



NEWS RELEASE

## Merck Receives CHMP Positive Opinion for KEYTRUDA® (pembrolizumab) for the Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC)

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Opinion Based on Data from KEYNOTE-010, Which Showed Superior Overall Survival Compared to Chemotherapy in Previously-Treated Patients Whose Tumors Express PD-L1

KENILWORTH, N.J.--**(BUSINESS WIRE)**--Merck (NYSE: MRK), known as MSD outside the United States and Canada, announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending approval of KEYTRUDA® (pembrolizumab), the company's anti-PD-1 therapy, for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) in adults whose tumors express PD-L1 and who have received at least one prior chemotherapy regimen. The CHMP positive opinion for KEYTRUDA will now be reviewed by the European Commission for marketing authorization in the European Union (EU).

"This news marks an important step in making KEYTRUDA available for appropriate patients suffering from locally advanced or metastatic non-small cell lung cancer," said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories. "We are grateful to patients and investigators around the world who participated in these studies and who are helping to advance this important new treatment."

Data supporting the CHMP positive opinion were based on findings from two studies, KEYNOTE-010, a pivotal study assessing overall survival (OS) and KEYNOTE-001, which assessed overall response rates (ORR).

The CHMP recommended approval of KEYTRUDA monotherapy at a dose of 2 mg/kg every three weeks, which is also the FDA-approved dose for metastatic NSCLC in the United States. Based on this recommendation, a final decision regarding the approval of KEYTRUDA (pembrolizumab) monotherapy is expected from the European Commission in the third-quarter of 2016.

KEYNOTE-010 is an open-label, randomized phase 2/3 trial assessing OS with two doses of KEYTRUDA (2 mg/kg or 10 mg/kg every three weeks) compared to docetaxel (75 mg/m<sup>2</sup> every three weeks), a standard of care chemotherapy, in patients with any level of PD-L1 expression (as defined by a tumor proportion score [TPS] of 1 percent or more). KEYNOTE-001 is a multicenter, open-label multi-cohort, activity-estimating study evaluating ORR of KEYTRUDA (2 mg/kg or 10 mg/kg every three weeks).

## About Lung Cancer

Lung cancer, which forms in the tissues of the lungs, usually within cells lining the air passages, is the leading cause of cancer death worldwide. Each year, more people die of lung cancer than die of colon, breast, and prostate cancers combined. The two main types of lung cancer are non-small cell and small cell. NSCLC is the most common type of lung cancer, accounting for about 85 percent of all cases. The five-year relative survival rate for patients suffering from highly advanced, metastatic (Stage IV) lung cancers is estimated to be two percent.

## About KEYTRUDA® (pembrolizumab) Injection 100 mg

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 indicated for the treatment of patients with unresectable or metastatic melanoma.

In the United States, KEYTRUDA is also 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. 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.

KEYTRUDA is administered at a dose of 2 mg/kg as an intravenous infusion over 30 minutes every three weeks for the approved indications.

## 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 (pembrolizumab). 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.

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%).

No formal pharmacokinetic drug interaction studies have been conducted with KEYTRUDA.

It is not known whether KEYTRUDA (pembrolizumab) 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 270 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](http://www.sec.gov)).

Please see Prescribing Information for KEYTRUDA (pembrolizumab) at [http://www.merck.com/product/usa/pi\\_circulars/k/keytruda/keytruda\\_pi.pdf](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](http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf).

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