Updated Data for Merck’s KEYTRUDA® (pembrolizumab) in Patients with Advanced Gastric Cancer Across Treatment Settings to Be Presented at ESMO 2017 Congress

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KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced the presentation of data from all three cohorts of the registrational, phase 2 KEYNOTE-059 trial investigating the use of KEYTRUDA® (pembrolizumab), the company’s anti-PD-1 therapy, in patients with advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma, including new data in treatment-naïve patients. Overall, results showed antitumor activity and durability of response with KEYTRUDA across multiple lines of therapy, with higher response rates observed in PD-L1-positive (CPS ≥1) patients:

- In heavily pre-treated patients, KEYTRUDA monotherapy (Cohort 1) showed an overall response rate (ORR) of 12 percent (95% CI, 8-17) in all patients and 16 percent (95% CI, 11-23) in patients with PD-L1 positive tumors.
- In treatment-naïve patients, KEYTRUDA in combination with chemotherapy (Cohort 2) showed an ORR of 60 percent (95% CI, 39-79) in all patients and 69 percent (95% CI, 41-89) in patients with PD-L1 positive tumors.
- In treatment-naïve patients with PD-L1 positive tumors, KEYTRUDA monotherapy (Cohort 3) showed an ORR of 26 percent (95% CI, 12-45).

Results are being presented at the European Society for Medical Oncology (ESMO) 2017 Congress in Madrid, Spain, in an oral presentation on Friday, Sept. 8 from 3:03-3:15 p.m. CEST (Location: Barcelona Auditorium) (Abstract #LBA28_PR).

“Outcomes can vary significantly among patients with gastric or GEJ cancer – across stages of disease and based on a variety of biological and molecular makeups of tumors,” said Charles S. Fuchs, M.D., MPH, lead investigator and director of Yale Cancer Center. “KEYNOTE-059 was designed to provide important insight across various treatment settings, simultaneously, and these results show encouraging activity with pembrolizumab in both previously treated and treatment-naïve patients, particularly in those with high levels of PD-L1 expression.”

“These findings across lines of therapy in gastric and GEJ cancers continue to support the potential for KEYTRUDA, and PD-L1 as a biomarker, in patients with this advanced stage disease,” said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories. “We are encouraged by the responses observed in heavily pre-treated patients and look forward to continued analysis of data in treatment-naïve patients.”

Merck’s broad clinical program encompasses multiple gastrointestinal disorders – such as gastroesophageal cancer and microsatellite instability-high (MSI-H) colorectal cancer – and includes four gastric/GEJ cancer registration-enabling studies and numerous other gastrointestinal cancer studies currently underway.

Data from KEYNOTE-059 Study Cohorts (Abstract #LBA28_PR)

Results presented from KEYNOTE-059 were based on an analysis of efficacy, safety and PD-L1 expression from 315 patients across the study’s three cohorts. Patients were considered PD-L1 positive if they had a PD-L1 combined positive score of one or more (CPS ≥1). Findings showed:

- Cohort 1: KEYTRUDA (pembrolizumab) as monotherapy in patients whose disease progressed on or after two or more prior lines of therapy (n=259). Forty-eight percent of these patients had received three or more lines of prior therapy. The efficacy analysis in all patients, with or without PD-L1 expression, showed an ORR of 12 percent (95% CI, 8-17), with complete responses (CR) in three percent (95% CI, 1-6) and partial responses (PR) in nine percent (95% CI, 6-13) of patients. In patients whose tumors expressed PD-L1 (n=148), the ORR was 16 percent (95% CI, 11-23), with CR in three percent (95% CI, 1-8) and PR in 13 percent (95% CI, 8-19) of patients. In PD-L1 negative patients (n=109), the ORR was six percent (95% CI, 3-13), with CR in three percent (95% CI, 1-8) and PR in four percent (95% CI, 1-9) of patients. Median duration of follow-up was 5.6 months (range: 0.5-24.7). In all patients, 42 percent (n=95) experienced a reduction in target lesion size. Median duration of response was 14.2 months (range: 2.4-19.4+).

In all patients, median progression-free survival (PFS) was two months (95% CI, 2.0-2.1), with a six-month PFS rate of
14.6 percent; the median overall survival (OS) was 5.5 months (95% CI, 4.2-6.5), with a six-month OS rate of 45.7 percent. In patients whose tumors expressed PD-L1, the median PFS was 2.1 months (95% CI, 2.0-2.1), with a six-month PFS rate of 18.2 percent; the median OS in these patients was 5.8 months (95% CI, 4.4-7.8), with a six-month OS rate of 48.4 percent. In PD-L1 negative patients, the median PFS was two months (95% CI, 1.9-2.0), with a six-month PFS rate of 9.9 percent; the median OS was 4.6 months (95% CI, 3.2-6.5), with a six-month OS rate of 42.9 percent.

- **Cohort 2**: KEYTRUDA (pembrolizumab) in combination with chemotherapy in treatment-naïve patients (n=31). The efficacy analysis showed an ORR of 26 percent (95% CI, 12-45), with CR in seven percent (95% CI, 1-21) and PR in 19 percent (95% CI, 8-38) of patients. Median duration of follow-up was 17.5 months (range: 1.7-20.7). Seventy-seven percent of patients (n=24) experienced a reduction in target lesion size. The median duration of response was 9.6 months (range: 2.1-17.8+). The median PFS was 3.3 months (95% CI, 2.0-6.0), with a six-month PFS rate of 34.9 percent; the median OS was 20.7 months (95% CI, 9.2-20.7), with a six-month OS rate of 72.9 percent.

The safety profile of KEYTRUDA was consistent with that observed in previously reported studies. In Cohorts 1, 2 and 3, Grade 3-5 treatment-related adverse events (TRAEs) occurred in 46 (18%), 19 (76%), and 7 (23%) patients, respectively. In Cohort 1, Grade 3-5 TRAEs were anemia (3%), fatigue (2%), and dehydration (1%); TRAEs led to discontinuation in seven patients (3%) and death in two patients (1%). In Cohort 2, Grade 3/4 TRAEs were neutropenia (24%), stomatitis (20%), anemia (8%), decreased platelet count (8%), decreased appetite (8%), and fatigue (8%). TRAEs in Cohort 2 led to discontinuation in three patients (12%); there were no treatment-related deaths. In Cohort 3, Grade 3-5 TRAEs occurred in seven patients (23%); there was one treatment-related death (3%) and no discontinuations due to TRAEs.

In Cohorts 1, 2 and 3, Grade 3 or higher immune-mediated adverse events occurred in 13, four, and three patients, respectively. In Cohort 1, Grade 3 immune-mediated adverse events were colitis (n=3), pneumonitis (n=2), thyroiditis (n=1), and hypothyroidism (n=1); there were no Grade 4-5 immune-mediated adverse events. In Cohort 2, Grade 3 immune-mediated adverse events were palmar-plantar erythrodysesthesia (n=2), nephrotic syndrome (n=1), rash (n=1), and maculopapular rash (n=1); there were no Grade 4-5 immune-mediated adverse events. In Cohort 3, Grade 3 immune-mediated adverse events were colitis (n=1) and rash (n=1); there was one Grade 5 adverse event (pneumonitis).

### About KEYNOTE-059

KEYNOTE-059 is a registrational, phase 2 non-randomized, multi-cohort study (Cohorts 1, 2 and 3) investigating KEYTRUDA (pembrolizumab) in patients with advanced gastric or GEJ adenocarcinoma. Patients in Cohort 1 received KEYTRUDA monotherapy after two or more prior lines of therapy. Patients in Cohort 2 had received no prior therapy and received KEYTRUDA in combination with cisplatin (80 mg/m² Q3W) and 5-fluorouracil (800 mg/m² Q3W) or capecitabine (in Japan only, 1000 mg/m² BID Q3W) as a first-line therapy. Patients in Cohort 3, which only enrolled patients whose tumors were positive for PD-L1, received KEYTRUDA monotherapy as a first-line therapy. In all cohorts, KEYTRUDA was given at 200 mg every three weeks for up to 24 months. The primary endpoints are safety (all cohorts) and ORR using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Key secondary endpoints are ORR and duration of response by RECIST v1.1, PFS, and OS. Data from Cohorts 1 and 2 were further assessed based on PD-L1 expression. Tumors were considered to have positive PD-L1 expression if the combined positive score (CPS) - as examined by tumor and immune cells - was equal to or greater than one.

### About Gastric Cancer

Gastric cancer, also called stomach cancer, is a type of cancer that begins in the stomach and tends to develop slowly over many years. Most gastric cancers are adenocarcinomas, which develop from the cells of the innermost lining (mucosa) of the stomach. Risk factors for gastric cancer include gender, age, ethnicity, geography and infection with *Helicobacter pylori*. Worldwide, gastric cancer is the fifth most common type of cancer and the third leading cause of cancer death. Each year there are approximately 952,000 newly diagnosed cases of gastric cancer resulting in approximately 723,000 deaths worldwide.

### 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. Studies of KEYTRUDA - from the largest immuno-oncology program in the industry with more than 550 trials - include a wide variety of cancers and treatment settings. The KEYTRUDA clinical program seeks to understand factors that predict a patient’s likelihood of benefiting from treatment with KEYTRUDA, including the exploration of several different biomarkers across a broad range of tumors.

### KEYTRUDA (pembrolizumab) 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) ≥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 ≥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.

KEYTRUDA, in combination with pembrolizumab, 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 (pembrolizumab) 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 adult and pediatric 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. In pediatric patients with HNSCC, 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.

**Urothelial Carcinoma**

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 duration 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 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.

**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 pediatric patients 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.

**Selected Important Safety Information for KEYTRUDA® (pembrolizumab)**

KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 94 (3.4%) of 2799
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 (pembrolizumab) 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 (pembrolizumab) and administer corticosteroids. For signs and 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 myocardiitis 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.
Based on its mechanism of action, KEYTRUDA (pembrolizumab) 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 (≥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.

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 pneumonia (1.8%). Adverse reactions leading to interruption of KEYTRUDA occurred in 23% of patients; the most common (≥1%) were diarrhea (1%), fatigue (1.3%), pneumonia (1%), liver enzyme elevation (1.2%), decreased appetite (1.3%), and neutropenia (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%).

When KEYTRUDA was administered in combination with carboplatin and pemetrexed (carbo/pem), KEYTRUDA was discontinued in 10% of 59 patients. The most common adverse reaction resulting in discontinuation of KEYTRUDA (≥2%) was acute kidney injury (3.4%). Adverse reactions leading to interruption of KEYTRUDA occurred in 39% of patients; the most common (≥2%) were fatigue (8%), neutrophil count decreased (8%), anemia (5%), dyspnea (3.4%), and pneumonia (3.4%). The most common adverse reactions (≥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%), diarrhea (39% vs 21%), 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 (pembrolizumab) as compared to carbo/pem alone for any specified adverse reaction.

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.

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 (≥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 ≥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 ≥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 (≥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 (≥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 uterine carcinoma. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA (pembrolizumab) was pneumonia (1.9%). Adverse reactions leading to discontinuation of KEYTRUDA occurred in 20% of patients; the most common (≥1%) were urinary tract infection (1.5%), diarrhea (1.5%), and colitis (1.1%). The most common adverse reactions (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 were occurring in 39% of KEYTRUDA-treated patients, the most frequent (≥2%) of which were urinary tract infection, pneumonia, anemia, and pneumonitis. There is limited experience in pediatric patients. Efficacy for pediatric patients was extrapolated from the results in the adult chL population. In a study of 40 pediatric patients with advanced melanoma, PD-L1–positive advanced, relapsed, or refractory solid tumors or lymphoma, patients were treated with KEYTRUDA for a median of 43 days (range 1-414 days), with 24 patients (60%) receiving treatment for 42 days or more. The safety profile in pediatric patients was similar to that seen in adults treated with KEYTRUDA. Toxicities that occurred at a higher rate (≥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%). 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.
Our 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. We are currently executing an expansive research program evaluating our anti-PD-1 therapy 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 healthcare 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 2016 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).

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