



NEWS RELEASE

New Data from Merck's Leading Immuno-Oncology Clinical Development Program in Over 25 Tumor Types to Be Presented at 2018 ASCO Annual Meeting

5/16/2018

New and Long-term Overall Survival Data for KEYTRUDA® (pembrolizumab) in Lung Cancer and Melanoma, Plus New Data in Renal Cell, Cervical, Merkel Cell, and Other Cancers

First-Time Lynparza® (olaparib) Data in Combination with Abiraterone in Metastatic Prostate Cancer Under Merck and AstraZeneca Strategic Collaboration

New Data in Four Tumor Types Evaluating LENVIMA® (lenvatinib) in Combination with KEYTRUDA Under Merck and Eisai Strategic Collaboration

Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that new combination and monotherapy data from Merck's oncology portfolio, anchored by anti-PD-1 therapy KEYTRUDA, will be presented at the 54th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago from June 1-5. More than 140 abstracts in over 25 tumor types have been accepted, including new and long-term data for KEYTRUDA across multiple types of cancer.

"With more data and longer follow-up across tumors and treatment settings, evidence continues to support the role of KEYTRUDA as a foundational treatment for many types of cancer," said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. "At ASCO, we will present new and long-term overall survival data for KEYTRUDA in advanced lung cancer and melanoma – as well as studies across our growing oncology portfolio in a number of new tumor types where we have adduced clinically meaningful results."



The abstracts accepted for the 2018 ASCO Annual Meeting include data for approved and investigational uses of KEYTRUDA, investigational uses of PARP inhibitor Lynparza and MEK inhibitor selumetinib (in collaboration with AstraZeneca), and investigational uses of kinase inhibitor LENVIMA (in collaboration with Eisai). Highlights to be presented at ASCO include:

Select Lung Cancer Presentations

- New overall survival (OS) data from the pivotal Phase 3 KEYNOTE-042 trial with KEYTRUDA monotherapy compared to chemotherapy alone as first-line treatment in patients with locally advanced or metastatic nonsquamous or squamous non-small cell lung cancer (NSCLC) with a PD-L1 tumor proportion score (TPS) of ≥ 1 percent are to be presented in the ASCO opening plenary session and press program on Sunday, June 3 (Abstract #LBA4). As previously announced, an interim analysis conducted by the independent Data Monitoring Committee (DMC) demonstrated that treatment with KEYTRUDA monotherapy resulted in significantly longer overall survival (OS) than that achieved with platinum-based chemotherapy (carboplatin plus paclitaxel or carboplatin plus pemetrexed) in patients with a PD-L1 TPS of ≥ 1 percent.
- First-time data of an early patient cohort (n=204) from the randomized, double-blind, placebo-controlled, Phase 3 KEYNOTE-407 trial investigating KEYTRUDA in combination with carboplatin-paclitaxel or nab-paclitaxel, compared with carboplatin-paclitaxel or nab-paclitaxel alone as first-line treatment in patients with metastatic squamous NSCLC (Abstract #105) are to be presented. An interim analysis of pre-specified secondary endpoints showed an alpha-controlled, overall response rate (ORR) of 58.4 percent for KEYTRUDA plus chemotherapy (n=101) compared to 35 percent for chemotherapy alone (n=103) (p-value, 0.0004) [(7.7 months median follow-up (range 0.4, 13.9)]. The duration of response (DOR) was ≥ 6 months in 65.8 percent of patients receiving KEYTRUDA plus chemotherapy compared to 45.6 percent receiving chemotherapy alone. Adverse events (grade ≥ 3) were 64.4 percent for KEYTRUDA plus chemotherapy and 74.5 percent for chemotherapy alone. No new safety concerns were reported. The primary endpoints of the study are OS and progression-free survival (PFS). As previously announced, based on these data, Merck has recently submitted a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA).

Select Combination Data Presentations

- First-time data from a Phase 2 trial in post-chemotherapy, metastatic castration-resistant prostate cancer with Lynparza in combination with standard of care, abiraterone, regardless of HRRm status (Abstract #5003) are to be featured as an oral presentation. This is the first data for a PARP inhibitor in combination with standard of care, abiraterone, in the treatment of prostate cancer.
- New and updated data for KEYTRUDA in combination with LENVIMA are to be presented including in advanced hepatocellular carcinoma (HCC), endometrial carcinoma, head and neck squamous cell carcinoma

(HNSCC) and renal cell carcinoma (RCC) from the KEYNOTE-524 (Study 116) and Phase 1b/2 KEYNOTE-146 (Study 111) studies (Abstracts #4076, #5596, #6016 and #4560, respectively). KEYTRUDA in combination with LENVIMA was previously granted Breakthrough Therapy Designation for the potential treatment of advanced and/or metastatic RCC.

Select Monotherapy Data Presentations

- Long-term (four- and five-year) OS data from KEYNOTE-006 and KEYNOTE-001 in advanced melanoma with KEYTRUDA monotherapy (Abstracts #9503 and #9516, respectively) are to be presented.
- First-time and long-term data for KEYTRUDA monotherapy are to be presented in eight tumor types. These data are in esophageal cancer (KEYNOTE-180, Abstract #4049), HCC (KEYNOTE-224, Abstract #4020), Merkel cell carcinoma (KEYNOTE-017, Abstract #9506), RCC (KEYNOTE-427, Abstract #4500), prostate cancer (KEYNOTE-199, Abstract #5007), ovarian cancer (KEYNOTE-100, Abstract #5511), cervical cancer (KEYNOTE-158, Abstract #5522) and small cell lung cancer (KEYNOTE-158, Abstract #8506).

Merck Investor Event

Merck will hold an investor event in conjunction with the 2018 ASCO Annual Meeting on Monday, June 4 at 5:45 p.m. CT. Those unable to attend in person will be able to listen to a live audio webcast of the presentation. Details of the event will be provided at a date closer to the event at <http://investors.merck.com/home/default.aspx>.

Details on Merck's Late-Breaking, Oral and Clinical Science Symposium ASCO Abstracts

Late-Breaking Presentation

- Abstract #LBA4 Late-Breaking Presentation: Pembrolizumab (pembro) versus platinum-based chemotherapy (chemo) as first-line therapy for advanced/metastatic NSCLC with a PD-L1 tumor proportion score (TPS) \geq 1%: Open-label, phase 3 KEYNOTE-042 study. G. Lopes. Sunday, June 3. 3:10-3:25 p.m. CT. Location: Hall B1.

Oral Presentations

- Abstract #4062 Oral Session: Pembrolizumab (pembro) vs paclitaxel (PTX) for previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer: Phase 3 KEYNOTE-061 trial. C. Fuchs. Monday, June 4. 5:24-5:36 p.m. CT. Location: Arie Crown Theater.
- Abstract #4500 Oral Session: Pembrolizumab monotherapy as first-line therapy in advanced clear cell renal cell carcinoma (accRCC): Results from cohort A of KEYNOTE-427. D. McDermott. Sunday, June 3. 8-8:12 a.m. CT. Location: Arie Crown Theater.
- Abstract #5003 Oral Session: Olaparib combined with abiraterone in patients (pts) with metastatic castration-

resistant prostate cancer (mCRPC): A randomized phase II trial. N. Clarke. Monday, June 4. 4-4:12 p.m. CT. Location: Hall D1.

- Abstract #5007 Oral Session: KEYNOTE-199: Pembrolizumab (pembro) for docetaxel-refractory metastatic castration-resistant prostate cancer (mCRPC). J. De Bono. Monday, June 4. 5:12-5:24 p.m. CT. Location: Hall D1.
- Abstract #8506 Oral Session: Phase 2 study of pembrolizumab in advanced small-cell lung cancer (SCLC): KEYNOTE-158. H. Chung. Monday, June 4. 10-10:12 a.m. CT. Location: Hall B1.
- Abstract #9503 Oral Session: 4-year survival and outcomes after cessation of pembrolizumab (pembro) after 2-years in patients (pts) with ipilimumab (ipi)-naive advanced melanoma in KEYNOTE-006. G. Long. Monday, June 4. 9-9:12 a.m. CT. Location: Arie Crown Theater.
- Abstract #9506 Oral Session: Durable tumor regression and overall survival (OS) in patients with advanced Merkel cell carcinoma (aMCC) receiving pembrolizumab as first-line therapy. P. Nghiem. Monday, June 4. 10-10:12 a.m. CT. Location: Arie Crown Theater.
- Abstract #10503 Oral Session: SPRINT: Phase II study of the MEK 1/2 inhibitor selumetinib (AZD6244, ARRY-142886) in children with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN). A. Gross. Saturday, June 2. 4-4:12 p.m. CT. Location: S504.

Clinical Symposium Presentations

- Abstract #105 Clinical Science Symposium: Phase 3 study of carboplatin-paclitaxel/nab-paclitaxel (Chemo) with or without pembrolizumab (Pembro) for patients (Pts) with metastatic squamous (Sq) non-small cell lung cancer (NSCLC). L. Paz-Ares. Sunday, June 3. 10:09-10:21 a.m. CT. Location: Hall D1.
- Abstract #106 Clinical Science Symposium: TOPACIO/KEYNOTE-162 (NCT02657889): A phase 1/2 study of niraparib + pembrolizumab in patients (pts) with advanced triple-negative breast cancer or recurrent ovarian cancer (ROC)—Results from ROC cohort. P. Konstantinopoulos. Sunday, June 3. 10:21-10:33 a.m. CT. Location: Hall D1.
- Abstract #108 Clinical Science Symposium: Epacadostat (E) plus pembrolizumab (P) versus pembrolizumab alone in patients (pts) with unresectable or metastatic melanoma: Results of the phase 3 ECHO-301/KEYNOTE-252 study. G. Long. Sunday, June 3. 10:33-10:45 a.m. CT. Location: Hall D1.
- Abstract #1011 Clinical Science Symposium: TOPACIO/KEYNOTE-162: Niraparib + pembrolizumab in patients (pts) with metastatic triple-negative breast cancer (TNBC), a phase 2 trial. S. Vinayak. Monday, June 4. 3:36-3:48 p.m. CT. Location: Hall D2.
- Abstract #5511 Clinical Science Symposium: Antitumor activity and safety of pembrolizumab in patients with advanced recurrent ovarian cancer: Interim results from the phase 2 KEYNOTE-100 study. U. Matulonis. Sunday, June 3. 10:21-10:33 a.m. CT. Location: S406.

For more information, including a complete list of abstract titles and presentation dates and times for Merck's oncology portfolio, please visit the ASCO website at <https://iplanner.asco.org/am2018>.

About KEYTRUDA® (pembrolizumab) Injection 100mg

KEYTRUDA is an anti-PD-1 therapy that works by increasing the ability of the body's immune system to help detect and fight tumor cells. KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumor cells and healthy cells.

Merck has the industry's largest immuno-oncology clinical research program, which currently involves more than 750 trials studying KEYTRUDA across a wide variety of cancers and treatment settings. The KEYTRUDA clinical program seeks to understand the role of KEYTRUDA across cancers and the factors that may predict a patient's likelihood of benefitting from treatment with KEYTRUDA, including exploring several different biomarkers.

KEYTRUDA Indications and Dosing

Melanoma

KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity.

Lung Cancer

KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS) $\geq 50\%$] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA, as a single agent, is also indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS $\geq 1\%$) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA (pembrolizumab).

KEYTRUDA, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

In metastatic NSCLC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

When administering KEYTRUDA in combination with chemotherapy, KEYTRUDA should be administered prior to chemotherapy when given on the same day. See also the Prescribing Information for pemetrexed and carboplatin.

Head and Neck Cancer

KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy. 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. In HNSCC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Classical Hodgkin Lymphoma

KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after three or more prior lines of therapy. 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. In adults with cHL, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression. In pediatric patients with cHL, KEYTRUDA (pembrolizumab) is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Urothelial Carcinoma

KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-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 the confirmatory trials.

KEYTRUDA is also indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

In locally advanced or metastatic urothelial carcinoma, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Microsatellite Instability-High (MSI-H) Cancer

KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or colorectal cancer that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan.

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. The safety and effectiveness of KEYTRUDA in pediatric patients with MSI-H central nervous system cancers have not been established.

In adult patients with MSI-H cancer, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. In children with MSI-H cancer, KEYTRUDA is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Gastric Cancer

KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy. 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. The recommended dose of KEYTRUDA is 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Selected Important Safety Information for KEYTRUDA (pembrolizumab)

KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 94 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 1 (0.8%), 2 (1.3%), 3 (0.9%), 4 (0.3%), and 5 (0.1%) pneumonitis, and occurred more frequently in patients with a history of prior thoracic radiation (6.9%) compared to those without (2.9%). Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected pneumonitis with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

KEYTRUDA can cause immune-mediated colitis. Colitis occurred in 48 (1.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.4%), 3 (1.1%), and 4 (<0.1%) colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

KEYTRUDA can cause immune-mediated hepatitis. Hepatitis occurred in 19 (0.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.4%), and 4 (<0.1%) hepatitis. Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

KEYTRUDA can cause hypophysitis. Hypophysitis occurred in 17 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.2%), 3 (0.3%), and 4 (<0.1%) hypophysitis. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids and hormone replacement as clinically indicated. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3 or 4 hypophysitis.

KEYTRUDA can cause thyroid disorders, including hyperthyroidism, hypothyroidism, and thyroiditis. Hyperthyroidism occurred in 96 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.8%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 237 (8.5%) of 2799 patients receiving KEYTRUDA, including Grade 2 (6.2%) and 3 (0.1%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in patients with HNSCC, occurring in 28 (15%) of 192 patients with HNSCC, including Grade 3 (0.5%) hypothyroidism. Thyroiditis occurred in 16 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.3%) thyroiditis. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer replacement hormones for hypothyroidism and manage hyperthyroidism with thionamides and beta-blockers as appropriate. Withhold or discontinue KEYTRUDA for Grade 3 or 4 hyperthyroidism.

KEYTRUDA can cause type 1 diabetes mellitus, including diabetic ketoacidosis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer antihyperglycemics in patients with severe hyperglycemia.

KEYTRUDA can cause immune-mediated nephritis. Nephritis occurred in 9 (0.3%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.1%), and 4 (<0.1%) nephritis. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

Immune-mediated rashes, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) (some cases with fatal outcome), exfoliative dermatitis, and bullous pemphigoid, can occur. Monitor patients for suspected severe skin reactions and based on the severity of the adverse reaction, withhold or permanently discontinue KEYTRUDA and administer corticosteroids. For signs or symptoms of SJS or TEN, withhold KEYTRUDA and refer the patient for specialized care for assessment and treatment. If SJS or TEN is confirmed, permanently discontinue KEYTRUDA.

KEYTRUDA can cause other clinically important immune-mediated adverse reactions. These immune-mediated reactions may occur in any organ system. For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold KEYTRUDA and administer corticosteroids. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Based on limited data from clinical studies in patients whose immune-related adverse reactions could not be controlled with corticosteroid use, administration of other systemic immunosuppressants can be considered. Resume KEYTRUDA when the adverse reaction remains at Grade 1 or less following corticosteroid taper. Permanently discontinue KEYTRUDA for any Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

The following clinically significant immune-mediated adverse reactions occurred in less than 1% (unless otherwise indicated) of 2799 patients: arthritis (1.5%), uveitis, myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, and partial seizures arising in a patient with inflammatory foci in brain parenchyma. In addition, myelitis and myocarditis were reported in other clinical trials, including classical Hodgkin lymphoma, and postmarketing use.

Solid organ transplant rejection has been reported in postmarketing use of KEYTRUDA. Treatment with KEYTRUDA may increase the risk of rejection in solid organ transplant recipients. Consider the benefit of treatment with KEYTRUDA vs the risk of possible organ rejection in these patients.

KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for signs and symptoms of infusion-related reactions, including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Immune-mediated complications, including fatal events, occurred in patients who underwent allogeneic hematopoietic stem cell transplantation (HSCT) after being treated with KEYTRUDA. Of 23 patients with cHL who proceeded to allogeneic HSCT after treatment with KEYTRUDA on any trial, 6 patients (26%) developed graft-versus-host disease (GVHD), one of which was fatal, and 2 patients (9%) developed severe hepatic veno-occlusive disease

(VOD) after reduced-intensity conditioning, one of which was fatal. Cases of fatal hyperacute GVHD after allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor–blocking antibody before transplantation.

These complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT. Follow patients closely for early evidence of transplant-related complications such as hyperacute GVHD, severe (Grade 3 to 4) acute GVHD, steroid-requiring febrile syndrome, hepatic VOD, and other immune-mediated adverse reactions, and intervene promptly.

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

Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (0.7%), allergic reaction (0.4%), polyneuropathy (0.4%), and cardiac failure (0.4%). Adverse reactions leading to interruption of KEYTRUDA occurred in 21% of patients; the most common ($\geq 1\%$) was diarrhea (2.5%). The most common adverse reactions with KEYTRUDA vs ipilimumab were fatigue (28% vs 28%), diarrhea (26% with KEYTRUDA), rash (24% vs 23%), and nausea (21% with KEYTRUDA). Corresponding incidence rates are listed for ipilimumab only for those adverse reactions that occurred at the same or lower rate than with KEYTRUDA.

In KEYNOTE-010, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 682 patients with metastatic NSCLC. The most common adverse event resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.8%). Adverse reactions leading to interruption of KEYTRUDA occurred in 23% of patients; the most common ($\geq 1\%$) were diarrhea (1%), fatigue (1.3%), pneumonia (1%), liver enzyme elevation (1.2%), decreased appetite (1.3%), and pneumonitis (1%). The most common adverse reactions (occurring in at least 20% of patients and at a higher incidence than with docetaxel) were decreased appetite (25% vs 23%), dyspnea (23% vs 20%), and nausea (20% vs 18%).

In KEYNOTE-021(G1), when KEYTRUDA was administered in combination with carboplatin and pemetrexed (carbo/pem) in advanced nonsquamous NSCLC, KEYTRUDA was discontinued in 10% of 59 patients. The most common adverse reaction resulting in discontinuation of KEYTRUDA ($\geq 2\%$) was acute kidney injury (3.4%). Adverse

reactions leading to interruption of KEYTRUDA occurred in 39% of patients; the most common ($\geq 2\%$) were fatigue (8%), neutrophil count decreased (8%), anemia (5%), dyspnea (3.4%), and pneumonitis (3.4%). The most common adverse reactions ($\geq 20\%$) with KEYTRUDA compared to carbo/pem alone were fatigue (71% vs 50%), nausea (68% vs 56%), constipation (51% vs 37%), rash (42% vs 21%), vomiting (39% vs 27%), dyspnea (39% vs 21%), diarrhea (37% vs 23%), decreased appetite (31% vs 23%), headache (31% vs 16%), cough (24% vs 18%), dizziness (24% vs 16%), insomnia (24% vs 15%), pruritus (24% vs 4.8%), peripheral edema (22% vs 18%), dysgeusia (20% vs 11%), alopecia (20% vs 3.2%), upper respiratory tract infection (20% vs 3.2%), and arthralgia (15% vs 24%). This study was not designed to demonstrate a statistically significant difference in adverse reaction rates for KEYTRUDA as compared to carbo/pem alone for any specified adverse reaction.

In KEYNOTE-012, KEYTRUDA was discontinued due to adverse reactions in 17% of 192 patients with HNSCC. Serious adverse reactions occurred in 45% of patients. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia, dyspnea, confusional state, vomiting, pleural effusion, and respiratory failure. The most common adverse reactions (reported in at least 20% of patients) were fatigue, decreased appetite, and dyspnea. Adverse reactions occurring in patients with HNSCC were generally similar to those occurring in patients with melanoma or NSCLC, with the exception of increased incidences of facial edema (10% all Grades; 2.1% Grades 3 or 4) and new or worsening hypothyroidism.

In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL, and treatment was interrupted due to adverse reactions in 26% of patients. Fifteen percent (15%) of patients had an adverse reaction requiring systemic corticosteroid therapy. Serious adverse reactions occurred in 16% of patients. The most frequent serious adverse reactions ($\geq 1\%$) included pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression; one from GVHD after subsequent allogeneic HSCT and one from septic shock. The most common adverse reactions (occurring in $\geq 20\%$ of patients) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).

In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (in $\geq 20\%$ of patients) were fatigue (38%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%). Eighteen patients (5%) died from causes other than disease progression. Five patients (1.4%) who were treated with KEYTRUDA experienced sepsis which led to death, and 3 patients (0.8%) experienced pneumonia which led to death. Adverse reactions leading to interruption of KEYTRUDA occurred in 22% of patients; the most common ($\geq 1\%$) were liver enzyme increase, diarrhea, urinary tract infection, acute kidney injury, fatigue, joint pain, and pneumonia. Serious adverse reactions occurred in 42% of patients, the most frequent ($\geq 2\%$) of which were urinary tract infection, hematuria, acute kidney injury, pneumonia, and urosepsis.

In KEYNOTE-045, KEYTRUDA was discontinued due to adverse reactions in 8% of 266 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.9%). Adverse reactions leading to interruption of KEYTRUDA occurred in 20% of patients; the most common ($\geq 1\%$) were urinary tract infection (1.5%), diarrhea (1.5%), and colitis (1.1%). The most common adverse reactions ($\geq 20\%$) in patients who received KEYTRUDA vs those who received chemotherapy were fatigue (38% vs 56%), musculoskeletal pain (32% vs 27%), pruritus (23% vs 6%), decreased appetite (21% vs 21%), nausea (21% vs 29%), and rash (20% vs 13%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients, the most frequent ($\geq 2\%$) of which were urinary tract infection, pneumonia, anemia, and pneumonitis.

It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA and for 4 months after the final dose.

There is limited experience in pediatric patients. In a study, 40 pediatric patients (16 children aged 2 years to younger than 12 years and 24 adolescents aged 12 years to 18 years) with advanced melanoma, lymphoma, or PD-L1-positive advanced, relapsed, or refractory solid tumors were administered KEYTRUDA 2 mg/kg every 3 weeks. Patients received KEYTRUDA for a median of 3 doses (range 1–17 doses), with 34 patients (85%) receiving KEYTRUDA for 2 doses or more. The safety profile in these pediatric patients was similar to that seen in adults treated with KEYTRUDA. Toxicities that occurred at a higher rate ($\geq 15\%$ difference) in these patients when compared to adults under 65 years of age were fatigue (45%), vomiting (38%), abdominal pain (28%), hypertransaminasemia (28%), and hyponatremia (18%).

About Lynparza® (olaparib) tablets, 150mg

Lynparza is a first-in-class poly ADP-ribose polymerase (PARP) inhibitor and the first targeted treatment to potentially exploit tumor DNA damage response (DDR)-pathway deficiencies to preferentially kill cancer cells. Specifically, in vitro studies have shown that Lynparza-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes, resulting in DNA damage and cancer cell death.

Indications for Lynparza in the U.S.

Lynparza is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

For the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm)

advanced ovarian cancer who have been treated with 3 or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

In patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have previously been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine treatment. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

Important Safety Information for Lynparza

Contraindications

There are no contraindications for Lynparza.

Warnings and Precautions

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in <1.5% of patients exposed to Lynparza monotherapy, and the majority of events had a fatal outcome. The duration of therapy in patients who developed secondary MDS/AML varied from <6 months to >2 years. All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy, and some also had a history of more than one primary malignancy or of bone marrow dysplasia.

Do not start Lynparza until patients have recovered from hematological toxicity caused by previous chemotherapy (\leq Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt Lynparza and monitor blood count weekly until recovery.

If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. Discontinue Lynparza (olaparib) if MDS/AML is confirmed.

Pneumonitis: Occurred in <1% of patients exposed to Lynparza, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt Lynparza treatment and initiate prompt investigation. Discontinue Lynparza if pneumonitis is confirmed and treat patient appropriately.

Embryo-Fetal Toxicity: Based on its mechanism of action and findings in animals, Lynparza can cause fetal harm. A pregnancy test is recommended for females of reproductive potential prior to initiating treatment.

Females

Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months following the last dose.

Males

Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of Lynparza and to not donate sperm during this time.

Adverse Reactions—Maintenance Setting

Most common adverse reactions (Grades 1-4) in $\geq 20\%$ of patients in clinical trials of Lynparza in the **maintenance setting** for **SOLO-2**: nausea (76%), fatigue (including asthenia) (66%), anemia (44%), vomiting (37%), nasopharyngitis/upper respiratory tract infection (URI)/influenza (36%), diarrhea (33%), arthralgia/myalgia (30%), dysgeusia (27%), headache (26%), decreased appetite (22%), and stomatitis (20%).

Study 19: nausea (71%), fatigue (including asthenia) (63%), vomiting (35%), diarrhea (28%), anemia (23%), respiratory tract infection (22%), constipation (22%), headache (21%), and decreased appetite (21%).

Most common laboratory abnormalities (Grades 1-4) in $\geq 25\%$ of patients in clinical trials of Lynparza in the **maintenance setting (SOLO-2/Study 19)** were: increase in mean corpuscular volume (89%/82%), decrease in hemoglobin (83%/82%), decrease in leukocytes (69%/58%), decrease in lymphocytes (67%/52%), decrease in absolute neutrophil count (51%/47%), increase in serum creatinine (44%/45%), and decrease in platelets (42%/36%).

Adverse Reactions—Advanced gBRCAm Ovarian Cancer

Most common adverse reactions (Grades 1-4) in $\geq 20\%$ of patients in clinical trials of Lynparza for **advanced gBRCAm ovarian cancer after 3 or more lines of chemotherapy** (pooled from 6 studies) were: fatigue (including asthenia) (66%), nausea (64%), vomiting (43%), anemia (34%), diarrhea (31%), nasopharyngitis/upper respiratory tract infection (URI) (26%), dyspepsia (25%), myalgia (22%), decreased appetite (22%), and arthralgia/musculoskeletal pain (21%).

Most common laboratory abnormalities (Grades 1-4) in $\geq 25\%$ of patients in clinical trials of Lynparza for **advanced gBRCAm ovarian cancer** (pooled from 6 studies) were: decrease in hemoglobin (90%), increase in mean corpuscular volume (57%), decrease in lymphocytes (56%), increase in serum creatinine (30%), decrease in platelets (30%), and decrease in absolute neutrophil count (25%).

Adverse Reactions—gBRCAm, HER2-Negative Breast Cancer

Most common adverse reactions (Grades 1-4) in $\geq 20\%$ of patients in **OlympiAD** were: nausea (58%), anemia (40%), fatigue (including asthenia) (37%), vomiting (30%), neutropenia (27%), respiratory tract infection (27%), leukopenia (25%), diarrhea (21%), and headache (20%).

Most common laboratory abnormalities (Grades 1-4) in $\geq 25\%$ of patients in **OlympiAD** were: decrease in hemoglobin (82%), decrease in lymphocytes (73%), decrease in leukocytes (71%), increase in mean corpuscular volume (71%), decrease in absolute neutrophil count (46%), and decrease in platelets (33%).

Drug Interactions

Anticancer Agents: Clinical studies of Lynparza in combination with other myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

CYP3A Inhibitors: Avoid concomitant use of strong or moderate CYP3A inhibitors. If a strong or moderate CYP3A inhibitor must be co-administered, reduce the dose of Lynparza. Advise patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during Lynparza treatment.

CYP3A Inducers: Avoid concomitant use of strong or moderate CYP3A inducers when using Lynparza (olaparib). If a moderate inducer cannot be avoided, there is a potential for decreased efficacy of Lynparza.

Use in Specific Populations

Lactation: No data are available regarding the presence of olaparib in human milk, its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infant, advise a lactating woman not to breastfeed during treatment with Lynparza and for 1 month after receiving the final dose.

Pediatric Use: The safety and efficacy of Lynparza have not been established in pediatric patients.

Hepatic Impairment: No adjustment to the starting dose is required in patients with mild hepatic impairment (Child-Pugh classification A). There are no data in patients with moderate or severe hepatic impairment.

Renal Impairment: No adjustment to the starting dose is necessary in patients with mild renal impairment (CLcr=51-80 mL/min). In patients with moderate renal impairment (CLcr=31-50 mL/min), reduce the dose to 200 mg twice daily. There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤30 mL/min).

Dosing and Administration

To avoid substitution errors and overdose, **do not substitute Lynparza tablets with Lynparza capsules** on a milligram-to-milligram basis due to differences in the dosing and bioavailability of each formulation.

Recommended tablet dose is 300 mg, taken orally twice daily, with or without food. Continue treatment until disease progression or unacceptable toxicity. For adverse reactions, consider dose interruption or dose reduction.

About LENVIMA® (lenvatinib)

LENVIMA® (lenvatinib) is a kinase inhibitor that is indicated for:

- Differentiated Thyroid Cancer (DTC): single agent for patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory DTC.
- Renal Cell Cancer (RCC): in combination with everolimus for patients with advanced RCC following one prior anti-angiogenic therapy.

Lenvatinib, discovered and developed by Eisai, is a receptor tyrosine kinase (RTK) inhibitor that inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4). Lenvatinib also inhibits other RTKs that have been implicated in pathogenic angiogenesis, tumor growth, and cancer progression in addition to their normal cellular functions, including fibroblast growth factor (FGF) receptors FGFR1-4; the platelet derived growth factor receptor alpha (PDGFR α), KIT, and RET

Important Safety Information

Warnings and Precautions

- In DTC, hypertension was reported in 73% of patients on LENVIMA vs 16% with placebo (44% vs 4% grade ≥3). In RCC, hypertension was reported in 42% of patients on LENVIMA + everolimus vs 10% with everolimus alone (13% vs 2% grade 3). Serious complications of poorly controlled hypertension, including aortic dissection, have been reported. Systolic blood pressure ≥160 mmHg occurred in 29% of patients, and 21% of patients had a diastolic blood pressure ≥100 mmHg in the LENVIMA + everolimus-treated group. Blood pressure should be controlled prior to treatment and monitored throughout. Withhold dose for grade 3 hypertension despite

optimal antihypertensive therapy; resume at reduced dose when controlled at grade ≤ 2 . Discontinue for life-threatening hypertension

- In DTC, cardiac dysfunction was reported in 7% of patients on LENVIMA vs 2% with placebo (2% vs 0% grade ≥ 3). In RCC, decreased ejection fraction and cardiac failure were reported in 10% of patients on LENVIMA + everolimus vs 6% with everolimus alone (3% vs 2% grade 3). Monitor for signs/symptoms of cardiac decompensation. Withhold LENVIMA for development of grade 3 cardiac dysfunction until improvement to grade 0, 1, or baseline. Resume at reduced dose or discontinue based on severity and persistence of cardiac dysfunction. Discontinue for grade 4 cardiac dysfunction
- In DTC, arterial thromboembolic events were reported in 5% of patients on LENVIMA vs 2% with placebo (3% vs 1% grade ≥ 3). In RCC, arterial thromboembolic events were reported in 2% of patients on LENVIMA + everolimus vs 6% with everolimus alone (2% vs 4% grade ≥ 3). Discontinue following an arterial thrombotic event. The safety of resuming LENVIMA after an arterial thromboembolic event has not been established, and LENVIMA has not been studied in patients who have had an arterial thromboembolic event within the previous 6 months
- Across clinical studies in which 1,160 patients received LENVIMA monotherapy, hepatic failure (including fatal events) was reported in 3 patients and acute hepatitis in 1 patient. In DTC, ALT and AST increases (grade ≥ 3) occurred in 4% and 5% of patients on LENVIMA, respectively, vs 0% with placebo. In RCC, ALT and AST increases (grade ≥ 3) occurred in 3% of patients on LENVIMA + everolimus vs 2% and 0% with everolimus alone, respectively. Monitor liver function before initiation, then every 2 weeks for the first 2 months, and at least monthly thereafter during treatment. Withhold dose for liver impairment grade ≥ 3 until resolved to grade 0, 1, or baseline. Resume at reduced dose or discontinue based on severity/persistence of hepatotoxicity. Discontinue for hepatic failure
- In DTC, proteinuria was reported in 34% of patients on LENVIMA vs 3% with placebo (11% vs 0% grade 3). In RCC, proteinuria was reported in 31% of patients on LENVIMA + everolimus vs 14% with everolimus alone (8% vs 2% grade 3). Monitor for proteinuria before and during treatment. Withhold dose for proteinuria ≥ 2 g/24 h. Resume at reduced dose when proteinuria is < 2 g/24 h. Discontinue for nephrotic syndrome
- In RCC, diarrhea was reported in 81% of patients on LENVIMA + everolimus vs 34% with everolimus alone (19% vs 2% grade ≥ 3). Initiate prompt medical management for the development of diarrhea. Monitor for dehydration. Withhold dose for diarrhea grade ≥ 3 . Resume at a reduced dose when diarrhea resolves to grade 1 or baseline. Permanently discontinue LENVIMA for grade 4 diarrhea despite medical management
- In DTC, events of renal impairment were reported in 14% of patients on LENVIMA vs 2% with placebo (3% vs 1% grade ≥ 3). In RCC, events of renal impairment were reported in 18% of patients on LENVIMA + everolimus vs 12% with everolimus alone (10% vs 2% grade ≥ 3). Withhold LENVIMA for grade 3 or 4 renal failure/impairment. Resume at reduced dose or discontinue, depending on severity/persistence of renal impairment. Active management of diarrhea and any other gastrointestinal (GI) symptoms should be initiated for grade 1 events

- In DTC, events of GI perforation or fistula were reported in 2% of patients on LENVIMA vs 0.8% with placebo. In RCC, events of GI perforation, abscess, or fistula (grade ≥ 3) were reported in 2% of patients on LENVIMA + everolimus vs 0% with everolimus alone. Discontinue in patients who develop GI perforation or life-threatening fistula
- In DTC, QT/QTc interval prolongation was reported in 9% of patients on LENVIMA vs 2% with placebo (2% vs 0% >500 ms). In RCC, QTc interval increases >60 ms were reported in 11% of patients on LENVIMA + everolimus (6% >500 ms) vs 0% with everolimus alone. Monitor electrocardiograms in patients with congenital long QT syndrome, congestive heart failure, bradyarrhythmias, or patients taking drugs known to prolong the QT interval. Monitor and correct electrolyte abnormalities in all patients. Withhold dose for QTc interval prolongation >500 ms. Resume at reduced dose when QTc prolongation resolves to baseline
- In DTC, hypocalcemia (grade ≥ 3) was reported in 9% of patients on LENVIMA vs 2% with placebo. In RCC, hypocalcemia (grade ≥ 3) was reported in 6% of patients on LENVIMA + everolimus vs 2% with everolimus alone. Monitor blood calcium levels at least monthly and replace calcium as necessary. Interrupt and adjust LENVIMA as necessary
- Across clinical studies in which 1,160 patients received LENVIMA monotherapy, reversible posterior leukoencephalopathy syndrome (RPLS) was reported in 4 patients. Withhold LENVIMA for RPLS until fully resolved. Resume at reduced dose or discontinue based on the severity and persistence of neurologic symptoms
- Across clinical studies in which 1,160 patients received LENVIMA monotherapy, hemorrhage (grade ≥ 3) was reported in 2% of patients. In DTC, hemorrhagic events occurred in 35% of patients on LENVIMA vs 18% with placebo (2% vs 3% grade ≥ 3). There was 1 fatal intracranial hemorrhage case among 16 patients who received LENVIMA and had central nervous system metastases at baseline. The most frequently reported hemorrhagic event was epistaxis (11% grade 1, 1% grade 2). Discontinuation due to hemorrhagic events occurred in 1% of patients on LENVIMA. In RCC, hemorrhagic events occurred in 34% of patients on LENVIMA + everolimus vs 26% with everolimus alone (8% vs 2% grade ≥ 3). The most frequently reported hemorrhagic event was epistaxis (23% for LENVIMA + everolimus vs 24% with everolimus alone). There was 1 fatal cerebral hemorrhage case. Discontinuation due to hemorrhagic events occurred in 3% of patients on LENVIMA + everolimus. Consider the risk of severe or fatal hemorrhage associated with tumor invasion/infiltration of major blood vessels (eg, carotid artery). Withhold LENVIMA for the development of grade 3 hemorrhage until resolved to grade 0 or 1. Resume at reduced dose or discontinue based on severity/persistence of hemorrhage. Discontinue for grade 4 hemorrhage
- In DTC patients with normal baseline thyroid-stimulating hormone (TSH), elevation of TSH level above 0.5 mU/L was observed postbaseline in 57% of patients on LENVIMA vs 14% with placebo. In RCC, grade 1 or 2 hypothyroidism occurred in 24% of patients on LENVIMA + everolimus vs 2% with everolimus alone. In RCC patients with normal or low TSH at baseline, elevation of TSH was observed postbaseline in 60% of patients on LENVIMA + everolimus vs 3% with everolimus alone. Monitor thyroid function before initiation of and at

least monthly throughout treatment. Treat hypothyroidism according to standard medical practice to maintain a euthyroid state

- Impaired wound healing, including fistula formation, has been reported in patients receiving LENVIMA. Temporary interruption of LENVIMA therapy should be considered in patients undergoing major surgical procedures
- LENVIMA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with LENVIMA and for at least 2 weeks following completion of therapy

Adverse Reactions

- In DTC, the most common adverse reactions ($\geq 30\%$) observed in LENVIMA-treated patients vs placebo-treated patients were hypertension (73% vs 16%), fatigue (67% vs 35%), diarrhea (67% vs 17%), arthralgia/myalgia (62% vs 28%), decreased appetite (54% vs 18%), weight decrease (51% vs 15%), nausea (47% vs 25%), stomatitis (41% vs 8%), headache (38% vs 11%), vomiting (36% vs 15%), proteinuria (34% vs 3%), palmar-plantar erythrodysesthesia syndrome (32% vs 1%), abdominal pain (31% vs 11%), and dysphonia (31% vs 5%)
- In DTC, adverse reactions led to dose reductions in 68% of patients receiving LENVIMA and in 5% of patients receiving placebo; 18% of patients discontinued LENVIMA and 5% discontinued placebo for adverse reactions. The most common adverse reactions ($\geq 10\%$) resulting in dose reductions of LENVIMA were hypertension (13%), proteinuria (11%), decreased appetite (10%), and diarrhea (10%); the most common adverse reactions ($\geq 1\%$) resulting in discontinuation of LENVIMA were hypertension (1%) and asthenia (1%)
- In RCC, the most common adverse reactions ($>30\%$) observed in patients treated with LENVIMA + everolimus vs everolimus alone were diarrhea (81% vs 34%), fatigue (73% vs 40%), arthralgia/myalgia (55% vs 32%), decreased appetite (53% vs 18%), vomiting (48% vs 12%), nausea (45% vs 16%), stomatitis/oral inflammation (44% vs 50%), hypertension/increased blood pressure (42% vs 10%), peripheral edema (42% vs 20%), cough (37% vs 30%), abdominal pain (37% vs 8%), dyspnea/exertional dyspnea (35% vs 28%), rash (35% vs 40%), weight decreased (34% vs 8%), hemorrhagic events (32% vs 26%), and proteinuria/urine protein present (31% vs 14%). The most common serious adverse reactions ($\geq 5\%$) were renal failure (11%), dehydration (10%), anemia (6%), thrombocytopenia (5%), diarrhea (5%), vomiting (5%), and dyspnea (5%)
- In RCC, adverse reactions led to dose reductions or interruption in 89% of patients receiving LENVIMA + everolimus and in 54% of patients receiving everolimus alone. The most common adverse reactions ($\geq 5\%$) resulting in dose reductions in the LENVIMA + everolimus-treated group were diarrhea (21%), fatigue (8%), thrombocytopenia (6%), vomiting (6%), nausea (5%), and proteinuria (5%). Treatment discontinuation due to an adverse reaction occurred in 29% of patients in the LENVIMA + everolimus-treated group and in 12% of patients in the everolimus-treated group

Use in Specific Populations

- Because of the potential for serious adverse reactions in nursing infants, advise women to discontinue breastfeeding during treatment
- LENVIMA may result in reduced fertility in females of reproductive potential and may result in damage to male reproductive tissues, leading to reduced fertility of unknown duration

For more information about LENVIMA, click [here](#) for the full Prescribing Information.

About the AstraZeneca and Merck Strategic Oncology Collaboration

In July 2017, AstraZeneca and Merck (known as MSD outside the United States and Canada) announced a global strategic oncology collaboration to co-develop and co-commercialize Lynparza, the world's first PARP inhibitor, and potential new medicine selumetinib, a MEK inhibitor, for multiple cancer types. The collaboration is based on increasing evidence that PARP and MEK inhibitors can be combined with PD-L1/PD-1 inhibitors for a range of tumor types. Working together, the companies will develop Lynparza and selumetinib in combination with other potential new medicines and as a monotherapy. Independently, the companies will develop Lynparza and selumetinib in combination with their respective PD-L1 and PD-1 medicines.

About the Eisai and Merck Strategic Collaboration

In March 2018, Eisai and Merck, through an affiliate, entered into a strategic collaboration for the worldwide co-development and co-commercialization of LENVIMA® (lenvatinib). Under the agreement, the companies will jointly develop and commercialize LENVIMA, both as monotherapy and in combination with Merck's anti-PD-1 therapy KEYTRUDA® (pembrolizumab). In addition to ongoing clinical studies of the combination, the companies will jointly initiate new clinical studies evaluating the combination to support 11 potential indications in six types of cancer, including bladder cancer endometrial cancer, hepatocellular carcinoma, head and neck cancer, melanoma and non-small cell lung cancer, as well as a basket trial targeting six additional cancer types. The LENVIMA/KEYTRUDA combination is not approved in any cancer types today.

Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck, helping people fight cancer is our passion and supporting accessibility to our cancer medicines is our commitment. Our focus is on pursuing research in immuno-oncology and we are accelerating every step in the journey – from lab to clinic – to potentially bring new hope to people with cancer.

As part of our focus on cancer, Merck is committed to exploring the potential of immuno-oncology with one of the fastest-growing development programs in the industry across more than 30 tumor types. We also continue to

strengthen our immuno-oncology portfolio through strategic acquisitions and are prioritizing the development of several promising immunotherapeutic candidates with the potential to improve the treatment of advanced cancers.

For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.merck.com and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of

new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2017 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

Please see Prescribing Information for KEYTRUDA at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf and Patient Information/Medication Guide for KEYTRUDA at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf.

Please see complete **Prescribing Information** for Lynparza, including Patient Information (Medication Guide).

For more information about Lenvima, click [here](#) for the full Prescribing Information.

Merck

Media:

Pamela Eisele, 267-305-3558

or

Claire Mulhearn, 908-740-6664

or

Investors:

Teri Loxam, 908-740-1986

or

Michael DeCarbo, 908-740-1807