November 14, 2016

Bristol-Myers Squibb's Opdivo® (nivolumab) is the First Immuno-Oncology Treatment to Receive FDA Approval Based on Overall Survival in Head and Neck Cancer

(PRINCETON, NJ, November, 10, 2016) – Bristol-Myers Squibb Company (NYSE: BMY) announced that the U.S. Food and Drug Administration (FDA) has approved Opdivo (nivolumab) injection, for intravenous use, for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy. Opdivo is the first and only Immuno-Oncology treatment proven in a Phase 3 trial to significantly extend overall survival (OS) for these patients. In oncology clinical trials, OS is considered the gold standard primary endpoint to evaluate the outcome of any therapy.

The approval was based on results from the Phase 3, CheckMate -141 trial in which Opdivo demonstrated statistically significant and clinically meaningful superior OS vs the comparator arm (investigator's choice of methotrexate, docetaxel or cetuximab), with a 30% reduction in the risk of death (HR=0.70 [95% CI: 0.53-0.92; p=0.0101]).1 The median OS was 7.5 months (95% CI: 5.5-9.1) for Opdivo compared to 5.1 months (95% CI: 4.0-6.0) for investigator's choice.

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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Bristol-Myers Squibb

Bristol-Myers Squibb's *Opdivo*® (nivolumab) is the First Immuno-Oncology Treatment to Receive FDA Approval Based on Overall Survival in Head and Neck Cancer

Opdivo *is the first and only Immuno-Oncology treatment proven in a Phase 3 trial to significantly extend overall survival for patients with recurrent or metastatic squamous cell head and neck cancer who had been previously treated with platinum-based therapy*[1]

***NCCN guidelines recently updated to include treatment with* Opdivo *as the only category 1 single-agent therapy for certain patients in this setting*[2]**

Opdivo *has now been approved in five tumor types in under two years*[1]

(PRINCETON, NJ, November, 10, 2016) – Bristol-Myers Squibb Company (NYSE: BMY) announced today that the U.S. Food and Drug Administration (FDA) has approved *Opdivo* (nivolumab) injection, for intravenous use, for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.[1] *Opdivo* is the first and only Immuno-Oncology treatment proven in a Phase 3 trial to significantly extend overall survival (OS) for these patients.[1] In oncology clinical trials, OS is considered the gold standard primary endpoint to evaluate the outcome of any therapy.[3]

The approval was based on results from the Phase 3, CheckMate -141 trial in which *Opdivo* demonstrated statistically significant and clinically meaningful superior OS vs the comparator arm (investigator's choice of methotrexate, docetaxel or cetuximab), with a 30% reduction in the risk of death (HR=0.70 [95% CI: 0.53-0.92; p=0.0101]).[1] The median OS was 7.5 months (95% CI: 5.5-9.1) for *Opdivo* compared to 5.1 months (95% CI: 4.0-6.0) for investigator's choice.[1] *Opdivo* is associated with immune-mediated: pneumonitis, colitis, hepatitis, endocrinopathies, nephritis and renal dysfunction, skin adverse reactions, encephalitis, other adverse reactions; infusion reactions; and embryo-fetal toxicity. Please see the Important Safety Information section below.

"With this approval in head and neck cancer, we continue to lead the field in bringing our Immuno-Oncology science and the potential for increasing survival to more people with cancer," said Chris Boerner, Head of U.S. Commercial, Bristol-Myers Squibb. "We take tremendous pride in the unprecedented speed and rigor with which we have brought *Opdivo* to market to address unmet needs across more tumor types than any other Immuno-Oncology treatment."

Squamous cell carcinoma of the head and neck (SCCHN) accounts for more than 90% of all head and neck cancers, and more than 50% of SCCHN patients present with Stage III or

higher disease (locally advanced or metastatic), which has higher potential for progression and recurrence.[4,5] The relative five-year survival rate for metastatic head and neck cancers is <38%, and can be as low as 4% for recurrent or metastatic Stage IV disease.[6,7]

"Squamous cell carcinoma of the head and neck that progresses on or after platinum-based therapy is a debilitating and hard-to-treat disease associated with a very poor prognosis," said Maura Gillison, M.D., Ph.D., lead investigator, Jeg Coughlin Chair of Cancer Research, The Ohio State University Wexner Medical Center. "This latest approval for *Opdivo* reinforces the potential to provide patients with improved overall survival, considered the gold standard in cancer care."

Based on a pre-planned interim analysis, CheckMate -141 was stopped early in January 2016 because an assessment conducted by the independent Data Monitoring Committee concluded the study met its primary endpoint of OS. In April 2016, the FDA granted Breakthrough Therapy Designation to *Opdivo* for recurrent or metastatic SCCHN after platinum-based therapy, underscoring the need for new treatment approaches for this disease. In October, the U.S. National Comprehensive Cancer Network (NCCN) updated its clinical practice guidelines to recommend treatment with *Opdivo* as the only category 1 single-agent therapy for patients with recurrent or metastatic head and neck cancer with disease progression on or after platinum-containing chemotherapy.[2] *Opdivo* has now been approved in five tumor types in under two years. [1]

CheckMate -141 Confirms Superior OS in SCCHN

CheckMate -141 was a global Phase 3, open-label, randomized, trial evaluating *Opdivo* versus investigator's choice of therapy in patients with recurrent or metastatic SCCHN who had tumor progression during or within six months of receiving platinum-based therapy administered in the adjuvant, neo-adjuvant, primary (unresectable locally advanced) or metastatic setting.[1,8] Patients were included regardless of their HPV or PD-L1 status.[1] Patients were randomized 2:1 to receive *Opdivo* 3 mg/kg intravenously over 60 minutes every two weeks (n=240), or investigator's choice (n=121) of: methotrexate 40 to 60 mg/m^2 intravenously weekly, docetaxel 30 to 40 mg/m^2 intravenously weekly, or cetuximab 400 mg/m^2 intravenously once then 250 mg/m^2 weekly.[1] Therapies chosen for investigator's choice represent the most commonly used therapies in the platinum refractory setting.[9,10] The primary endpoint was OS.[1] The trial's secondary endpoints included progression-free survival (PFS) and objective response rate (ORR).[11]

In the trial, *Opdivo* demonstrated statistically significant superior OS with a 30% reduction in the risk of death (HR=0.70 [95% CI: 0.53-0.92; *p*=0.0101]), and a median OS of 7.5 months (95% CI: 5.5-9.1) for *Opdivo* compared to 5.1 months (95% CI: 4.0-6.0) for the investigator's choice arm.[1] There were no statistically significant differences between the two arms for PFS (HR=0.89; 95% CI: 0.70, 1.13) or ORR (13.3% [95% CI: 9.3, 18.3] vs 5.8% [95% CI: 2.4, 11.6] for *Opdivo* and investigator's choice, respectively.[1] Data from CheckMate -141 were published in *The New England Journal of Medicine* in October.[8]

"We are excited to see the continued benefits of ongoing Immuno-Oncology research from a company with a long-standing commitment to head and neck cancer like Bristol-Myers Squibb," said Brian Hill, oral cancer survivor and founder, The Oral Cancer Foundation. "Today's approval provides hope for the thousands of previously treated SCCHN patients and their loved ones by bringing a new treatment option that has the potential to extend lives."

The safety profile of *Opdivo* in CheckMate -141 was consistent with prior studies in patients with melanoma and non-small cell lung cancer.[8] *Opdivo* was discontinued in 14% of patients and was delayed in 24% of patients for an adverse reaction.[1] Serious adverse reactions occurred in 49% of patients receiving *Opdivo*.[1] The most frequent serious adverse reactions reported in at least 2% of patients receiving *Opdivo* were pneumonia, dyspnea, aspiration pneumonia, respiratory failure, respiratory tract infection, and sepsis.[1] Please see the Important Safety Information section below.

About Head & Neck Cancer

Cancers that are known as head and neck cancers usually begin in the squamous cells that line the moist mucosal surfaces inside the head and neck, such as inside the mouth and the throat.[12] In 2016, approximately 64,000 new cases of head and neck cancer are estimated to be diagnosed in the U.S., resulting in more than 13,000 deaths.[4,13,14] Head and neck cancers are more than twice as common among men as they are among women.[4]

Bristol-Myers Squibb & Immuno-Oncology: Advancing Oncology Research

At Bristol-Myers Squibb, we have a vision for the future of cancer care that is focused on Immuno-Oncology, now considered a major treatment modality alongside surgery, radiation and chemotherapy for certain types of cancer.

We have a comprehensive clinical portfolio of investigational and approved Immuno-Oncology agents, many of which were discovered and developed by our scientists. We

pioneered the research leading to the first regulatory approval for the combination of two Immuno-Oncology agents and continue to study the role of combinations in cancer.

Our collaboration with academia as well as small and large biotech companies is responsible for researching the potential Immuno-Oncology and non-Immuno-Oncology combinations, with the goal of providing new treatment options in clinical practice.

At Bristol-Myers Squibb, we are committed to changing expectations in hard-to-treat cancers and the way patients live with cancer.

U.S. FDA APPROVED INDICATIONS FOR OPDIVO®

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 the confirmatory trials

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

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.

OPDIVO® (nivolumab) is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

Bristol-Myers Squibb

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), adrenocorticotropic 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

OPDIVO can cause immune-mediated pneumonitis. Fatal cases have been reported. Monitor patients for signs with radiographic imaging and for symptoms of pneumonitis. Administer corticosteroids for Grade 2 or more severe pneumonitis. Permanently discontinue for Grade 3 or 4 and withhold until resolution for Grade 2. In patients receiving OPDIVO monotherapy, fatal cases of immune-mediated pneumonitis have occurred. Immune-mediated pneumonitis occurred in 3.1% (61/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated pneumonitis occurred in 6% (25/407) of patients.

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

OPDIVO can cause immune-mediated colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO monotherapy for Grade 2 or 3 and permanently discontinue for Grade 4 or recurrent colitis upon re-initiation of OPDIVO. When administered with YERVOY, withhold OPDIVO and YERVOY for Grade 2 and permanently discontinue for Grade 3 or 4 or recurrent colitis. In patients receiving OPDIVO monotherapy, immune-mediated colitis occurred in 2.9% (58/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated colitis occurred in 26% (107/407) of patients including three fatal cases.

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

OPDIVO can cause immune-mediated hepatitis. 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 patients receiving OPDIVO monotherapy, immune-mediated hepatitis occurred in 1.8% (35/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated hepatitis occurred in 13% (51/407) of patients.

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 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

OPDIVO can cause immune-mediated hypophysitis, immune-mediated adrenal insufficiency, autoimmune thyroid disorders, and Type 1 diabetes mellitus. Monitor patients for signs and symptoms of hypophysitis, signs and symptoms of adrenal insufficiency, thyroid function prior to and periodically during treatment, and hyperglycemia. Administer hormone replacement as clinically indicated and 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. Withhold OPDIVO for Grade 3 and permanently discontinue for Grade 4 hyperglycemia.

In patients receiving OPDIVO monotherapy, hypophysitis occurred in 0.6% (12/1994) of patients. In patients receiving OPDIVO with YERVOY, hypophysitis occurred in 9% (36/407) of patients. In patients receiving OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/1994) of patients. In patients receiving OPDIVO with YERVOY, adrenal insufficiency occurred in 5% (21/407) of patients. In patients receiving OPDIVO monotherapy, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 9% (171/1994) of patients. Hyperthyroidism occurred in 2.7% (54/1994) of patients receiving OPDIVO monotherapy. In patients receiving OPDIVO with YERVOY, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 22% (89/407) of patients. Hyperthyroidism occurred in 8% (34/407) of patients receiving OPDIVO with YERVOY. In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients. In patients receiving OPDIVO with YERVOY, diabetes occurred in 1.5% (6/407) of patients.

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

OPDIVO can cause immune-mediated nephritis. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grades 2-4 increased serum creatinine. Withhold OPDIVO for Grade 2 or 3 and permanently discontinue for Grade 4 increased serum creatinine. In patients receiving OPDIVO monotherapy, immune-mediated nephritis and renal dysfunction occurred in 1.2% (23/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated nephritis and renal dysfunction occurred in 2.2% (9/407) of patients.

Immune-Mediated Skin Adverse Reactions and Dermatitis

OPDIVO can cause immune-mediated rash, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some cases with fatal outcome. Administer corticosteroids for Grade 3 or 4 rash. Withhold for Grade 3 and permanently discontinue for Grade 4 rash. For symptoms or signs of SJS or TEN, withhold OPDIVO and refer the patient for specialized care for assessment and treatment; if confirmed, permanently discontinue. In patients receiving OPDIVO monotherapy, immune-mediated rash occurred in 9% (171/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated rash occurred in 22.6% (92/407) of patients.

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 Encephalitis

OPDIVO can cause immune-mediated encephalitis. Evaluation of patients with neurologic symptoms may include, but not be limited to, consultation with a neurologist, brain MRI, and lumbar puncture. 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 patients receiving OPDIVO monotherapy, encephalitis occurred in 0.2% (3/1994) of patients. Fatal limbic encephalitis occurred in one patient after 7.2 months of exposure despite discontinuation of OPDIVO and administration of corticosteroids. Encephalitis occurred in one patient receiving OPDIVO with YERVOY (0.2%) after 1.7 months of exposure.

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. Across clinical trials of OPDIVO the following clinically significant immune-mediated adverse reactions occurred in <1.0% of patients receiving OPDIVO: uveitis, iritis, pancreatitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome, hypopituitarism, systemic inflammatory

response syndrome, gastritis, duodenitis, sarcoidosis, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), myositis, myocarditis, rhabdomyolysis, motor dysfunction, vasculitis, and myasthenic syndrome.

Infusion Reactions

OPDIVO can cause severe infusion reactions, which have been reported in <1.0% of patients in clinical trials. 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 patients receiving OPDIVO monotherapy, infusion-related reactions occurred in 6.4% (127/1994) of patients. In patients receiving OPDIVO with YERVOY, infusion-related reactions occurred in 2.5% (10/407) of patients.

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 HSCT 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 037, serious adverse reactions occurred in 41% of patients receiving OPDIVO (n=268). 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 (n=206). Grade 3 and 4 adverse reactions occurred in 41% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse reactions reported in ≥2% of patients receiving OPDIVO were gamma-glutamyltransferase increase (3.9%) and diarrhea (3.4%). 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 (n=313) relative to the OPDIVO arm (n=313). The most frequent (≥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 017 and 057, serious adverse reactions occurred in 46% of patients receiving OPDIVO (n=418). The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were pneumonia, pulmonary embolism, dyspnea, pyrexia, pleural effusion, pneumonitis, and respiratory failure. In Checkmate 025, serious adverse reactions occurred in 47% of patients receiving OPDIVO (n=406). The most frequent serious adverse reactions reported in ≥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 ≥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]). In Checkmate 141, serious adverse reactions occurred in 49% of patients receiving OPDIVO. The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were pneumonia, dyspnea, respiratory failure, respiratory tract infections, and sepsis.

Common Adverse Reactions

In Checkmate 037, the most common adverse reaction (≥20%) reported with OPDIVO (n=268) was rash (21%). In Checkmate 066, the most common adverse reactions (≥20%) reported with OPDIVO (n=206) vs dacarbazine (n=205) were fatigue (49% vs 39%), musculoskeletal pain (32% vs 25%), rash (28% vs 12%), and pruritus (23% vs 12%). In Checkmate 067, the most common (≥20%) adverse reactions in the OPDIVO plus YERVOY arm (n=313) were fatigue (59%), rash (53%), diarrhea (52%), nausea (40%), pyrexia (37%), vomiting (28%), and dyspnea (20%). The most common (≥20%) adverse reactions in the OPDIVO (n=313) arm were fatigue (53%), rash (40%), diarrhea (31%), and nausea (28%). In Checkmate 017 and 057, the most common adverse reactions (≥20%) in patients receiving

OPDIVO (n=418) were fatigue, musculoskeletal pain, cough, dyspnea, and decreased appetite. In Checkmate 025, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=406) vs everolimus (n=397) 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 (≥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 Checkmate 141, the most common adverse reactions (≥10%) in patients receiving OPDIVO were cough and dyspnea at a higher incidence than investigator's choice.

In a separate Phase 3 study of YERVOY 3 mg/kg, the most common adverse reactions (≥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 067 - advanced melanoma alone or in combination with YERVOY; **Checkmate 037 and 066** - advanced melanoma; **Checkmate 017** - squamous non-small cell lung cancer (NSCLC); **Checkmate 057** - non-squamous NSCLC; **Checkmate 025** - renal cell carcinoma; **Checkmate 205/039** - classical Hodgkin lymphoma; **Checkmate 141** – squamous cell carcinoma of the head and neck.

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

About the *Opdivo* Clinical Development Program

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.

About Bristol-Myers Squibb's Patient Support Programs for *Opdivo*

Bristol-Myers Squibb remains committed to helping patients through treatment with *Opdivo*. For support and assistance, patients and physicians may call 1-855-OPDIVO-1. This number offers a 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 *Opdivo* 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.

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 2014, Ono and Bristol-Myers Squibb 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. 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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