Bristol-Myers Squibb Research at ESMO Demonstrates Breadth of Oncology Development Program and Focus on Improving Overall Survival Across Multiple Cancers

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Overall survival data from CheckMate -227 Part 1 evaluating Opdivo (nivolumab) plus low-dose Yervoy (ipilimumab) in advanced non-small cell lung cancer featured in ESMO Presidential Symposium

Five-year survival data on Opdivo plus Yervoy in advanced melanoma from CheckMate -067, the longest follow-up from a dual Immuno-Oncology Phase 3 trial

New data exploring potential of Opdivo and Opdivo plus Yervoy in esophageal, cervical and prostate cancers

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced the presentation of clinical, translational and health outcomes research across 18 tumor types, highlighting the breadth of the company’s innovative oncology development program at the European Society for Medical Oncology (ESMO) 2019 Congress in Barcelona, Spain, September 27 to October 1. Research will be presented from over 66 Bristol-Myers Squibb-sponsored studies, investigator-sponsored studies and collaborations, and includes new data on Opdivo and the Opdivo (nivolumab) plus Yervoy (ipilimumab) combination that adds to the existing body of clinical evidence for these regimens to improve survival outcomes and quality of life for patients with cancer.

- Final analysis of CheckMate -227 Part 1, which met its co-primary endpoint of overall survival, demonstrating a superior benefit for Opdivo plus low-dose Yervoy versus chemotherapy in first-line non-small cell lung cancer (NSCLC) patients whose tumors express PD-L1 ≥1%.
- Five-year survival outcomes data from CheckMate -067 evaluating Opdivo plus Yervoy in advanced melanoma.
- Three-year results on recurrence-free survival and distant metastasis-free survival from the Phase 3 CheckMate -238 trial investigating adjuvant Opdivo versus Yervoy in resected stage III/IV melanoma.
- First presentation of Phase 3 data evaluating Opdivo versus chemotherapy in advanced esophageal cancer, which will be featured in an ESMO Presidential Symposium.
- Innovative translational research examining novel biomarkers and diagnostic pathways geared towards enabling a more precise and customized approach to care based on each patient’s unique disease biology.
- Health economic outcomes research encompassing real-world evidence in second-line lung cancer, head and neck cancer, and melanoma, as well as other novel types of evidence demonstrating the clinical value of Opdivo plus Yervoy versus targeted therapies in advanced melanoma and renal cell carcinoma.

“The breadth of data we are presenting at ESMO demonstrates our focus on research that delivers transformative therapies, explores new approaches in difficult-to-treat tumors and highlights the commitment we have to patients with cancer,” said Fouad Namouni, head, Oncology Development, Bristol-Myers Squibb. “We look forward to sharing five-year overall survival data in advanced melanoma and final results from CheckMate -227 Part 1 in the first-line treatment of patients with non-small cell lung cancer, data from two of the three types of cancer where the Opdivo plus Yervoy regimen has shown an overall survival benefit in randomized Phase 3 trials.”

Key Bristol-Myers Squibb data being presented at the ESMO 2019 Congress include:
Non-Small Cell Lung Cancer
Final efficacy and safety results from Part 1 of the Phase 3 CheckMate -227 study evaluating Opdivo plus low-dose Yervoy in patients with first-line NSCLC. These data (Presentation #LBA4_PR) will be featured in the official Press Programme and in a Presidential Symposium on Saturday, September 28 from 4:30-6:20 PM CEST.

**Melanoma**

- Five-year survival outcomes from the Phase 3 CheckMate -067 trial evaluating the durability and sustained clinical benefit of Opdivo plus Yervoy in advanced melanoma. These data (Presentation #LBA68_PR) will be featured in the official Press Programme and in a Proffered Paper session on Saturday, September 28 from 8:30-10:15 AM CEST.
- Three-year efficacy and biomarker results from the Phase 3 CheckMate -238 trial investigating adjuvant Opdivo versus Yervoy in resected stage III/IV melanoma. These data (Presentation #1310O) will be featured in a Proffered Paper session on Saturday, September 28 from 8:30-10:15 AM CEST.

**Prostate Cancer**

- Phase 2 results from the CheckMate -9KD study assessing the clinical activity seen with Opdivo in combination with docetaxel in male patients with metastatic castration-resistant prostate cancer. These data (Presentation #LBA52) will be featured in a Poster Discussion on Sunday, September 29 from 8:30-9:45 AM CEST.

**Gastrointestinal Cancer**

- First presentation of the final analysis from the randomized Phase 3 ATTRACTION-3 study evaluating Opdivo versus chemotherapy in patients with unresectable advanced or recurrent esophageal squamous cell carcinoma that is refractory to or intolerant of one prior fluoropyrimidine/platinum-based therapy. These data (Presentation #LBA11) will be featured in a Presidential Symposium on Monday, September 30 from 4:30-6:15 PM CEST.
- Phase 3 results from the CheckMate -459 study of Opdivo compared to standard of care sorafenib as a first-line treatment in patients with advanced hepatocellular carcinoma. These data (Presentation #LBA38_PR) will be featured on Friday, September 27 in a Proffered Paper Session from 2-3:30 PM CEST.

**Cervical Cancer**

- Interim analysis from the Opdivo plus Yervoy cohort of the Phase 1/2 CheckMate -358 study in patients with recurrent or metastatic cervical cancer. These data (Presentation #LBA62) will be featured in a Proffered Paper Session on Sunday, September 29 from 8:30-10 AM CEST.

**Translational Medicine and Early Assets**

- Translational data from a clinical study will highlight a potential predictive composite biomarker approach to aid in the biology-driven selection of patients for Immuno-Oncology (I-O) therapy. These data (Presentation #1874O) will be featured in a Proffered Paper session on Saturday, September 28 from 8:30-10 AM CEST.
- New findings featuring emerging technologies that enable deeper exploration of tumor biology and the tumor microenvironment, and may ultimately inform our approach to I-O resistance, will also be presented. Research on how spatial analysis of immune and tumor cells in gastric and urothelial tumors may impact use of predictive biomarkers for I-O therapy (Presentation #128P) will be presented in a Poster Display session on Monday, September 30 from 12-1 PM CEST. Data highlighting the application of an artificial intelligence-based computed tomography imaging platform to detect early radiomic changes associated with sensitivity to treatment in patients with squamous NSCLC (Presentation #1910P) and the development of a multiplex chromogenic immunohistochemistry approach for simultaneous quantitation, spatial analysis and checkpoint expression of tumor infiltrating lymphocytes (Presentation #128P) will be presented in a Poster Display session on Monday, September 30 from 12-1 PM CEST.

**Bristol-Myers Squibb-sponsored and collaborative data at the ESMO 2019 Congress**

*All times noted are Central European Summer Time (CEST)*

**Melanoma**

- 5-year survival outcomes of the CheckMate 067 phase 3 trial of nivolumab plus ipilimumab (NIVO+IPI) combination therapy in advanced melanoma
  Author: Larkin
  Presentation Number: #LBA68_PR
  Session: Proffered Paper – Melanoma and other skin tumours
  Session Time: Saturday, September 28, 8:30-10:15 AM, Cordoba Auditorium (Hall 7)
  Presentation Time: 9:21-9:33 AM

- Adjuvant nivolumab (NIVO) versus ipilimumab (IPI) in resected stage III/IV melanoma: 3-year efficacy and biomarker results from the phase 3 CheckMate 238 trial
  Author: Weber
  Presentation Number: #1310O
  Session: Proffered Paper – Melanoma and other skin tumours
  Session Time: Saturday, September 28, 8:30-10:15 AM, Cordoba Auditorium (Hall 7)
  Presentation Time: 8:54-9:06 AM

- Mixture-cure modeling for resected stage III/IV melanoma in the phase 3 CheckMate 238 trial
  Author: Weber
  Presentation Number: #1331P
  Session: Poster Display Session 3
  Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

- Long-term efficacy of combination nivolumab and ipilimumab for first-line treatment of advanced melanoma: a network meta-analysis
Long-term real-world (RW) outcomes in patients with advanced melanoma (MEL) treated with ipilimumab (IPI) and non-IPI therapies: IMAGE study
Author: Dalle
Presentation Number: #1348P
Session: Poster Display Session 3
Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

Health-related quality of life of advanced melanoma survivors treated with CTLA-4 immune checkpoint inhibition: a matched cohort study
Author: Boekhout
Presentation Number: #1621P
Session: Poster Display Session 1
Session Time: Saturday, September 28, 12-1 PM, Poster Area (Hall 4)

Renal Cell Carcinoma

Association between depth of response and overall survival: exploratory analysis in patients with previously untreated advanced renal cell carcinoma (aRCC) in CheckMate 214
Author: Grünwald
Presentation Number: #950P
Session: Poster Display Session 3
Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

Quality of life in previously untreated patients with advanced renal cell carcinoma (aRCC) in CheckMate 214: updated results
Author: Cella
Presentation Number: #951P
Session: Poster Display Session 3
Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

Treatment-free survival, with and without toxicity, as a novel outcome applied to immunoncology agents in advanced renal cell carcinoma
Author: Regan
Presentation Number: #971P
Session: Poster Display Session 3
Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

Tailored immunotherapy approach with nivolumab in advanced renal cell carcinoma (TITAN-RCC)
Author: Grimm
Presentation Number: #LBA57
Session: Proffered Paper 2 – Genitourinary tumours, non-prostate
Session Time: Saturday, September 28, 2:45-4 PM, Sevilla Auditorium (Hall 2)
Presentation Time: 3-3:15 PM

NIVOREN GETUG-AFU 26 translational study: CD8 infiltration and PD-L1 expression are associated with outcome in patients (pts) with metastatic clear cell renal cell carcinoma (mccRCC) treated with nivolumab (N)
Author: Vano
Presentation Number: #909PD
Session: Poster Discussion – Genitourinary tumours, non-prostate
Session Time: Sunday, September 29, 3-4:15 PM, Pamplona Auditorium (Hall 2)
Discussion Time: 3:20-3:35 PM

A phase II trial of TKI induction followed by a randomized comparison between nivolumab or TKI continuation in renal cell carcinoma (NIVOSWITCH)
Author: Grünwald
Presentation Number: #959P
Session: Poster Display Session 3
Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

Genitourinary

Efficacy and safety of nivolumab in combination with docetaxel in men with metastatic castration-resistant prostate cancer in CheckMate 9KD
Author: Fizazi
Presentation Number: #LBA52
Session: Poster Discussion – Genitourinary tumours, prostate
Session Time: Sunday, September 29, 8:30-9:45 AM, Malaga Auditorium (Hall 5)
Discussion Time: 8:55-9:10 AM

Lung Cancer

Nivolumab (NIVO) + low-dose ipilimumab (IPI) vs platinum-doublet chemotherapy (chemo) as first-line (1L) treatment (tx) for advanced non-small cell lung cancer (NSCLC): CheckMate 227 Part 1
Impact of second-line (2L) immune checkpoint inhibitors (ICIs) on the treatment (Tx) of advanced non-small cell lung cancer (NSCLC) in a UK centre: a REAL-Oncoanalysis from the I-O Optimise initiative

Real-world effectiveness of nivolumab monotherapy after prior systemic therapy in advanced non-small cell lung cancer (NSCLC) in the United States

Nivolumab treatment in advanced non-small cell lung cancer (aNSCLC): a French nationwide retrospective cohort (UNIVOC Study)

IO-Synthesise NSCLC: A pooled analysis of real-world survival outcomes for non-small cell lung cancer patients treated with nivolumab in France and Germany

Effectiveness and safety of nivolumab in the treatment of lung cancer patients in France: Updated survival and subgroup analysis from the real-world EVIDENS study

Nivolumab versus chemotherapy in patients with previously treated advanced esophageal squamous cell carcinoma: the ATTRACTION-3 trial

CheckMate 459: a randomized, multi-center phase 3 study of nivolumab (NIVO) versus sorafenib (SOR) as first-line treatment in patients (pts) with advanced hepatocellular carcinoma (aHCC)

Efficacy and safety of nivolumab (Nivo) + ipilimumab (Ipi) in patients (pts) with recurrent/metastatic (R/M) cervical cancer: Results from CheckMate 358

Clinical and analytical accuracy of a 523 gene panel next-generation sequencing (NGS) assay on formalin-fixed paraffin-embedded (FFPE) solid tumor samples
- **Microsatellite Instability Testing and Lynch Syndrome Screening For Colorectal Cancer Patients Through Tumor Sequencing**
  Author: Liu
  Presentation Number: #1406P
  Session: Poster Display Session 3
  Session Time: Monday, September 30, Poster Display: 12-1 PM, Poster Area (Hall 4)

- **Interferon γ (IFN-γ) gene signature and tryptophan 2,3-dioxygenase 2 (TDO2) gene expression: a potential predictive composite biomarker for linrodostat mesylate (BMS-986205; indoleamine 2,3-dioxygenase 1 inhibitor [IDO1i]) + nivolumab (NIVO)**
  Author: Luke
  Presentation Number: #1874O
  Session: Proffered Paper – Translational research
  Session Time: Saturday, September 28, 8:30-10 AM, Pamplona Auditorium (Hall 2)
  Presentation Time: 9:15-9:30 AM

- **Comparison of platforms for determining tumor mutational burden (TMB) in patients with non-small cell lung cancer (NSCLC)**
  Author: Baden
  Presentation Number: #90PD
  Session: Poster Discussion 1 – Translational research
  Session Time: Sunday, September 29, 8:45-9:45 AM, Salamanca Auditorium (Hall 3)
  Discussion Time: 9:15-9:35 AM

- **Comparison of platforms for determining tumor mutational burden (TMB) from blood samples in patients with non-small cell lung cancer (NSCLC)**
  Author: Baden
  Presentation Number: #99P
  Session: Poster Display Session 3
  Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

- **Multiplex chromogenic immunohistochemistry (IHC) for spatial analysis of checkpoint-positive tumor infiltrating lymphocytes (TILs)**
  Author: Ely
  Presentation Number: #128P
  Session: Poster Display Session 3
  Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

- **Radiomic signatures for identification of tumors sensitive to nivolumab or docetaxel in squamous non-small cell lung cancer (sqNSCLC)**
  Author: Dercle
  Presentation Number: #1910P
  Session: Poster Display Session 3
  Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

- **Cell phenotypes associated with response and toxicity defined by high resolution flow cytometry in melanoma patients receiving checkpoint inhibition**
  Author: Weber
  Presentation Number: #1314PD
  Session: Poster Discussion – Melanoma and other skin tumours
  Session Time: Saturday, September 28, 2:45-4 PM, Granada Auditorium (Hall 3)
  Discussion Time: 3:39-3:54 PM

- **Pathologic scoring of pre-treatment H&E biopsies predicts overall survival in patients with metastatic clear cell renal cell carcinoma receiving nivolumab monotherapy**
  Author: Stein
  Presentation Number: #1251P
  Session: Poster Display Session 3
  Session Time: Monday, September 30, 12-1 PM, Poster Area (Hall 4)

- **Quantitative spatial profiling of lymphocyte-activation gene 3 (LAG-3)/major histocompatibility complex class II (MHC II) interaction in gastric and urothelial tumors**
  Author: Hedvat
  Presentation Number: #2021P
  Session: Poster Display Session 1
  Session Time: Saturday, September 28, 12-1 PM, Poster Area (Hall 4)

**Cross-Tumor**

- **Analysis of tumor hyperprogression (HP) with nivolumab (nivo) in randomized, placebo (pbo)-controlled trials**
  Author: Reck
  Presentation Number: #1193PD
  Session: Poster Discussion 2 – Immunotherapy of cancer
  Session Time: Monday, September 30, 8:45-9:45 AM, Malaga Auditorium (Hall 5)
  Discussion Time: 9:25-9:40 AM

**Collaborations**
• **SPICE, a phase I study of enadenotucirev in combination with nivolumab in tumors of epithelial origin: analysis of the metastatic colorectal cancer patients in the dose escalation phase**

  Author: Fakih  
  Presentation Number: #612P  
  Session: Poster Display Session 2  
  Session Time: Sunday, September 29, 12-1 PM, Poster Area (Hall 4)

**Bristol-Myers Squibb: Advancing Oncology Research**

At Bristol-Myers Squibb, patients are at the center of everything we do. The focus of our research is to increase quality, long-term survival for patients and make cure a possibility. Through a unique multidisciplinary approach powered by translational science, we harness our deep scientific experience in oncology and Immuno-Oncology (I-O) research to identify novel treatments tailored to individual patient needs. Our researchers are developing a diverse, purposefully built pipeline designed to target different immune system pathways and address the complex and specific interactions between the tumor, its microenvironment and the immune system. We source innovation internally, and in collaboration with academia, government, advocacy groups and biotechnology companies, to help make the promise of transformational medicines, like I-O, a reality for patients.

**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 35,000 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 65 countries, including the United States, the European Union, Japan and China. 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 50 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 unresectable or metastatic melanoma.

**OPDIVO®** (nivolumab), in combination with **YERVOY®** (ipilimumab), is indicated for the treatment of patients with unresectable or metastatic melanoma.

**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 metastatic small cell lung cancer (SCLC) with progression after platinum-based chemotherapy and at least one other line of therapy. This indication is approved under accelerated approval based on overall response rate and duration of response. 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 advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

**OPDIVO®** (nivolumab), in combination with **YERVOY®** (ipilimumab), is indicated for the treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma (RCC).

**OPDIVO®** (nivolumab) is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin or after 3 or more lines of systemic therapy that includes autologous HSCT. 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.

**OPDIVO®** (nivolumab) is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

**OPDIVO®** (nivolumab), as a single agent, is indicated for the treatment of adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. This indication is approved under
OPDIVO® (nivolumab), in combination with YERVOY® (ipilimumab), is indicated for the treatment of adults and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. This indication is approved under accelerated approval based on overall response rate and duration of response. 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 hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

OPDIVO® (nivolumab) is indicated for the adjuvant treatment of patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

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 1 mg/kg with YERVOY 3 mg/kg, immune-mediated pneumonitis occurred in 6% (25/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated pneumonitis occurred in 4.4% (24/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated pneumonitis occurred in 1.7% (2/119) of patients.

In Checkmate 205 and 039, pneumonitis, including interstitial lung disease, occurred in 6.0% (16/266) of patients receiving OPDIVO. Immune-mediated pneumonitis occurred in 4.9% (13/266) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 2 (n=12).

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 recurrent colitis. In patients receiving OPDIVO monotherapy, immune-mediated colitis occurred in 2.9% (58/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated colitis occurred in 26% (107/407) of patients including three fatal cases. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated colitis occurred in 10% (52/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated colitis occurred in 7% (8/119) 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 4.9% (13/266) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 2 (n=12). 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. For patients without HCC, withhold OPDIVO for Grade 2 and permanently discontinue OPDIVO for Grade 3 or 4. For patients with HCC, withhold OPDIVO and administer corticosteroids if AST/ALT is within normal limits at baseline and increases to >3 and up to 5 times the upper limit of normal (ULN), if AST/ALT is >1 and up to 3 times ULN at baseline and increases to >5 and up to 10 times the ULN, and if AST/ALT is >3 and up to 5 times ULN at baseline and increases to >8 and up to 10 times the ULN. Permanently discontinue OPDIVO and administer corticosteroids if AST or ALT increases to >10 times the ULN or total bilirubin increases >3 times the ULN. In patients receiving OPDIVO monotherapy, immune-mediated hepatitis occurred in 1.8% (35/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated hepatitis occurred in 13% (51/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated hepatitis occurred in 7% (38/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated hepatitis
occurred in 8% (10/119) of patients.

In Checkmate 040, immune-mediated hepatitis requiring systemic corticosteroids occurred in 5% (8/154) of patients receiving OPDIVO.

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% (2/154) of patients, with fatal hepatic failure in 0.6% 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. 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% (12/2094) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, hypophysitis occurred in 9% (36/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, hypophysitis occurred in 4.6% (25/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated hypophysitis occurred in 3.4% (4/119) of patients. In patients receiving OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/2094) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, adrenal insufficiency occurred in 5% (21/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, adrenal insufficiency occurred in 7% (41/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, adrenal insufficiency occurred in 5.9% (7/119) 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 1 mg/kg with YERVOY 3 mg/kg, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 22% (89/407) of patients. Hyperthyroidism occurred in 8% (34/407) of patients receiving this dose of OPDIVO with YERVOY. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 22% (119/547) of patients. Hyperthyroidism occurred in 12% (14/119) of patients. In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, diabetes occurred in 1.5% (6/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, diabetes occurred in 2.7% (15/547) 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. Six 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. Patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, immune-mediated nephritis and renal dysfunction occurred in 2.2% (9/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated nephritis and renal dysfunction occurred in 4.6% (25/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated nephritis and renal dysfunction occurred in 7% (41/547) of patients. In patients receiving YERVOY 3 mg/kg with OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/2094) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 1 mg/kg, adrenal insufficiency occurred in 5% (21/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, adrenal insufficiency occurred in 7% (41/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, adrenal insufficiency occurred in 5.9% (7/119) 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 1 mg/kg with YERVOY 3 mg/kg, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 22% (89/407) of patients. Hyperthyroidism occurred in 8% (34/407) of patients receiving this dose of OPDIVO with YERVOY. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 22% (119/547) of patients. Hyperthyroidism occurred in 12% (14/119) of patients. In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg, diabetes occurred in 1.5% (6/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, diabetes occurred in 2.7% (15/547) 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. Six of the 9 patients were hospitalized for severe endocrinopathies.

**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 1 mg/kg with YERVOY 3 mg/kg, immune-mediated rash occurred in 22.6% (92/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated rash occurred in 16.6% (91/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, immune-mediated rash occurred in 14% (17/121) 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 1 mg/kg with YERVOY 3 mg/kg (0.2%) after 1.7 months of exposure. Encephalitis occurred in one RCC patient receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg (0.2%) after approximately 4 months of exposure. Encephalitis occurred in one MSI-H/dMMR mCRC patient (0.8%) receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg after 15 days of exposure.

Other Immune-Mediated Adverse Reactions

Based on the severity of the adverse reaction, permanently discontinue or withhold OPDIVO, administer high-dose corticosteroids, and, if appropriate, initiate hormone-replacement therapy. Across clinical trials of OPDIVO monotherapy or in combination with YERVOY, the following clinically significant immune-mediated adverse reactions, some with fatal outcome, occurred in <1.0% of patients receiving OPDIVO: myocarditis, rhabdomyolysis, myositis, uveitis, iritis, pancreatitis, and abdominal nerve parestis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome, hypopituitarism, systemic inflammatory response syndrome, gastritis, duodenitis, sarcoidosis, histiciocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), motor dysfunction, vasculitis, aplastic anemia, pericarditis, and myasthenic syndrome.

If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, which has been observed in patients receiving OPDIVO and may require treatment with systemic steroids to reduce the risk of permanent vision loss.

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 as a 60-minute infusion, infusion-related reactions occurred in 6.4% (12/191) of patients. In a separate study in which patients received OPDIVO monotherapy as a 60-minute infusion or a 30-minute infusion, infusion-related reactions occurred in 2.2% (8/368) and 2.7% (10/369) of patients, respectively. Additionally, 0.5% (2/368) and 1.4% (5/369) of patients, respectively, experienced adverse reactions within 48 hours of infusion that led to dose delay, permanent discontinuation or withholding of OPDIVO. In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 2.5% (10/407) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, infusion-related reactions occurred in 5.1% (28/547) of patients. In MSI-H/dMMR mCRC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg, infusion-related reactions occurred in 4.2% (5/119) of patients.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1 receptor blocking antibody. Transplant-related complications include hyperacutae graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1 receptor blocking antibody prior to or after an allogeneic HSCT.

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.

Increased Mortality in Patients with Multiple Myeloma when OPDIVO is Added to a Thalidomide Analogue and Dexamethasone

In clinical trials in patients with multiple myeloma, the addition of OPDIVO to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.

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 breastfeeding 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 (74% and 44%), adverse reactions leading to permanent discontinuation (47%
and 18%) or to dosing delays (58% and 36%), and Grade 3 or 4 adverse reactions (72% and 51%) 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 2.2%), colitis (10% and 1.9%), and pyrexia (10% and 1.0%). In Checkmate 017 and 057, serious adverse reactions occurred in 46% of patients receiving OPDIVO (n=318). The most frequent serious adverse reactions reported in ≥2% of patients receiving OPDIVO were pneumonia, pulmonary embolism, dyspnea, pyrexia, pleural effusion, pneumonitis, and respiratory failure. In Checkmate 032, serious adverse reactions occurred in 45% of patients receiving OPDIVO (n=245). The most frequent serious adverse reactions reported in ≥2% of patients receiving OPDIVO were fatigue (41%), diarrhea (32%), pruritus (31%), rash (30%), and colitis (18%). In Checkmate 205 and 039, serious adverse reactions occurred in 47% of patients (n=236). Serious adverse reactions occurred in 26% of patients. The most frequent serious adverse reactions reported in ≥2% of patients were pneumonia, infusion-related reaction, pyrexia, colitis or diarrhea, pleural effusion, pneumonitis, and rash. Eleven patients died from causes other than disease progression: 3 from adverse reactions within 30 days of the last OPDIVO dose, 2 from infection 8 to 9 months after completing OPDIVO, and 6 from complications of allogeneic HCT. In Checkmate 141, serious adverse reactions occurred in 49% of patients receiving OPDIVO (n=326). The most frequent serious adverse reactions reported in ≥2% of patients receiving OPDIVO were pneumonia, dyspnea, respiratory failure, respiratory tract infection, and sepsis. In Checkmate 275, serious adverse reactions occurred in 54% of patients receiving OPDIVO (n=270). The most frequent serious adverse reactions reported in ≥2% of patients receiving OPDIVO were urinary tract infection, sepsis, diarrhea, small intestine obstruction, and general physical health deterioration. In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO with YERVOY, serious adverse reactions occurred in 47% of patients. The most frequent serious adverse reactions reported in ≥2% of patients were colitis/diarrhea, hepatic events, abdominal pain, acute kidney injury, pyrexia, and dehydration. In Checkmate 040, serious adverse reactions occurred in 49% of patients (n=154). The most frequent serious adverse reactions reported in ≥2% of patients were pyrexia, ascites, back pain, general physical health deterioration, abdominal pain, and pneumonia. In Checkmate 238, Grade 3 or 4 adverse reactions occurred in 52% of OPDIVO-treated patients (n=452). The most frequent Grade 3 and 4 adverse reactions reported in ≥2% of OPDIVO-treated patients were diarrhea and increased lipase and amylase. Serious adverse reactions occurred in 18% of OPDIVO-treated patients.

### 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 reaction (≥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 (62%), diarrhea (54%), rash (53%), nausea (44%), pyrexia (40%), pruritus (39%), musculoskeletal pain (32%), vomiting (31%), decreased appetite (29%), cough (27%), headache (26%), dyspnea (24%), upper respiratory tract infection (23%), arthralgia (21%), and increased transaminases (25%). In Checkmate 067, the most common (≥20%) adverse reactions in the OPDIVO arm (n=313) were fatigue (59%), rash (40%), musculoskeletal pain (42%), diarrhea (36%), nausea (30%), cough (28%), pruritus (27%), upper respiratory tract infection (22%), decreased appetite (22%), headache (22%), constipation (21%), arthralgia (21%), and vomiting (20%). 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 032, the most common adverse reactions (≥20%) in patients receiving OPDIVO (n=245) were fatigue (45%), decreased appetite (27%), musculoskeletal pain (25%), dyspnea (22%), nausea (22%), diarrhea (21%), constipation (20%), and cough (20%). In Checkmate 025, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=406) vs everolimus (n=397) were fatigue (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 214, the most common adverse reactions (≥20%) reported in patients treated with OPDIVO plus YERVOY (n=547) vs sunitinib (n=535) were fatigue (58% vs 69%), rash (39% vs 25%), diarrhea (38% vs 58%), musculoskeletal pain (37% vs 40%), pruritus (33% vs 11%), nausea (30% vs 43%), cough (28% vs 25%), pyrexia (25% vs 17%), arthralgia (23% vs 16%), decreased appetite (21% vs 29%), dyspnea (20% vs 21%), and vomiting (20% vs 28%). In Checkmate 205 and 039, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=266) were upper respiratory tract infection (44%), fatigue (39%), cough (36%), diarrhea (33%), pyrexia (29%), musculoskeletal pain (26%), rash (24%), nausea (20%) and pruritus (20%). In Checkmate 141, the most common adverse reactions (≥10%) in patients receiving OPDIVO (n=236) were cough and dyspnea at a higher incidence than investigator’s choice. In Checkmate 275, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=270) were fatigue (46%), musculoskeletal pain (30%), nausea (22%), and decreased appetite (22%). In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO as a single agent, the most common adverse reactions (≥20%) were fatigue (54%), diarrhea (43%), abdominal pain (34%), nausea (34%), vomiting (28%), musculoskeletal pain (28%), cough (26%), pyrexia (24%), rash (23%), constipation (20%), and upper respiratory tract infection (20%). In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO with YERVOY, the most common adverse reactions (≥20%) were fatigue (49%), diarrhea (45%), pyrexia (36%), musculoskeletal pain (36%), abdominal pain (30%), pruritus (28%), nausea (26%), rash (25%), decreased appetite (20%), and vomiting (20%). In Checkmate 040, the most common adverse reactions (≥20%) in patients receiving OPDIVO (n=154) were fatigue (38%), musculoskeletal pain (36%), abdominal pain (34%), pruritus (27%), diarrhea (27%), rash (26%), cough (23%), and decreased appetite (22%). In Checkmate 238, the most common adverse reactions (≥20%) reported in OPDIVO-treated patients (n=452) vs ipilimumab-treated patients (n=453) were fatigue (57% vs 55%), diarrhea (37% vs 55%), rash (35% vs 47%), musculoskeletal pain (32% vs 27%), pruritus (28% vs 37%), headache (23% vs 31%), nausea (23% vs 28%), upper respiratory infection (22% vs 15%), and abdominal pain (21% vs 23%). The most common immune-mediated adverse reactions were rash (16%), diarrhea/colic (6%), and hepatitis (3%).

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

Checkmate Trials and Patient Populations

Checkmate 037 – previously treated metastatic melanoma; Checkmate 066 – previously untreated metastatic melanoma; Checkmate 067 – previously untreated metastatic melanoma, as a single agent or in combination with YERVOY; Checkmate 017 – second-line treatment of metastatic squamous non-small cell lung cancer; Checkmate 057 – second-line treatment of metastatic non-squamous non-small cell lung cancer; Checkmate 032 – small cell lung cancer; Checkmate 025 – previously treated renal cell carcinoma; Checkmate 214 – previously untreated renal cell carcinoma, in combination with YERVOY; Checkmate 205/039 – classical Hodgkin lymphoma; Checkmate 141 – recurrent or metastatic squamous cell carcinoma of the head and neck; Checkmate 275 – urothelial carcinoma; Checkmate 142 – MSI-H or dMMR metastatic colorectal cancer, as a single agent or in combination with YERVOY; Checkmate 040 – hepatocellular carcinoma; Checkmate 238 – adjuvant treatment of melanoma.

About the Bristol-Myers Squibb and Ono Pharmaceutical Collaboration

In 2011, through a collaboration agreement with Ono Pharmaceutical Co., Bristol-Myers Squibb expanded its territorial rights to develop and commercialize Opdivo globally, except in Japan, South Korea and Taiwan, where Ono had retained all rights to the compound at the time. On July 23, 2014, 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.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development and commercialization of pharmaceutical products. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on historical performance and current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These risks, assumptions, uncertainties and other factors include, among others, that future study results will be consistent with the results to date, that Opdivo, alone or in combination with Yervoy, may not achieve their primary study endpoints or receive regulatory approval for the indications described in this release in the currently anticipated timeline or at all and, if approved, whether such product candidates for such indications described in this release will be commercially successful. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect Bristol-Myers Squibb’s business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol-Myers Squibb’s Annual Report on Form 10-K for the year ended December 31, 2018, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, Bristol-Myers Squibb undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

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