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Two Major Studies to Be Presented at ESMO 2016 Congress Presidential Symposium Demonstrate Potential of Merck's KEYTRUDA® (pembrolizumab) for the First-Line Treatment of Metastatic Non-Small Cell Lung Cancer in a Broad Range of Patients

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KEYNOTE-024, Published in The New England Journal of Medicine, Showed KEYTRUDA as Monotherapy Demonstrated Superior Progression-Free and Overall Survival Compared to Chemotherapy as First-Line Treatment in Patients with High Levels of PD-L1 Expression

KEYNOTE-021, Cohort G, Published in The Lancet Oncology, Showed KEYTRUDA in Combination with Chemotherapy Demonstrated Superior Efficacy Compared to Chemotherapy Alone as First-Line Treatment; Trial Enrolled Patients Regardless of PD-L1 Expression

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced results from two major studies of KEYTRUDA® (pembrolizumab), the company's anti-PD-1 therapy, in the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) at the ESMO 2016 Congress, the annual meeting of the European Society for Medical Oncology:

- In KEYNOTE-024, which evaluated squamous and non-squamous NSCLC patients whose tumors expressed high levels of PD-L1 (tumor proportion score, or TPS, of 50 percent or more), KEYTRUDA provided a 50 percent reduction in the risk of disease progression or death and a 40 percent reduction in the risk of death compared to platinum doublet, the current standard of care. These data were also published today in *The New England Journal of Medicine*. Based upon the results observed from KEYNOTE-024, to date KEYTRUDA is the only anti-PD-1 to demonstrate superior progression-free survival (PFS) and overall survival (OS) compared to chemotherapy for the first-line treatment of both squamous and non-squamous NSCLC in patients whose tumors express high levels of PD-L1 and do not express EGFR or ALK genetic aberrations.
- In KEYNOTE-021, Cohort G, which included patients with metastatic non-squamous NSCLC regardless of PD-L1 expression level, KEYTRUDA (pembrolizumab) plus chemotherapy (carboplatin plus pemetrexed) achieved a 55 percent objective response rate (ORR) compared to 29 percent for chemotherapy alone, the standard of care, and reduced the risk of disease progression or death by 47 percent. To date, KEYTRUDA is the only anti-PD-1 therapy to demonstrate superior efficacy in combination with chemotherapy compared to chemotherapy alone in patients receiving first-line treatment. These data were published today in *The Lancet Oncology*.

"Chemotherapy has been the standard treatment for most patients with advanced non-small cell lung cancer for decades, but survival rates remain low," said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. "Our new data suggest that KEYTRUDA treatment can offer meaningful improvement over chemotherapy in a broad array of patients. In this sense, these studies may represent a turning point in worldwide efforts to control lung cancer. We sincerely thank the patients and the clinical investigators for their participation in our studies. Together we are working to improve the health of more and more patients with cancer."

Merck has submitted KEYNOTE-024 data to regulatory agencies in the United States, Europe, and Japan. The U.S. Food and Drug Administration has granted Breakthrough Therapy Designation and Priority Review, with a PDUFA, or target action, date of Dec. 24, 2016.

Merck is currently advancing multiple registration-enabling studies in NSCLC with KEYTRUDA as monotherapy and in combination, including the combination of KEYTRUDA plus a platinum/pemetrexed-based chemotherapy regimen in patients with previously untreated, non-squamous NSCLC in the ongoing phase 3 KEYNOTE-189 trial. The KEYTRUDA clinical development program includes more than 350 clinical trials across more than 30 tumor types, including more than 100 trials

that combine KEYTRUDA with other cancer treatments.

KEYNOTE-024: Data Showed KEYTRUDA was Superior to Chemotherapy for PFS and OS in First-Line Treatment of Metastatic NSCLC

KEYNOTE-024 included 305 patients who were previously untreated and whose tumors expressed high levels of PD-L1 (TPS of 50 percent or more). Patients were randomized to receive a 200 mg fixed dose of KEYTRUDA every three weeks (n=154) or four to six cycles of investigator's choice of one of five platinum-based chemotherapy regimens (n=151): carboplatin or cisplatin plus pemetrexed, carboplatin or cisplatin plus gemcitabine, or carboplatin plus paclitaxel. Pemetrexed maintenance therapy was permitted for patients with non-squamous histologies. Patients randomized to the control arm had the option of crossing over to KEYTRUDA (pembrolizumab) upon disease progression. The median follow-up was 11.2 months (range, 6.3-19.7). The primary endpoint was PFS; secondary endpoints were OS, ORR, and safety.

The findings published in *The New England Journal of Medicine* demonstrated that KEYTRUDA reduced the risk of progression or death by 50 percent compared to chemotherapy (HR, 0.50 [95% CI, 0.37-0.68]; p<0.001). The median PFS for KEYTRUDA was 10.3 months (95% CI, 6.7-not reached) compared to 6.0 months for chemotherapy (95% CI, 4.2-6.2). At six months, 62.1 percent of patients treated with KEYTRUDA were alive and had no disease progression (95% CI, 53.8-69.4) compared to 50.3 percent of those receiving chemotherapy (95% CI, 41.9-58.2). This benefit was observed in all study subgroups.

Additionally, KEYTRUDA resulted in a 40 percent reduction in the risk of death compared with chemotherapy (HR, 0.60 [95% CI, 0.41-0.89]; p=0.005); this finding includes the 66 patients (43.7%) on the chemotherapy arm who crossed over in-study to receive KEYTRUDA once their cancer had progressed; median OS was not reached in either group. Further, ORR was 44.8 percent for patients receiving KEYTRUDA (95% CI, 36.8-53.0), including six complete responses, compared to 27.8 percent with chemotherapy (95% CI, 20.8-35.7), including one complete response.

"These data from KEYNOTE-024 demonstrate the potential of KEYTRUDA to change the way non-small cell lung cancer is currently treated," said Dr. Martin Reck, head of the thoracic oncology dept., LungenClinic Grosshansdorf, Germany, and lead author of *The New England Journal of Medicine* paper. "This provides additional evidence that testing for PD-L1 levels should become standard in lung cancer at first diagnosis to guide treatment decisions."

Additional Findings and Safety Information from KEYNOTE-024

The safety of KEYTRUDA was consistent with what has been seen in previous trials among patients with metastatic NSCLC. The most common treatment-related adverse events for KEYTRUDA were diarrhea (n=22), fatigue (n=16), and pyrexia (n=16). Grade 3-5 treatment-related adverse events for KEYTRUDA included diarrhea (n=6) and pneumonitis (n=4). There was one treatment-related death in a patient receiving KEYTRUDA (cause unknown).

Additionally, based on an analysis of duration of response, a pre-specified exploratory endpoint, the median duration of response was not reached with KEYTRUDA (range, 1.9+ to 14.5+ months). The median duration of response with the chemotherapy group was 6.3 months (range, 2.1+ to 12.6+). Median time to response was 2.2 months for both groups.

About KEYNOTE-024

KEYNOTE-024 is a randomized, phase 3 study (ClinicalTrials.gov, NCT02142738) evaluating KEYTRUDA (pembrolizumab) as monotherapy compared to standard of care platinum-based chemotherapy in the treatment of patients with metastatic NSCLC. Patients enrolled were those who had received no prior systemic chemotherapy treatment for their advanced disease, whose tumors did not harbor an EGFR sensitizing mutation or ALK translocation, and whose tumors expressed high levels of PD-L1 (TPS of 50 percent or more) as determined by a central laboratory using an FDA approved companion diagnostic, the Dako PD-L1 IHC 22C3 PharmDx test, from Agilent Technologies.

KEYNOTE-021, Cohort G: KEYTRUDA Combined with Chemotherapy Showed Higher Response Rates Compared to Chemotherapy Alone as First-Line Treatment of Metastatic NSCLC

KEYNOTE-021, Cohort G, included 123 previously untreated patients with metastatic non-squamous NSCLC regardless of PD-L1 expression and whose tumors did not have EGFR mutations or ALK translocations. Patients were randomized to receive KEYTRUDA plus platinum doublet chemotherapy with pemetrexed and carboplatin (n=60) or platinum doublet chemotherapy alone (n=63). Patients randomized to the chemotherapy-only arm had the option of crossing over to KEYTRUDA monotherapy upon disease progression. The median follow-up was 10.6 months (range, 0.8-19.3).

The findings published in *The Lancet Oncology* demonstrated that ORR nearly doubled by adding KEYTRUDA to chemotherapy, with an ORR of 55 percent (n=33/60) compared to 29 percent (n=18/63) for chemotherapy alone (treatment difference 26%, 95% CI, 9-42%, p=0.0016); all responses were partial. Median duration of response was not reached in either group (range, 1.4+-13.0+ for KEYTRUDA plus chemotherapy; 1.4+-15.2+ for chemotherapy alone). Responses in both groups were durable, with 88 percent (n=29/33) of responders in the KEYTRUDA plus chemotherapy group and 78 percent (n=14/18) of responders in the chemotherapy alone group experiencing ongoing response at the time of data cut-off.

Additionally, the KEYTRUDA combination significantly reduced the risk of disease progression or death compared to chemotherapy alone (hazard ratio 0.53, 95% CI, 0.31-0.91, p=0.0102). Median PFS was 13.0 months with KEYTRUDA plus chemotherapy compared to 8.9 months with chemotherapy alone. OS was similar between the two arms, with 92 percent survival at six months in both, and 75 percent and 72 percent survival at 12 months in the KEYTRUDA combination and chemotherapy alone, respectively.

Of treated patients on the KEYTRUDA (pembrolizumab) plus chemotherapy arm, 47 percent remained on treatment as of the cut-off date, compared to 31 percent on chemotherapy alone. Of the treated patients who discontinued treatment on the chemotherapy-only arm, 52 percent (n=32/62) subsequently received anti-PD-L1 therapy, with 32 percent crossing over to KEYTRUDA monotherapy as allowed by the study protocol and 19 percent receiving it outside of study crossover.

"The results from KEYNOTE-021 show that pembrolizumab plus chemotherapy nearly doubled the number of patients responding to treatment than chemotherapy alone," said Dr. Corey Langer, director of thoracic oncology and professor of medicine at the Hospital of the University of Pennsylvania and lead author of *The Lancet Oncology* paper. "We are now gaining a better understanding that pembrolizumab combined with chemotherapy may play an important role in the first-line treatment of patients with non-small cell lung cancer."

Additional Safety Information from KEYNOTE-021, Cohort G

The most common treatment-related adverse events (occurring in at least 15% of patients) for KEYTRUDA plus chemotherapy were fatigue, nausea, anemia, rash, vomiting, diarrhea, increased AST, constipation, decreased appetite, increased ALT, dysgeusia, and decreased neutrophils. Grade 3-4 treatment-related adverse events in this arm included fatigue, nausea, anemia, rash, vomiting, increased AST, increased ALT, and decreased neutrophils. The most common immune-mediated adverse events in patients receiving KEYTRUDA plus chemotherapy were hypothyroidism and hyperthyroidism. Additionally, pneumonitis, infusion reactions, and severe skin toxicity were noted. These immune-mediated adverse events occurred at similar rates to patients receiving KEYTRUDA as a single agent. There was one treatment-related death from sepsis in a patient receiving KEYTRUDA plus chemotherapy, and two (one from sepsis and one from pancytopenia) in patients receiving chemotherapy alone.

About KEYNOTE-021, Cohort G

Cohort G of the multicenter, open-label, phase 1/2 multi-cohort KEYNOTE-021 study evaluated the efficacy and safety of KEYTRUDA in combination with pemetrexed and carboplatin compared with pemetrexed and carboplatin in patients with metastatic, non-squamous, EGFR- and ALK-negative NSCLC in the first-line treatment setting. Patients were randomized 1:1 to four cycles of KEYTRUDA (200 mg plus carboplatin AUC 5 (5 mg/mL/min) plus pemetrexed 500 mg/m^2 every three weeks), or carboplatin plus pemetrexed alone, followed by maintenance pemetrexed with or without KEYTRUDA. Randomization was stratified by PD-L1 expression (positive expression defined as TPS of one percent or more; negative expression defined as TPS of less than one percent). Patients randomized to the chemotherapy arm were allowed to cross over to KEYTRUDA (pembrolizumab) monotherapy if they experienced disease progression. Response was assessed by blinded, independent central review using RECIST 1.1 every six weeks for the first 18 weeks, every nine weeks through the first year, and every 12 weeks in the second year. The primary endpoint was ORR; secondary endpoints included PFS, duration of response, and OS.

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 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 occurred in 19 (3.5%) of 550 patients, including Grade 2 (1.1%), 3 (1.3%), 4 (0.4%), or 5 (0.2%) pneumonitis and occurred 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 for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

Immune-mediated colitis occurred in 4 (0.7%) of 550 patients, 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. 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 1 (0.2%) of 550 patients, 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 10 (1.8%) of 550 patients, including Grade 2 (0.7%) or 3 (0.3%) hyperthyroidism. Hypothyroidism occurred in 38 (6.9%) of 550 patients, including Grade 2 (5.5%) or 3 (0.2%) 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. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA (pembrolizumab) for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 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% of 550 patients: 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.

KEYTRUDA was discontinued due to adverse reactions in 14% of 550 patients. 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%).

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.

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 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).

Please see Prescribing Information for KEYTRUDA (pembrolizumab) 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 .

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