate 205 and 039, hypersensitivity/infusion-related reactions occurred in 16% (42/263) of patients receiving OPDIVO: Grade 3 (n=2), Grade 2 (n=24), and Grade 1 (n=16).

Complications of Allogeneic HSCT after OPDIVO

Complications, including fatal events, occurred in patients who received allogeneic HSCT after OPDIVO. Outcomes were evaluated in 17 patients from CheckMate 205 and 039, who underwent allogeneic HSCT after discontinuing OPDIVO (15 with reduced-intensity conditioning, 2 with myeloablative conditioning). Thirty-five percent (6/17) of patients died from complications of allogeneic HSCT after OPDIVO. Five deaths occurred in the setting of severe or refractory GVHD. Grade 3 or higher acute GVHD was reported in 29% (5/17) of patients. Hyperacute GVHD was reported in 20% (n=2) of patients. A steroid-requiring febrile syndrome, without an identified infectious cause, was reported in 35% (n=6) of patients. Two cases of encephalitis were reported: Grade 3 (n=1) lymphocytic encephalitis without an identified infectious cause, and Grade 3 (n=1) suspected viral encephalitis. Hepatic veno-occlusive disease (VOD) occurred in one patient, who received reduced-intensity conditioned allogeneic SCT and died of GVHD and multi-organ failure. Other cases of hepatic VOD after reduced-intensity conditioned allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor blocking antibody before transplantation. Cases of fatal hyperacute GVHD have also been reported. These

complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT.

Follow patients closely for early evidence of transplant-related complications such as hyperacute GVHD, severe (Grade 3 to 4) acute GVHD, steroid-requiring febrile syndrome, hepatic VOD, and other immune-mediated adverse reactions, and intervene promptly.

Embryo-fetal Toxicity

Based on their mechanisms of action, OPDIVO and YERVOY 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 an OPDIVO- or YERVOY- containing regimen and for at least 5 months after the last dose of OPDIVO.

Lactation

It is not known whether OPDIVO or YERVOY 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 an OPDIVO-containing regimen, advise women to discontinue breastfeeding during treatment. Advise women to discontinue nursing during treatment with YERVOY and for 3 months following the final dose.

Serious Adverse Reactions

In CheckMate 067, serious adverse reactions (73% and 37%), adverse reactions leading to permanent discontinuation (43% and 14%) or to dosing delays (55% and 28%), and Grade 3 or 4 adverse reactions (72% and 44%) all occurred more frequently in the OPDIVO plus YERVOY arm relative to the OPDIVO arm. The most frequent ($\geq 10\%$) serious adverse reactions in the OPDIVO plus YERVOY arm and the OPDIVO arm, respectively, were diarrhea (13% and 2.6%), colitis (10% and 1.6%), and pyrexia (10% and 0.6%). 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 066, serious adverse reactions occurred in 36% of patients receiving OPDIVO. Grade 3 and 4 adverse reactions occurred in 41% of patients receiving

OPDIVO. The most frequent Grade 3 and 4 adverse reactions reported in $\geq 2\%$ of patients receiving OPDIVO were gamma-glutamyltransferase increase (3.9%) and diarrhea (3.4%). 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. In CheckMate 025, serious adverse reactions occurred in 47% of patients receiving OPDIVO. The most frequent serious adverse reactions reported in $\geq 2\%$ of patients were acute kidney injury, pleural effusion, pneumonia, diarrhea, and hypercalcemia. In CheckMate 205 and 039, among all patients (safety population [n=263]), adverse reactions leading to discontinuation (4.2%) or to dosing delays (23%) occurred. The most frequent serious adverse reactions reported in $\geq 1\%$ of patients were infusion-related reaction, pneumonia, pleural effusion, pyrexia, rash and pneumonitis. Ten patients died from causes other than disease progression, including 6 who died from complications of allogeneic HSCT. Serious adverse reactions occurred in 21% of patients in the safety population (n=263) and 27% of patients in the subset of patients evaluated for efficacy (efficacy population [n=95]).

Common Adverse Reactions

In CheckMate 067, the most common ($\geq 20\%$) adverse reactions in the OPDIVO plus YERVOY arm were fatigue (59%), rash (53%), diarrhea (52%), nausea (40%), pyrexia (37%), vomiting (28%), and dyspnea (20%). The most common ($\geq 20\%$) adverse reactions in the OPDIVO arm were fatigue (53%), rash (40%), diarrhea (31%), and nausea (28%). In CheckMate 037, the most common adverse reaction ($\geq 20\%$) reported with OPDIVO was rash (21%). In CheckMate 066, the most common adverse reactions ($\geq 20\%$) reported with OPDIVO vs dacarbazine were fatigue (49% vs 39%), musculoskeletal pain (32% vs 25%), rash (28% vs 12%), and pruritus (23% vs 12%). 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%). In CheckMate 025, the most common adverse reactions ($\geq 20\%$) reported in patients receiving OPDIVO vs everolimus were asthenic conditions (56% vs 57%), cough (34% vs 38%), nausea (28% vs 29%), rash (28% vs 36%), dyspnea (27% vs 31%), diarrhea (25% vs 32%), constipation (23% vs 18%), decreased appetite (23% vs 30%), back pain (21% vs 16%), and arthralgia (20% vs 14%). In CheckMate 205 and 039, among all patients (safety population [n=263]) and the subset of patients in the efficacy population (n=95), respectively, the most common adverse

reactions (reported in at least 20%) were fatigue (32% and 43%), upper respiratory tract infection (28% and 48%), pyrexia (24% and 35%), diarrhea (23% and 30%), and cough (22% and 35%). In the subset of patients in the efficacy population (n=95), the most common adverse reactions also included rash (31%), musculoskeletal pain (27%), pruritus (25%), nausea (23%), arthralgia (21%), and peripheral neuropathy (21%).

In a separate Phase 3 study of YERVOY 3 mg/kg, 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%).

CheckMate Trials and Patient Populations

CheckMate 069 and 067 – advanced melanoma alone or in combination with YERVOY; **CheckMate 037 and 066** – advanced melanoma; **CheckMate 057** – non-squamous non-small cell lung cancer (NSCLC); **CheckMate 025** – renal cell carcinoma; **CheckMate 205/039** – classical Hodgkin lymphoma

About the Bristol-Myers Squibb and Ono Pharmaceutical Co., Ltd. Collaboration

In 2011, through a collaboration agreement with Ono Pharmaceutical Co., Ltd (Ono), 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 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 us at BMS.com or follow us on [LinkedIn](#), [Twitter](#), [YouTube](#) and [Facebook](#).

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. 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, 2015 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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