New KEYTRUDA® (pembrolizumab) Data in Advanced Urothelial Cancer Demonstrate Overall Response Rate of 24 Percent in Cisplatin-Ineligible Patients

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Results from Interim Analysis of Phase 2 KEYNOTE-052 Study to be Presented at ESMO 2016 Congress and Highlighted in ESMO Press Program

First Presentation of Data Investigating KEYTRUDA in the Front Line Treatment of Bladder Cancer

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced positive findings from the phase 2 KEYNOTE-052 study investigating the use of KEYTRUDA® (pembrolizumab), the company’s anti-PD-1 therapy, in previously untreated patients with unresectable (inoperable) or metastatic urothelial cancer who are ineligible for cisplatin-based therapy. Data presented at the ESMO 2016 Congress, the annual meeting of the European Society for Medical Oncology, showed an overall response rate (ORR) of 24 percent (n=24/100) (95% CI, 16-34) in the total study population, which included patients with and without PD-L1 expression.

“We have a growing body of evidence of KEYTRUDA’s activity in a range of cancers and treatment settings including the first-line treatment of patients with advanced urothelial cancer who will not tolerate cisplatin-based therapy,” said Dr. Roger Dansey, senior vice president, oncology late-stage development, Merck Research Laboratories.

The KEYTRUDA clinical development program includes more than 30 tumor types in more than 350 clinical studies, including more than 100 trials that combine KEYTRUDA with other cancer treatments. Merck has the largest immuno-oncology clinical development program in bladder cancer with 27 trials involving KEYTRUDA, including four
registration-enabling studies currently underway.

“There have been very few advancements in the treatment of bladder cancer in the past several decades, and patients with urothelial cancer who are ineligible for cisplatin-based therapy are in significant need of new approaches to care,” said Dr. Dean F. Bajorin, study investigator and medical oncologist at Memorial Sloan Kettering Cancer Center. “These data are exciting and demonstrate the potential for an anti-PD-1 therapy, such as pembrolizumab, to address the unmet treatment need that exists today for cisplatin-ineligible patients with this type of urothelial cancer.”

Findings from KEYNOTE-052 are being presented at the ESMO 2016 Congress by Dr. Arjun V. Balar, medical oncologist and assistant professor of medicine at the Perlmutter Cancer Center at NYU Langone Medical Center, on Oct. 8 from 9:30 – 9:45 a.m. CEST (Abstract: # LBA32_PR) and are featured in the official ESMO press program.

**Additional Findings from KEYNOTE-052**

KEYNOTE-052 is an open-label, phase 2 study evaluating KEYTRUDA (pembrolizumab) (200 mg every three weeks) monotherapy as a first-line treatment in an estimated 350 patients with unresectable (inoperable) or metastatic urothelial cancer (a type of bladder cancer) who are ineligible for cisplatin-based therapy. The primary endpoints include ORR in all patients enrolled in the study (total study population) and in patients with PD-L1 positive tumors (expression of one percent or more). Secondary endpoints include duration of response, progression-free survival (PFS), and overall survival (OS). Tumor response was measured according to RECIST (Response Evaluation Criteria in Solid Tumors) v1.1 as assessed by blinded independent central review.

Findings presented at the ESMO 2016 Congress are from the planned interim analysis of the first 100 patients, which was intended to evaluate ORR and determine the PD-L1-high expression cut-point as examined by expression in tumor and immune cells. Forty-five percent of patients (n=45/100) had an ECOG (Eastern Cooperative Oncology Group) Performance Status (PS) score of two, 30 percent (n=30/100) had a PS score of one, and 24 percent (n=24/100) had a PS score of zero.

In the total study population, ORR was 24 percent (n=24/100) (95% CI, 16-34) with a complete response rate of six percent (n=6/100) (95% CI, 2-13). Review of the outcomes based on PD-L1 expression showed that in patients with PD-L1 expression of less than one percent, ORR was 18 percent (n=6/33) (95% CI, 7-36) with a complete response rate of three percent (n=1/33) (95% CI, 0.1-16); in patients with PD-L1 expression greater than or equal to one percent and less than 10 percent, ORR was 15 percent (n=5/33) (95% CI, 5-32) with no complete responses; and, in patients expressing PD-L1 at levels equal to or greater than 10 percent, ORR was 37 percent (n=11/30) (95% CI, 20-56) with a complete response rate of 13 percent (n=4/30) (95% CI, 4-31). Among the 24 percent of patients in the total study population who were responding to treatment, the median duration of response had not been reached.
(range 1.4+ to 9.8+ months), with 83 percent of patients (n=20/24) having responses of six months or longer.

The safety profile of KEYTRUDA (pembrolizumab) was consistent with that observed in previously reported KEYTRUDA studies. The treatment-related adverse events observed in this trial (any grade occurring in five percent or more of patients) were fatigue (n=14), pruritus (n=12), pyrexia (n=8), decreased appetite (n=7), diarrhea (n=7), rash (n=7), chills (n=6), hypothyroidism (n=6), and nausea (n=6). Grade 3-4 treatment-related adverse events observed (occurring in 2 or more patients) were fatigue (n=4), muscle spasms (n=2), decreased appetite (n=1), and diarrhea (n=1). Immune-mediated adverse events of Grade 3-4 were nephritis (n=1) and pneumonitis (n=2). Five patients discontinued due to a treatment-related adverse event; there were no treatment-related deaths.

About Bladder Cancer

Bladder cancer begins when cells in the urinary bladder start to grow uncontrollably. As more cancer cells develop, they can form a tumor and spread to other areas of the body. Urothelial carcinoma, the most common type of bladder cancer, starts in the urothelial cells that line the inside of the bladder. In 2012, approximately 430,000 people worldwide were diagnosed with bladder cancer and 165,000 died from the disease. The incidence of bladder cancer is elevated in North America, Europe, North Africa, the Middle East, Australia and New Zealand.

About KEYTRUDA ® (pembrolizumab)

KEYTRUDA is a humanized monoclonal antibody that works by increasing the ability of the body's immune system to help detect and fight tumor cells. KEYTRUDA 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.

KEYTRUDA is administered as an intravenous infusion over 30 minutes every three weeks for the approved indications. KEYTRUDA for injection is supplied in a 100 mg single use vial.

KEYTRUDA (pembrolizumab) Indications and Dosing

Melanoma

KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma at a dose of 2 mg/kg every three weeks.

Lung Cancer

KEYTRUDA is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose
tumors express PD-L1 as determined by an FDA-approved test with disease progression on or after platinum-containing chemotherapy, at a dose of 2 mg/kg every three weeks. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA. This indication is approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

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 at a fixed dose of 200 mg every three weeks. 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.

Selected Important Safety Information for KEYTRUDA® (pembrolizumab)

Immune-mediated pneumonitis, including fatal cases, occurred in patients receiving KEYTRUDA. Pneumonitis occurred in 32 (2.0%) of 1567 patients with melanoma, including Grade 1 (0.8%), 2 (0.8%), and 3 (0.4%) pneumonitis. Pneumonitis occurred in 19 (3.5%) of 550 patients with NSCLC, including Grade 2 (1.1%), 3 (1.3%), 4 (0.4%), or 5 (0.2%) pneumonitis and more frequently in patients with a history of asthma/chronic obstructive pulmonary disease (5.4%) or prior thoracic radiation (6.0%). 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 (pembrolizumab) for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

Immune-mediated colitis occurred in 31 (2%) of 1567 patients with melanoma, including Grade 2 (0.5%), 3 (1.1%), and 4 (0.1%) colitis. Immune-mediated colitis occurred in 4 (0.7%) of 550 patients with NSCLC, including Grade 2 (0.2%) or 3 (0.4%) 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.

Immune-mediated hepatitis occurred in patients receiving KEYTRUDA. Hepatitis occurred in 16 (1%) of 1567 patients with melanoma, including Grade 2 (0.1%), 3 (0.7%), 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.
Hypophysitis occurred in 13 (0.8%) of 1567 patients with melanoma, including Grade 2 (0.3%), 3 (0.3%), and 4 (0.1%) hypophysitis. Hypophysitis occurred in 1 (0.2%) of 550 patients with NSCLC, which was Grade 3 in severity. 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.

Hyperthyroidism occurred in 51 (3.3%) of 1567 patients with melanoma, including Grade 2 (0.6%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 127 (8.1%) of 1567 patients with melanoma, including Grade 3 (0.1%) hypothyroidism. Hyperthyroidism occurred in 10 (1.8%) of 550 patients with NSCLC, including Grade 2 (0.7%) or 3 (0.3%) hyperthyroidism. Hypothyroidism occurred in 38 (6.9%) of 550 patients with NSCLC, including Grade 2 (5.5%) or 3 (0.2%) hypothyroidism. New or worsening hypothyroidism occurred in 28 (14.6%) of 192 patients with HNSCC, including Grade 3 (0.5%) hypothyroidism. Thyroid disorders can occur at any time during treatment. 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.

Type 1 diabetes mellitus, including diabetic ketoacidosis, occurred in 3 (0.1%) of 2117 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer anti-hyperglycemics in patients with severe hyperglycemia.

Immune-mediated nephritis occurred in patients receiving KEYTRUDA (pembrolizumab). Nephritis occurred in 7 (0.4%) of 1567 patients with melanoma including, Grade 2 (0.2%), 3 (0.2%), 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 greater nephritis.

Other clinically important immune-mediated adverse reactions can occur. 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 1567 patients with melanoma: arthritis (1.6%), exfoliative dermatitis, bullous pemphigoid, uveitis,
myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, and partial seizures arising in a patient with inflammatory foci in brain parenchyma. The following clinically significant, immune-mediated adverse reactions occurred in less than 1% of 550 patients with NSCLC: rash, vasculitis, hemolytic anemia, serum sickness, and myasthenia gravis.

Severe and life-threatening infusion-related reactions have been reported in 3 (0.1%) of 2117 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.

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 (pembrolizumab) 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.

In KEYNOTE-002, KEYTRUDA was discontinued due to adverse reactions in 12% of 357 patients with advanced melanoma; the most common (≥1%) were general physical health deterioration (1%), asthenia (1%), dyspnea (1%), pneumonitis (1%), and generalized edema (1%). Adverse reactions leading to interruption of KEYTRUDA occurred in 14% of patients; the most common (≥1%) were dyspnea (1%), diarrhea (1%), and maculopapular rash (1%). The most common adverse reactions with KEYTRUDA vs chemotherapy were fatigue (43% with KEYTRUDA), pruritus (28% vs 8%), rash (24% vs 8%), constipation (22% vs 20%), nausea (22% with KEYTRUDA), diarrhea (20% vs 20%), and decreased appetite (20% with KEYTRUDA). Corresponding incidence rates are listed for chemotherapy only for those adverse reactions that occurred at the same or lower rate than with KEYTRUDA.

KEYTRUDA was discontinued due to adverse reactions in 14% of 550 patients with NSCLC. Serious adverse reactions occurred in 38% of patients. The most frequent serious adverse reactions reported in at least 2% of patients were pleural effusion, pneumonia, dyspnea, pulmonary embolism, and pneumonitis. The most common adverse reactions (reported in at least 20% of patients) were fatigue (44%), cough (29%), decreased appetite (25%), and
dyspnea (23%).

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 (46%), decreased appetite (22%), and dyspnea (20%).

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.

Safety and effectiveness of KEYTRUDA have not been established in pediatric patients.

**Our Focus on Cancer**

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck Oncology, 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 that includes more than 350 clinical trials 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](http://www.merck.com/clinicaltrials).

**About Merck**

For 125 years, Merck has been a global health care leader working to help the world be well. Merck is known as MSD outside the United States and Canada. 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. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on Twitter, Facebook, 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 2015 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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