

# Bristol Myers Squibb to Showcase Data Demonstrating Improved Outcomes in Earlier Stages of Cancer, Durable Long-Term Benefits with Opdivo-Based Regimens, and Addressing High Unmet Needs in Multiple Tumor Types at ESMO 2023

10/12/2023

First presentation of results from CheckMate -901 show survival benefit with Opdivo (nivolumab) + chemotherapy in the first-line treatment of patients with unresectable or metastatic urothelial carcinoma who are eligible for cisplatin-based therapies; selected for ESMO Presidential Symposium

First presentation of results from CheckMate - 77T demonstrate benefit with perioperative regimen of neoadjuvant Opdivo + chemotherapy followed by surgery and adjuvant Opdivo in patients with resectable non-small cell lung cancer; selected for ESMO Presidential Symposium

Data to be presented reinforce benefits of Opdivo and Opdivo-based combinations in both earlier stages of cancer and advanced disease

Additional data demonstrate potential of repotrectinib in patients with NTRK-positive advanced solid tumors

PRINCETON, N.J.--(BUSINESS WIRE)-- **Bristol Myers Squibb** (NYSE: BMY) today announced the presentation of data from over 55 Bristol Myers Squibb-sponsored, investigator-sponsored, and collaboration studies across our

oncology portfolio in more than 10 tumor types at the European Society for Medical Oncology (ESMO) Congress 2023 to be held from October 20-24 in Madrid, Spain. Data from the Phase 3 CheckMate -901 and CheckMate -77T studies have been selected for presentation in Presidential Symposium sessions.

Data to be presented support the role of Opdivo and Opdivo-based combinations in both earlier and metastatic stages of multiple cancer types, especially in patient groups with high unmet needs. Additional data will highlight the potential of repotrectinib in patients with TKI-naïve and -pretreated NTRK-positive solid tumors, including non-small cell lung cancer (NSCLC), as well as the benefit of treatment with Opdualag, the dual immunotherapy fixed-dose combination of the PD-1 inhibitor nivolumab and the LAG-3-blocking antibody relatlimab, in advanced melanoma.

“We are eager to share research during this year’s ESMO Congress on our immunotherapies and targeted therapies in both metastatic disease and earlier stages of several tumor types, including bladder cancer, melanoma and lung cancer,” said **Samit Hirawat, M.D.**, executive vice president, chief medical officer, Global Drug Development, Bristol Myers Squibb. “These new data highlight our leading development program for Opdivo and Opdivo-based combinations in earlier stages of cancer, as well as our commitment to meeting the challenging treatment needs of cancer patients by both continuing to study the potential of our existing medicines as well as advancing new assets that may target cancer’s vulnerabilities more precisely.”

### Key data highlighting approved or investigational therapies from Bristol Myers Squibb at ESMO 2023 include:

- First presentation of overall survival (OS) and progression-free survival (PFS) data from the Phase 3 CheckMate -901 trial of Opdivo in combination with cisplatin-based chemotherapy followed by Opdivo monotherapy in the first-line treatment of patients with unresectable or metastatic urothelial carcinoma demonstrating survival benefits over standard-of-care cisplatin-based chemotherapy. CheckMate -901 is the first Phase 3 trial with an immunotherapy-based combination to demonstrate a survival benefit compared to standard-of-care cisplatin-based chemotherapy in the first-line treatment of this patient population. These data will be presented at the Presidential Symposium on Sunday, October 22.
- First presentation of data from the Phase 3 CheckMate -77T trial of the perioperative regimen of neoadjuvant Opdivo with chemotherapy followed by surgery and adjuvant Opdivo in patients with resectable stage IIA to IIIB NSCLC. CheckMate -77T is the second positive Phase 3 trial of an Opdivo-based combination for the treatment of non-metastatic NSCLC. These data will be presented at the Presidential Symposium on Saturday, October 21.
- Late-breaking results from the Phase 3 CheckMate -816 study of neoadjuvant Opdivo with chemotherapy showing improved clinical benefit according to PD-L1 expression status in patients with resectable NSCLC.

Additional CheckMate -816 results will also be presented showing efficacy benefits with Opdivo plus Yervoy in resectable NSCLC.

- Updated results from the registrational TRIDENT-1 trial demonstrating clinical benefit with repotrectinib in patients with NTRK-positive advanced solid tumors, including NSCLC, who often develop resistance to existing therapies.
- Seven-year efficacy results from the Phase 3 CheckMate -238 trial of adjuvant Opdivo in resected stage III/IV melanoma pointing to sustained benefits and reinforcing BMS' leadership in earlier stages of melanoma.
- Subgroup data from the Phase 2/3 RELATIVITY-047 trial showing consistent benefit across subgroups with the company's third distinct checkpoint inhibitor Opdualag (nivolumab and relatlimab-rmbw) in the first-line treatment of patients with advanced melanoma.

## Summary of Select Presentations:

Abstract Title	Author	Presentation Type/#	Session Title	Session/Poster Discussion Date/Time@
<b>Adrenocortical Carcinoma</b>				
EO2401 (E) peptide immunotherapy + nivolumab (N) in adrenocortical carcinoma (ACC) and metastatic pheochromocytoma/paraganglioma (MPP); EOADR1-19/SPENCER	Eric Baudin	Proffered Paper Abstract #724O	Proffered paper session - NETs and endocrine tumors	Sunday, October 22 08:30 - 10:00 CEST / 2:30 - 4:00 AM EDT
<b>Gastrointestinal</b>				
Factors associated with uptake of adjuvant nivolumab in a nationwide esophageal cancer patient cohort	Robert Verhoeven	Poster Abstract #1575P	Oesophagogastric cancer	Monday, October 23 Onsite poster display
<b>Genitourinary</b>				
Nivolumab plus gemcitabine-cisplatin vs gemcitabine-cisplatin alone for previously untreated unresectable or metastatic urothelial carcinoma: results for cisplatin-eligible patients in the phase 3 CheckMate 901 trial	Michiel van der Heijden	Proffered Paper Abstract #LBA7	Presidential 2	Sunday, October 22 16:30 - 18:15 CEST / 10:30 AM - 12:15 PM EDT
Clinical management and outcomes of patients with advanced renal cell carcinoma (aRCC) treated with nivolumab+ipilimumab (N+I): a real-world study	Tom Geldart	Poster Abstract #1896P	Renal cancer	Monday, October 23 Onsite poster display
Treatment patterns among novel hormonal therapy-experienced patients with metastatic castration-resistant prostate cancer	Vivek Narayan	Poster Abstract #1824P	Prostate cancer	Sunday, October 22 Onsite poster display
STELLAR-304: A randomized phase 3 study of zanzalintinib (XL092) and nivolumab in non-clear cell renal cell carcinoma (nccRCC)	Sumanta Pal	Poster Abstract #1912TIP	Renal cancer	Monday, October 23 Onsite poster display
<b>Glioblastoma</b>				
Trotabresib (CC-90010) combined with concomitant temozolomide (TMZ) plus radiotherapy (RT) and adjuvant TMZ in patients (pts) with newly diagnosed primary glioblastoma (ndGBM): updated results from a phase 1b/2 study	Maria Vieito Villar	Proffered Paper Abstract #500O	Proffered paper session - CNS tumors	Friday, October 20 16:00 - 17:30 CEST / 10:00-11:30 AM EDT
<b>Gynecological</b>				
Antitumor activity of farletuzumab ecteribulin in a panel of endometrial cancer patient-derived xenografts with four different molecular subtypes	Kosei Hasegawa	Poster	Gynecological cancers	Sunday, October 22

		Abstract #786P		Onsite poster display
A randomized, double-blind trial of nivolumab (NIVO) vs placebo (PBO) with neoadjuvant chemotherapy (NACT) followed by adjuvant endocrine therapy (ET) ± NIVO in patients (pts) with high-risk, ER+ HER2- primary breast cancer (BC)	Sherene Loi	Proffered Paper Abstract #LBA20	Proffered paper session – Breast cancer, early stage	Friday, October 20 14:00 – 15:40 CEST / 8:00 – 9:40 AM EDT
<b>Head and Neck</b>				
Nivolumab (nivo) in recurrent and/or metastatic squamous cell carcinoma of head and neck (R/M SCCHN): real-world effectiveness, quality of life (QoL) of patients and their caregivers in France (ProNiHN study)	Christophe Le Tourneau	Poster Abstract #938P	Head and neck cancers, excl. thyroid	Sunday, October 22 Onsite poster display
Patients (pts) with recurrent and/or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) treated with nivolumab (NIVO) in the first-line (1L) or later-line (2L+) settings in Germany: Updated results from the real-world HANNA study	Boris Kubuschok	Poster Abstract #927P	Head and neck cancers, excl. thyroid	Sunday, October 22 Onsite poster display
<b>Thoracic</b>				
CheckMate 77T: Phase 3 study comparing neoadjuvant nivolumab (NIVO) plus chemotherapy (chemo) vs neoadjuvant placebo plus chemo followed by surgery and adjuvant NIVO or placebo for previously untreated, resectable stage II–IIIB NSCLC	Tina Cascone	Proffered Paper Abstract #LBA1	Presidential 1	Saturday, October 21 16:30 - 18:15 CEST / 10:30 AM - 12:15 PM EDT
Neoadjuvant nivolumab (N) + ipilimumab (I) vs chemotherapy in the phase 3 CheckMate 816 trial	Mark Awad	Proffered Paper Abstract #1261O	Proffered paper session – non-metastatic NSCLC and other thoracic malignancies	Friday, October 20 14:00 – 15:45 CEST / 8:00 – 9:45 AM EDT
Neoadjuvant nivolumab (N) + chemotherapy (C) in the phase 3 CheckMate 816 study: 3-y results by tumor PD-L1 expression	Mariano Provencio Pulla	Mini Oral Abstract #LBA57	Mini oral session 2 – non-metastatic NSCLC and other thoracic malignancies	Monday, October 23 14:45 - 15:55 CEST / 8:45 - 9:55 AM EDT
Repotrectinib in patients (pts) with NTRK fusion-positive (NTRK+) advanced solid tumors, including NSCLC: Update from the phase 1/2 TRIDENT-1 trial	Ben Solomon	Poster Abstract #1372P	NSCLC, metastatic	Monday, October 23 Onsite poster display
Nivolumab (nivo) resumption in patients with advanced or metastatic non-small cell lung cancer (aNSCLC): Survival outcomes based on France and Germany real-world data (RWD)	Maurice Pérol	Poster Abstract #1455P	NSCLC, metastatic	Monday, October 23 Onsite poster display
First-line nivolumab (NIVO) plus ipilimumab (IPI) with two cycles of chemotherapy in patients with metastatic non-small cell lung cancer (NSCLC): Results from an interim analysis of the non-interventional FINN study	Jonas Kuon	Poster Abstract #1448P	NSCLC, metastatic	Monday, October 23 Onsite poster display
SAPPHIRE: Phase 3 Study of sitravatinib Plus nivolumab Versus Docetaxel in Patients with Previously Treated Advanced Non-Squamous Non-Small Cell Lung Cancer	Hossein Borghaei	Proffered Paper Abstract #LBA63	Proffered paper session – NSCLC, metastatic	Friday, October 20 16:00 - 17:30 CEST / 10:00 - 11:30 AM EDT
<b>Melanoma</b>				
Adjuvant nivolumab (NIVO) vs ipilimumab (IPI) in resected stage III/IV melanoma: 7-y results from CheckMate 238	Paolo Ascierto	Poster Abstract #1089P	Melanoma and other skin tumors	Sunday, October 22 Onsite poster display
Nivolumab (NIVO) plus relatlimab (RELA) vs NIVO in previously untreated metastatic or unresectable melanoma: 2-year subgroup analyses from RELATIVITY-047	Georgina Long	Poster Abstract #1103P	Melanoma and other skin tumors	Sunday, October 22 Onsite poster display
Comparison of intracranial (IC) response assessment criteria in patients (pts) with melanoma brain metastases (MBM) treated with combination nivolumab (NIVO) plus ipilimumab (IPI) in CheckMate 204	Raymond Huang	Poster Abstract #1135P	Melanoma and other skin tumors	Sunday, October 22 Onsite poster display
Unraveling relatlimab (RELA)-specific biology using biomarker analyses in patients with advanced melanoma treated with nivolumab (NIVO)+RELA or NIVO alone in RELATIVITY-047	Evan Lipson	Mini Oral Abstract #LBA51	Mini oral session – Melanoma and other skin tumors	Saturday, October 21 14:45 – 16:10 CEST / 8:45 – 10:10 AM EDT
Evaluation of surrogate endpoints for overall survival within the RELATIVITY-047 trial	Peter Mohr	Poster Abstract #1102P	Melanoma and other skin tumors	Sunday, October 22 Onsite poster display

Cross-Tumor/Solid Tumor				
Recommended phase 2 dose (RP2D) selection and pharmacodynamic (PD) data of the first-in-human immune-stimulating antibody conjugate (ISAC) BDC-1001 in patients (pts) with advanced HER2-expressing solid tumors	Bob Li	Mini Oral Abstract #657MO	Mini oral session – Developmental therapeutics	Monday, October 23 16:30 – 18:00 CEST / 10:30 AM – 12:00 PM EDT
Clinical benefit of immunotherapies in advanced cancer in France: a population-based estimate from 2014 to 2021	Isabelle Borget	Poster Abstract #1752P	Policy and preventive strategies	Sunday, October 22 Onsite poster display
Early Assets				
GUIDE.MRD: A Consortium Guiding Multi-Modal Therapies Against Minimal Residual Disease (MRD) by Liquid Biopsy to Assess Implementation of circulating tumor DNA (ctDNA) in Clinical Practice to Improve Patient Outcomes	Klaus Pantel	Poster Abstract #237TiP	Biomarkers (agnostic)	Saturday, October 21 Onsite poster display

All abstracts except late-breaking abstracts will be available on the ESMO website at 00:05 CEST Monday, October 16 (6:05 PM EDT on Sunday, October 15). All late-breaking abstracts will be available on the ESMO website at 00:05 CEST on Thursday, October 19 (6:05 PM EDT on Wednesday, October 18).

## Bristol Myers Squibb: Creating a Better Future for People with Cancer

Bristol Myers Squibb is inspired by a single vision — transforming patients' lives through science. The goal of the company's cancer research is to deliver medicines that offer each patient a better, healthier life and to make cure a possibility. Building on a legacy across a broad range of cancers that have changed survival expectations for many, Bristol Myers Squibb researchers are exploring new frontiers in personalized medicine and, through innovative digital platforms, are turning data into insights that sharpen their focus. Deep understanding of causal human biology, cutting-edge capabilities and differentiated research platforms uniquely position the company to approach cancer from every angle.

Cancer can have a relentless grasp on many parts of a patient's life, and Bristol Myers Squibb is committed to taking actions to address all aspects of care, from diagnosis to survivorship. As a leader in cancer care, Bristol Myers Squibb is working to empower all people with cancer to have a better future.

## 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 treated 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 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.

## **OPDIVO U.S. INDICATIONS**

OPDIVO® (nivolumab), as a single agent, is indicated for the treatment of adult and pediatric patients 12 years of age and older with unresectable or metastatic melanoma.

OPDIVO® (nivolumab), in combination with YERVOY® (ipilimumab), is indicated for the treatment of adult and pediatric patients 12 years of age and older with unresectable or metastatic melanoma.

OPDIVO® (nivolumab) is indicated for the adjuvant treatment of adult and pediatric patients 12 years of age and older with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.

OPDIVO® (nivolumab), in combination with platinum-doublet chemotherapy, is indicated as neoadjuvant treatment of adult patients with resectable (tumors  $\geq 4$  cm or node positive) non-small cell lung cancer (NSCLC).

OPDIVO® (nivolumab), in combination with YERVOY® (ipilimumab), is indicated for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 ( $\geq 1\%$ ) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

OPDIVO® (nivolumab), in combination with YERVOY® (ipilimumab) and 2 cycles of platinum-doublet chemotherapy, is indicated for the first-line treatment of adult patients with metastatic or recurrent non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

OPDIVO® (nivolumab) is indicated for the treatment of adult 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), in combination with YERVOY® (ipilimumab), is indicated for the first-line treatment of adult

patients with unresectable malignant pleural mesothelioma (MPM).

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

OPDIVO® (nivolumab), in combination with cabozantinib, is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC).

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

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 adult 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 adult 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.

OPDIVO® (nivolumab), as a single agent, is indicated for the adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC.

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 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), 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), in combination with YERVOY® (ipilimumab), is indicated for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. 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 the confirmatory trials.

OPDIVO® (nivolumab) is indicated for the treatment of adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

OPDIVO® (nivolumab) is indicated for the adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in adult patients who have received neoadjuvant chemoradiotherapy (CRT).

OPDIVO® (nivolumab), in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

OPDIVO® (nivolumab), in combination with YERVOY® (ipilimumab), is indicated for the first-line treatment of adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC).

OPDIVO® (nivolumab), in combination with fluoropyrimidine- and platinum- containing chemotherapy, is indicated for the treatment of adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma.

## **IMPORTANT SAFETY INFORMATION**

### **Severe and Fatal Immune-Mediated Adverse Reactions**

Immune-mediated adverse reactions listed herein may not include all possible severe and fatal immune- mediated adverse reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. While immune-mediated adverse reactions usually manifest during treatment, they can also occur after discontinuation



of OPDIVO or YERVOY. Early identification and management are essential to ensure safe use of OPDIVO and YERVOY. Monitor for signs and symptoms that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotrophic hormone (ACTH) level, and thyroid function at baseline and periodically during treatment with OPDIVO and before each dose of YERVOY. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue OPDIVO and YERVOY depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). In general, if OPDIVO or YERVOY interruption or discontinuation is required, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

#### Immune-Mediated Pneumonitis

OPDIVO and YERVOY can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation. In patients receiving OPDIVO monotherapy, immune-mediated pneumonitis occurred in 3.1% (61/1994) of patients, including Grade 4 (<0.1%), Grade 3 (0.9%), and Grade 2 (2.1%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated pneumonitis occurred in 7% (31/456) of patients, including Grade 4 (0.2%), Grade 3 (2.0%), and Grade 2 (4.4%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated pneumonitis occurred in 3.9% (26/666) of patients, including Grade 3 (1.4%) and Grade 2 (2.6%). In NSCLC patients receiving OPDIVO 3 mg/kg every 2 weeks with YERVOY 1 mg/kg every 6 weeks, immune-mediated pneumonitis occurred in 9% (50/576) of patients, including Grade 4 (0.5%), Grade 3 (3.5%), and Grade 2 (4.0%). Four patients (0.7%) died due to pneumonitis.

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, including Grade 3 (n=1) and Grade 2 (n=12).

#### Immune-Mediated Colitis

OPDIVO and YERVOY can cause immune-mediated colitis, which may be fatal. A common symptom included in the

definition of colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. In patients receiving OPDIVO monotherapy, immune-mediated colitis occurred in 2.9% (58/1994) of patients, including Grade 3 (1.7%) and Grade 2 (1%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated colitis occurred in 25% (115/456) of patients, including Grade 4 (0.4%), Grade 3 (14%) and Grade 2 (8%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated colitis occurred in 9% (60/666) of patients, including Grade 3 (4.4%) and Grade 2 (3.7%).

#### Immune-Mediated Hepatitis and Hepatotoxicity

OPDIVO and YERVOY can cause immune-mediated hepatitis. In patients receiving OPDIVO monotherapy, immune-mediated hepatitis occurred in 1.8% (35/1994) of patients, including Grade 4 (0.2%), Grade 3 (1.3%), and Grade 2 (0.4%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated hepatitis occurred in 15% (70/456) of patients, including Grade 4 (2.4%), Grade 3 (11%), and Grade 2 (1.8%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated hepatitis occurred in 7% (48/666) of patients, including Grade 4 (1.2%), Grade 3 (4.9%), and Grade 2 (0.4%). OPDIVO in combination with cabozantinib can cause hepatic toxicity with higher frequencies of Grade 3 and 4 ALT and AST elevations compared to OPDIVO alone. Consider more frequent monitoring of liver enzymes as compared to when the drugs are administered as single agents. In patients receiving OPDIVO and cabozantinib, Grades 3 and 4 increased ALT or AST were seen in 11% of patients.

#### Immune-Mediated Endocrinopathies

OPDIVO and YERVOY can cause primary or secondary adrenal insufficiency, immune-mediated hypophysitis, immune-mediated thyroid disorders, and Type 1 diabetes mellitus, which can present with diabetic ketoacidosis. Withhold OPDIVO and YERVOY depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism; initiate hormone replacement as clinically indicated. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism; initiate hormone replacement or medical management as clinically indicated. Monitor patients for hyperglycemia or other signs and symptoms of diabetes; initiate treatment with insulin as clinically indicated.

In patients receiving OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/1994), including Grade 3 (0.4%) and Grade 2 (0.6%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, adrenal insufficiency

occurred in 8% (35/456), including Grade 4 (0.2%), Grade 3 (2.4%), and Grade 2 (4.2%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, adrenal insufficiency occurred in 7% (48/666) of patients, including Grade 4 (0.3%), Grade 3 (2.5%), and Grade 2 (4.1%). In patients receiving OPDIVO and cabozantinib, adrenal insufficiency occurred in 4.7% (15/320) of patients, including Grade 3 (2.2%) and Grade 2 (1.9%).

In patients receiving OPDIVO monotherapy, hypophysitis occurred in 0.6% (12/1994) of patients, including Grade 3 (0.2%) and Grade 2 (0.3%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, hypophysitis occurred in 9% (42/456), including Grade 3 (2.4%) and Grade 2 (6%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, hypophysitis occurred in 4.4% (29/666) of patients, including Grade 4 (0.3%), Grade 3 (2.4%), and Grade 2 (0.9%).

In patients receiving OPDIVO monotherapy, thyroiditis occurred in 0.6% (12/1994) of patients, including Grade 2 (0.2%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, thyroiditis occurred in 2.7% (22/666) of patients, including Grade 3 (4.5%) and Grade 2 (2.2%).

In patients receiving OPDIVO monotherapy, hyperthyroidism occurred in 2.7% (54/1994) of patients, including Grade 3 (<0.1%) and Grade 2 (1.2%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, hyperthyroidism occurred in 9% (42/456) of patients, including Grade 3 (0.9%) and Grade 2 (4.2%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, hyperthyroidism occurred in 12% (80/666) of patients, including Grade 3 (0.6%) and Grade 2 (4.5%).

In patients receiving OPDIVO monotherapy, hypothyroidism occurred in 8% (163/1994) of patients, including Grade 3 (0.2%) and Grade 2 (4.8%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, hypothyroidism occurred in 20% (91/456) of patients, including Grade 3 (0.4%) and Grade 2 (11%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, hypothyroidism occurred in 18% (122/666) of patients, including Grade 3 (0.6%) and Grade 2 (11%).

In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients, including Grade 3 (0.4%) and Grade 2 (0.3%), and 2 cases of diabetic ketoacidosis. In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, diabetes occurred in 2.7% (15/666) of patients, including Grade 4 (0.6%), Grade 3 (0.3%), and Grade 2 (0.9%).

#### Immune-Mediated Nephritis with Renal Dysfunction

OPDIVO and YERVOY can cause immune-mediated nephritis. In patients receiving OPDIVO monotherapy, immune-mediated nephritis and renal dysfunction occurred in 1.2% (23/1994) of patients, including Grade 4 (<0.1%), Grade 3 (0.5%), and Grade 2 (0.6%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-

mediated nephritis with renal dysfunction occurred in 4.1% (27/666) of patients, including Grade 4 (0.6%), Grade 3 (1.1%), and Grade 2 (2.2%).

### Immune-Mediated Dermatologic Adverse Reactions

OPDIVO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate nonexfoliative rashes.

YERVOY can cause immune-mediated rash or dermatitis, including bullous and exfoliative dermatitis, SJS, TEN, and DRESS. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-bullous/exfoliative rashes.

Withhold or permanently discontinue OPDIVO and YERVOY depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).

In patients receiving OPDIVO monotherapy, immune-mediated rash occurred in 9% (171/1994) of patients, including Grade 3 (1.1%) and Grade 2 (2.2%). In patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, immune-mediated rash occurred in 28% (127/456) of patients, including Grade 3 (4.8%) and Grade 2 (10%). In patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, immune-mediated rash occurred in 16% (108/666) of patients, including Grade 3 (3.5%) and Grade 2 (4.2%).

### Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received OPDIVO monotherapy or OPDIVO in combination with YERVOY or were reported with the use of other PD-1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions: cardiac/vascular: myocarditis, pericarditis, vasculitis; nervous system: meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy; ocular: uveitis, iritis, and other ocular inflammatory toxicities can occur; gastrointestinal: pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis; musculoskeletal and connective tissue: myositis/polymyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica; endocrine: hypoparathyroidism; other (hematologic/immune): hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis (HLH), systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

In addition to the immune-mediated adverse reactions listed above, across clinical trials of YERVOY monotherapy or in combination with OPDIVO, the following clinically significant immune-mediated adverse reactions, some with fatal outcome, occurred in <1% of patients unless otherwise specified: nervous system: autoimmune neuropathy (2%), myasthenic syndrome/myasthenia gravis, motor dysfunction; cardiovascular: angiopathy, temporal arteritis; ocular: blepharitis, episcleritis, orbital myositis, scleritis; gastrointestinal: pancreatitis (1.3%); other (hematologic/immune): conjunctivitis, cytopenias (2.5%), eosinophilia (2.1%), erythema multiforme, hypersensitivity vasculitis, neurosensory hypoacusis, psoriasis.

Some ocular IMAR cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. 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 YERVOY, as this may require treatment with systemic corticosteroids to reduce the risk of permanent vision loss.

## Infusion-Related Reactions

OPDIVO and YERVOY can cause severe infusion-related reactions. Discontinue OPDIVO and YERVOY in patients with severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild (Grade 1) or moderate (Grade 2) infusion-related reactions. In patients receiving OPDIVO monotherapy as a 60-minute infusion, infusion-related reactions occurred in 6.4% (127/1994) of patients. In a separate trial 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 melanoma 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 HCC patients receiving OPDIVO 1 mg/kg with YERVOY 3 mg/kg every 3 weeks, infusion-related reactions occurred in 8% (4/49) of patients. In RCC patients receiving OPDIVO 3 mg/kg with YERVOY 1 mg/kg every 3 weeks, 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 every 3 weeks, infusion-related reactions occurred in 4.2% (5/119) of patients. In MPM patients receiving OPDIVO 3 mg/kg every 2 weeks with YERVOY 1 mg/kg every 6 weeks, infusion-related reactions occurred in 12% (37/300) 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 OPDIVO or YERVOY. Transplant-related complications include hyperacute 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 OPDIVO or YERVOY and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with OPDIVO and YERVOY prior to or after an allogeneic HSCT.

## Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal studies, OPDIVO and YERVOY can cause fetal harm when administered to a pregnant woman. The effects of YERVOY are likely to be greater during the second and third trimesters of pregnancy. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with OPDIVO and YERVOY and for at least 5 months after the last dose.

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

In randomized 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

There are no data on the presence of OPDIVO or YERVOY in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 5 months after the last 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  $\geq 2\%$  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 ( $\geq 10\%$ ) 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 238, serious adverse reactions occurred in 18% of patients receiving OPDIVO (n=452). Grade 3 or 4 adverse reactions occurred in 25% of OPDIVO-treated patients (n=452). The most frequent Grade 3 and 4 adverse reactions reported in  $\geq 2\%$  of OPDIVO-treated patients were diarrhea and increased lipase and amylase. In Checkmate 816, serious adverse reactions occurred in 30% of patients (n=176) who were treated with OPDIVO in combination with platinum-doublet chemotherapy. Serious adverse reactions in  $>2\%$  included pneumonia and vomiting. No fatal adverse reactions occurred in patients who received OPDIVO in combination with platinum-doublet chemotherapy. In Checkmate 227, serious adverse reactions occurred in 58% of patients (n=576). The most frequent ( $\geq 2\%$ ) serious adverse reactions were pneumonia, diarrhea/colitis, pneumonitis, hepatitis, pulmonary embolism, adrenal insufficiency, and hypophysitis. Fatal adverse reactions occurred in 1.7% of patients; these included events of pneumonitis (4 patients), myocarditis, acute kidney injury, shock, hyperglycemia, multi-system organ failure, and renal failure. In Checkmate 9LA, serious adverse reactions occurred in 57% of patients (n=358). The most frequent ( $>2\%$ ) serious adverse reactions were pneumonia, diarrhea, febrile neutropenia, anemia, acute kidney injury, musculoskeletal pain, dyspnea, pneumonitis, and respiratory failure. Fatal adverse reactions occurred in 7 (2%) patients, and included hepatic toxicity, acute renal failure, sepsis, pneumonitis, diarrhea with hypokalemia, and massive hemoptysis in the setting of thrombocytopenia. 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  $\geq 2\%$  of patients receiving OPDIVO were pneumonia, pulmonary embolism, dyspnea, pyrexia, pleural effusion, pneumonitis, and respiratory failure. In Checkmate 057, fatal adverse reactions occurred; these included events of infection (7 patients, including one case of *Pneumocystis jirovecii* pneumonia), pulmonary embolism (4 patients), and limbic encephalitis (1 patient). In Checkmate 743, serious adverse reactions occurred in 54% of patients receiving OPDIVO plus YERVOY. The most frequent serious adverse reactions reported in  $\geq 2\%$  of patients were pneumonia, pyrexia, diarrhea, pneumonitis, pleural effusion, dyspnea, acute kidney injury, infusion-related reaction, musculoskeletal pain, and pulmonary embolism. Fatal adverse reactions occurred in 4 (1.3%) patients and included pneumonitis, acute heart failure, sepsis, and encephalitis. In Checkmate 214, serious adverse reactions occurred in 59% of patients receiving OPDIVO plus YERVOY (n=547). The most frequent serious adverse reactions reported in  $\geq 2\%$  of patients were diarrhea, pyrexia, pneumonia, pneumonitis, hypophysitis, acute kidney injury, dyspnea, adrenal insufficiency, and colitis. In Checkmate 9ER, serious adverse reactions occurred in 48% of patients receiving OPDIVO and cabozantinib (n=320). The most frequent serious adverse reactions reported in  $\geq 2\%$  of patients were diarrhea, pneumonia, pneumonitis, pulmonary embolism, urinary tract infection, and hyponatremia. Fatal intestinal perforations occurred in 3 (0.9%) patients. In Checkmate 025, serious adverse reactions occurred in 47% of patients receiving OPDIVO (n=406). 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, adverse reactions leading to discontinuation occurred in 7% and dose delays due to adverse reactions occurred in 34% of patients (n=266). Serious adverse reactions occurred in 26% of patients. The most frequent serious adverse reactions reported in  $\geq 1\%$  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 HSCT. In Checkmate 141, serious adverse reactions occurred in 49% of patients receiving OPDIVO (n=236). The most frequent serious adverse reactions reported in  $\geq 2\%$  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  $\geq 2\%$  of patients receiving OPDIVO were urinary tract infection, sepsis, diarrhea, small intestine obstruction, and general physical health deterioration. In Checkmate 274, serious adverse reactions occurred in 30% of patients receiving OPDIVO (n=351). The most frequent serious adverse reaction reported in  $\geq 2\%$  of patients receiving OPDIVO was urinary tract infection. Fatal adverse reactions occurred in 1% of patients; these included events of pneumonitis (0.6%). In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO with YERVOY (n=119), serious adverse reactions occurred in 47% of patients. The most frequent serious adverse reactions reported in  $\geq 2\%$  of patients were colitis/diarrhea, hepatic events, abdominal pain, acute kidney injury, pyrexia, and dehydration. In Checkmate 040, serious adverse reactions occurred in 59% of patients receiving OPDIVO with YERVOY (n=49). Serious adverse reactions reported in  $\geq 4\%$  of patients were pyrexia, diarrhea, anemia, increased AST, adrenal insufficiency, ascites, esophageal varices hemorrhage, hyponatremia, increased blood bilirubin, and pneumonitis. In Attraction-3, serious adverse reactions occurred in 38% of patients receiving OPDIVO (n=209). Serious adverse reactions reported in  $\geq 2\%$  of patients who received OPDIVO were pneumonia, esophageal fistula, interstitial lung disease, and pyrexia. The following fatal adverse reactions occurred in patients who received OPDIVO: interstitial lung disease or pneumonitis (1.4%), pneumonia (1.0%), septic shock (0.5%), esophageal fistula (0.5%), gastrointestinal hemorrhage (0.5%), pulmonary embolism (0.5%), and sudden death (0.5%). In Checkmate 577, serious adverse reactions occurred in 33% of patients receiving OPDIVO (n=532). A serious adverse reaction reported in  $\geq 2\%$  of patients who received OPDIVO was pneumonitis. A fatal reaction of myocardial infarction occurred in one patient who received OPDIVO. In Checkmate 648, serious adverse reactions occurred in 62% of patients receiving OPDIVO in combination with chemotherapy (n=310). The most frequent serious adverse reactions reported in  $\geq 2\%$  of patients who received OPDIVO with chemotherapy were pneumonia (11%), dysphagia (7%), esophageal stenosis (2.9%), acute kidney injury (2.9%), and pyrexia (2.3%). Fatal adverse reactions occurred in 5 (1.6%) patients who received OPDIVO in combination with chemotherapy; these included pneumonitis, pneumatosis intestinalis, pneumonia, and acute kidney injury. In Checkmate 648, serious adverse reactions occurred in 69% of patients receiving OPDIVO in combination with YERVOY (n=322). The most frequent serious adverse reactions reported in  $\geq 2\%$  who received



OPDIVO in combination with YERVOY were pneumonia (10%), pyrexia (4.3%), pneumonitis (4.0%), aspiration pneumonia (3.7%), dysphagia (3.7%), hepatic function abnormal (2.8%), decreased appetite (2.8%), adrenal insufficiency (2.5%), and dehydration (2.5%). Fatal adverse reactions occurred in 5 (1.6%) patients who received OPDIVO in combination with YERVOY; these included pneumonitis, interstitial lung disease, pulmonary embolism, and acute respiratory distress syndrome. In Checkmate 649, serious adverse reactions occurred in 52% of patients treated with OPDIVO in combination with chemotherapy (n=782). The most frequent serious adverse reactions reported in  $\geq 2\%$  of patients treated with OPDIVO in combination with chemotherapy were vomiting (3.7%), pneumonia (3.6%), anemia (3.6%), pyrexia (2.8%), diarrhea (2.7%), febrile neutropenia (2.6%), and pneumonitis (2.4%). Fatal adverse reactions occurred in 16 (2.0%) patients who were treated with OPDIVO in combination with chemotherapy; these included pneumonitis (4 patients), febrile neutropenia (2 patients), stroke (2 patients), gastrointestinal toxicity, intestinal mucositis, septic shock, pneumonia, infection, gastrointestinal bleeding, mesenteric vessel thrombosis, and disseminated intravascular coagulation.

## Common Adverse Reactions

In Checkmate 037, the most common adverse reaction ( $\geq 20\%$ ) reported with OPDIVO (n=268) was rash (21%). In Checkmate 066, the most common adverse reactions ( $\geq 20\%$ ) 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 ( $\geq 20\%$ ) 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 ( $\geq 20\%$ ) 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 238, the most common adverse reactions ( $\geq 20\%$ ) 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/colitis (6%), and hepatitis (3%). In Checkmate 816, the most common ( $>20\%$ ) adverse reactions in the OPDIVO plus chemotherapy arm (n=176) were nausea (38%), constipation (34%), fatigue (26%), decreased appetite (20%), and rash (20%). In Checkmate 227, the most common ( $\geq 20\%$ ) adverse reactions were fatigue (44%), rash (34%), decreased appetite (31%), musculoskeletal pain (27%), diarrhea/colitis (26%), dyspnea (26%), cough (23%), hepatitis (21%), nausea (21%), and pruritus (21%). In Checkmate 9LA, the most common ( $>20\%$ ) adverse reactions were fatigue (49%), musculoskeletal pain (39%), nausea (32%), diarrhea (31%), rash (30%), decreased appetite (28%), constipation (21%), and pruritus (21%). In Checkmate 017 and 057, the most common adverse reactions ( $\geq 20\%$ ) in patients receiving

OPDIVO (n=418) were fatigue, musculoskeletal pain, cough, dyspnea, and decreased appetite. In Checkmate 743, the most common adverse reactions ( $\geq 20\%$ ) in patients receiving OPDIVO plus YERVOY were fatigue (43%), musculoskeletal pain (38%), rash (34%), diarrhea (32%), dyspnea (27%), nausea (24%), decreased appetite (24%), cough (23%), and pruritus (21%). In Checkmate 214, the most common adverse reactions ( $\geq 20\%$ ) reported in patients treated with OPDIVO plus YERVOY (n=547) were fatigue (58%), rash (39%), diarrhea (38%), musculoskeletal pain (37%), pruritus (33%), nausea (30%), cough (28%), pyrexia (25%), arthralgia (23%), decreased appetite (21%), dyspnea (20%), and vomiting (20%). In Checkmate 9ER, the most common adverse reactions ( $\geq 20\%$ ) in patients receiving OPDIVO and cabozantinib (n=320) were diarrhea (64%), fatigue (51%), hepatotoxicity (44%), palmar-plantar erythrodysesthesia syndrome (40%), stomatitis (37%), rash (36%), hypertension (36%), hypothyroidism (34%), musculoskeletal pain (33%), decreased appetite (28%), nausea (27%), dysgeusia (24%), abdominal pain (22%), cough (20%) and upper respiratory tract infection (20%). In Checkmate 025, the most common adverse reactions ( $\geq 20\%$ ) 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 205 and 039, the most common adverse reactions ( $\geq 20\%$ ) 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 ( $\geq 10\%$ ) in patients receiving OPDIVO (n=236) were cough (14%) and dyspnea (14%) at a higher incidence than investigator's choice. In Checkmate 275, the most common adverse reactions ( $\geq 20\%$ ) reported in patients receiving OPDIVO (n=270) were fatigue (46%), musculoskeletal pain (30%), nausea (22%), and decreased appetite (22%). In Checkmate 274, the most common adverse reactions ( $\geq 20\%$ ) reported in patients receiving OPDIVO (n=351) were rash (36%), fatigue (36%), diarrhea (30%), pruritus (30%), musculoskeletal pain (28%), and urinary tract infection (22%). In Checkmate 142 in MSI-H/dMMR mCRC patients receiving OPDIVO as a single agent (n=74), the most common adverse reactions ( $\geq 20\%$ ) 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 (n=119), the most common adverse reactions ( $\geq 20\%$ ) 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 ( $\geq 20\%$ ) in patients receiving OPDIVO with YERVOY (n=49), were rash (53%), pruritus (53%), musculoskeletal pain (41%), diarrhea (39%), cough (37%), decreased appetite (35%), fatigue (27%), pyrexia (27%), abdominal pain (22%), headache (22%), nausea (20%), dizziness (20%), hypothyroidism (20%), and weight decreased (20%). In Attraction-3, the most common adverse reactions ( $\geq 20\%$ ) in OPDIVO-treated patients (n=209) were rash (22%) and decreased appetite (21%). In Checkmate 577, the most common adverse reactions ( $\geq 20\%$ ) in patients receiving OPDIVO (n=532) were fatigue (34%), diarrhea (29%), nausea (23%), rash (21%), musculoskeletal pain (21%), and cough (20%). In Checkmate 648, the most common adverse reactions ( $\geq 20\%$ ) in patients treated with OPDIVO in combination with chemotherapy (n=310) were nausea (65%), decreased appetite

(51%), fatigue (47%), constipation (44%), stomatitis (44%), diarrhea (29%), and vomiting (23%). In Checkmate 648, the most common adverse reactions reported in  $\geq 20\%$  of patients treated with OPDIVO in combination with YERVOY were rash (31%), fatigue (28%), pyrexia (23%), nausea (22%), diarrhea (22%), and constipation (20%). In Checkmate 649, the most common adverse reactions ( $\geq 20\%$ ) in patients treated with OPDIVO in combination with chemotherapy (n=782) were peripheral neuropathy (53%), nausea (48%), fatigue (44%), diarrhea (39%), vomiting (31%), decreased appetite (29%), abdominal pain (27%), constipation (25%), and musculoskeletal pain (20%).

Please see US Full Prescribing Information for **OPDIVO** and **YERVOY**.

## Clinical Trials and Patient Populations

Checkmate 227—previously untreated metastatic non-small cell lung cancer, in combination with YERVOY; Checkmate 9LA—previously untreated recurrent or metastatic non-small cell lung cancer in combination with YERVOY and 2 cycles of platinum-doublet chemotherapy by histology; Checkmate 649—previously untreated advanced or metastatic gastric cancer, gastroesophageal junction and esophageal adenocarcinoma; Checkmate 577—adjuvant treatment of esophageal or gastroesophageal junction cancer; Checkmate 238—adjuvant treatment of melanoma; Checkmate 274—adjuvant treatment of urothelial carcinoma; Checkmate 275—previously treated advanced or metastatic urothelial carcinoma; Checkmate 142—MSI-H or dMMR metastatic colorectal cancer, as a single agent or in combination with YERVOY; Checkmate 142—MSI-H or dMMR metastatic colorectal cancer, as a single agent or in combination with YERVOY; Attraction-3—esophageal squamous cell carcinoma; Checkmate 648—previously untreated, unresectable advanced recurrent or metastatic esophageal squamous cell carcinoma; Checkmate 648—previously untreated, unresectable advanced recurrent or metastatic esophageal squamous cell carcinoma; Checkmate 040—hepatocellular carcinoma, in combination with YERVOY; Checkmate 743—previously untreated unresectable malignant pleural mesothelioma, in combination with YERVOY; 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 816—neoadjuvant non-small cell lung cancer, in combination with platinum-doublet chemotherapy; Checkmate 141—recurrent or metastatic squamous cell carcinoma of the head and neck; Checkmate 025—previously treated renal cell carcinoma; Checkmate 214—previously untreated renal cell carcinoma, in combination with YERVOY; Checkmate 9ER—previously untreated renal cell carcinoma, in combination with cabozantinib; Checkmate 205/039—classical Hodgkin lymphoma

## OPDUALAG U.S. INDICATION

Opdualag™ (nivolumab and relatlimab-rmbw) is indicated for the treatment of adult and pediatric patients 12 years of age or older with unresectable or metastatic melanoma.

## OPDUALAG IMPORTANT SAFETY INFORMATION

### Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions (IMARs) listed herein may not include all possible severe and fatal immune-mediated adverse reactions.

IMARs which may be severe or fatal, can occur in any organ system or tissue. IMARs can occur at any time after starting treatment with a LAG-3 and PD-1/PD-L1 blocking antibodies. While IMARs usually manifest during treatment, they can also occur after discontinuation of Opdualag. Early identification and management of IMARs are essential to ensure safe use. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying IMARs. Evaluate clinical chemistries including liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected IMARs, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue Opdualag depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information). In general, if Opdualag requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose IMARs are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

#### Immune-Mediated Pneumonitis

Opdualag can cause immune-mediated pneumonitis, which may be fatal. In patients treated with other PD-1/PD-L1 blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.7% (13/355) of patients receiving Opdualag, including Grade 3 (0.6%), and Grade 2 (2.3%) adverse reactions. Pneumonitis led to permanent discontinuation of Opdualag in 0.8% and withholding of Opdualag in 1.4% of patients.

#### Immune-Mediated Colitis

Opdualag can cause immune-mediated colitis, defined as requiring use of corticosteroids and no clear alternate etiology. A common symptom included in the definition of colitis was diarrhea. Cytomegalovirus

infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated diarrhea or colitis occurred in 7% (24/355) of patients receiving Opdualag, including Grade 3 (1.1%) and Grade 2 (4.5%) adverse reactions. Colitis led to permanent discontinuation of Opdualag in 2% and withholding of Opdualag in 2.8% of patients.

#### Immune-Mediated Hepatitis

Opdualag can cause immune-mediated hepatitis, defined as requiring the use of corticosteroids and no clear alternate etiology.

Immune-mediated hepatitis occurred in 6% (20/355) of patients receiving Opdualag, including Grade 4 (0.6%), Grade 3 (3.4%), and Grade 2 (1.4%) adverse reactions. Hepatitis led to permanent discontinuation of Opdualag in 1.7% and withholding of Opdualag in 2.3% of patients.

#### Immune-Mediated Endocrinopathies

Opdualag can cause primary or secondary adrenal insufficiency, hypophysitis, thyroid disorders, and Type 1 diabetes mellitus, which can be present with diabetic ketoacidosis. Withhold or permanently discontinue Opdualag depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).

For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. In patients receiving Opdualag, adrenal insufficiency occurred in 4.2% (15/355) of patients receiving Opdualag, including Grade 3 (1.4%) and Grade 2 (2.5%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of Opdualag in 1.1% and withholding of Opdualag in 0.8% of patients.

Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism; initiate hormone replacement as clinically indicated. Hypophysitis occurred in 2.5% (9/355) of patients receiving Opdualag, including Grade 3 (0.3%) and Grade 2 (1.4%) adverse reactions. Hypophysitis led to permanent discontinuation of Opdualag in 0.3% and withholding of Opdualag in 0.6% of patients.

Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism; initiate hormone replacement or medical management as clinically indicated. Thyroiditis occurred in 2.8% (10/355) of patients receiving Opdualag, including Grade 2 (1.1%) adverse reactions. Thyroiditis did not lead to permanent

discontinuation of Opdualag. Thyroiditis led to withholding of Opdualag in 0.3% of patients. Hyperthyroidism occurred in 6% (22/355) of patients receiving Opdualag, including Grade 2 (1.4%) adverse reactions. Hyperthyroidism did not lead to permanent discontinuation of Opdualag. Hyperthyroidism led to withholding of Opdualag in 0.3% of patients. Hypothyroidism occurred in 17% (59/355) of patients receiving Opdualag, including Grade 2 (11%) adverse reactions. Hypothyroidism led to the permanent discontinuation of Opdualag in 0.3% and withholding of Opdualag in 2.5% of patients.

Monitor patients for hyperglycemia or other signs and symptoms of diabetes; initiate treatment with insulin as clinically indicated. Diabetes occurred in 0.3% (1/355) of patients receiving Opdualag, a Grade 3 (0.3%) adverse reaction, and no cases of diabetic ketoacidosis. Diabetes did not lead to the permanent discontinuation or withholding of Opdualag in any patient.

#### Immune-Mediated Nephritis with Renal Dysfunction

Opdualag can cause immune-mediated nephritis, which is defined as requiring use of steroids and no clear etiology. In patients receiving Opdualag, immune-mediated nephritis and renal dysfunction occurred in 2% (7/355) of patients, including Grade 3 (1.1%) and Grade 2 (0.8%) adverse reactions. Immune-mediated nephritis and renal dysfunction led to permanent discontinuation of Opdualag in 0.8% and withholding of Opdualag in 0.6% of patients.

Withhold or permanently discontinue Opdualag depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).

#### Immune-Mediated Dermatologic Adverse Reactions

Opdualag can cause immune-mediated rash or dermatitis, defined as requiring use of steroids and no clear alternate etiology. Exfoliative dermatitis, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and Drug Rash with eosinophilia and systemic symptoms has occurred with PD-1/L-1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.

Withhold or permanently discontinue Opdualag depending on severity (please see section 2 Dosage and Administration in the accompanying Full Prescribing Information).

Immune-mediated rash occurred in 9% (33/355) of patients, including Grade 3 (0.6%) and Grade 2 (3.4%) adverse reactions. Immune-mediated rash did not lead to permanent discontinuation of Opdualag. Immune-mediated rash led to withholding of Opdualag in 1.4% of patients.

#### Immune-Mediated Myocarditis

Opdualag can cause immune-mediated myocarditis, which is defined as requiring use of steroids and no clear alternate etiology. The diagnosis of immune-mediated myocarditis requires a high index of suspicion. Patients with cardiac or cardio-pulmonary symptoms should be assessed for potential myocarditis. If myocarditis is suspected, withhold dose, promptly initiate high dose steroids (prednisone or methylprednisolone 1 to 2 mg/kg/day) and promptly arrange cardiology consultation with diagnostic workup. If clinically confirmed, permanently discontinue Opdualag for Grade 2-4 myocarditis.

Myocarditis occurred in 1.7% (6/355) of patients receiving Opdualag, including Grade 3 (0.6%), and Grade 2 (1.1%) adverse reactions. Myocarditis led to permanent discontinuation of Opdualag in 1.7% of patients.

### Other Immune-Mediated Adverse Reactions

The following clinically significant IMARs occurred at an incidence of <1% (unless otherwise noted) in patients who received Opdualag or were reported with the use of other PD-1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions: Cardiac/Vascular: pericarditis, vasculitis; Nervous System: meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy; Ocular: uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other IMARs, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss; Gastrointestinal: pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis; Musculoskeletal and Connective Tissue: myositis/polymyositis, rhabdomyolysis (and associated sequelae including renal failure), arthritis, polymyalgia rheumatica; Endocrine: hypoparathyroidism; Other (Hematologic/Immune): hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

### **Infusion-Related Reactions**

Opdualag can cause severe infusion-related reactions. Discontinue Opdualag in patients with severe or life-threatening infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild to moderate infusion-related reactions. In patients who received Opdualag as a 60-minute intravenous infusion, infusion-related reactions occurred in 7% (23/355) of patients.

### **Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)**

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/PD-L1 receptor blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 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/PD-L1 receptor blocking antibody prior to or after an allogeneic HSCT.

## Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, Opdualag 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 Opdualag for at least 5 months after the last dose of Opdualag.

## Lactation

There are no data on the presence of Opdualag in human milk, the effects on the breastfed child, or the effect on milk production. Because nivolumab and relatlimab may be excreted in human milk and because of the potential for serious adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with Opdualag and for at least 5 months after the last dose.

## Serious Adverse Reactions

In Relativity-047, fatal adverse reaction occurred in 3 (0.8%) patients who were treated with Opdualag; these included hemophagocytic lymphohistiocytosis, acute edema of the lung, and pneumonitis. Serious adverse reactions occurred in 36% of patients treated with Opdualag. The most frequent serious adverse reactions reported in  $\geq 1\%$  of patients treated with Opdualag were adrenal insufficiency (1.4%), anemia (1.4%), colitis (1.4%), pneumonia (1.4%), acute myocardial infarction (1.1%), back pain (1.1%), diarrhea (1.1%), myocarditis (1.1%), and pneumonitis (1.1%).

## Common Adverse Reactions and Laboratory Abnormalities

The most common adverse reactions reported in  $\geq 20\%$  of the patients treated with Opdualag were musculoskeletal pain (45%), fatigue (39%), rash (28%), pruritus (25%), and diarrhea (24%).



The most common laboratory abnormalities that occurred in  $\geq 20\%$  of patients treated with Opdualag were decreased hemoglobin (37%), decreased lymphocytes (32%), increased AST (30%), increased ALT (26%), and decreased sodium (24%).

Please see U.S. Full Prescribing Information for **OPDUALAG**.

### 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**, **Facebook** and **Instagram**.

### 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 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 may not be consistent with the results to date, that the treatments and combination treatments may not receive regulatory approval for the indications described in this release in the currently anticipated timeline or at all, that any marketing approvals, if granted, may have significant limitation on their use, and, if approved, whether such treatments or combination treatments 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, 2022, 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.

corporatefinancial-news

## Bristol Myers Squibb

### Media Inquiries:

**[media@bms.com](mailto:media@bms.com)**

### Investors:

**[investor.relations@bms.com](mailto:investor.relations@bms.com)**

Source: Bristol Myers Squibb