



NEWS RELEASE

FDA Approves KEYTRUDA® (pembrolizumab) for the Treatment of Patients with Metastatic Non-Small Cell Lung Cancer Whose Tumors Express PD-L1 with Disease Progression On or After Platinum-Containing Chemotherapy

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Patients with EGFR or ALK Genomic Tumor Aberrations Should Have Disease Progression on FDA-Approved Therapy for These Aberrations Prior to Receiving KEYTRUDA

Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved KEYTRUDA® (pembrolizumab) monotherapy, the company's anti-PD-1 (programmed death receptor-1) therapy, at a dose of 2 mg/kg every three weeks, 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 and who have 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. Under FDA's accelerated approval regulations, this indication for KEYTRUDA is approved 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 the first and only anti-PD-1 therapy approved for both squamous and non-squamous metastatic NSCLC. In addition to approving KEYTRUDA for NSCLC, FDA approved the first companion diagnostic that will enable physicians to determine the level of PD-L1 expression in a patient's tumor. In KEYNOTE-001, the clinical



study supporting the FDA Breakthrough Designation for KEYTRUDA and this approval, KEYTRUDA demonstrated an overall response rate of 41 percent (n=25/61) in patients with a PD-L1 expression tumor proportion score (TPS) of 50 percent or more; all responses were partial responses (95% CI, 29, 54). Eighty-four percent (n=21/25) of those who responded had ongoing responses, including 11 patients with ongoing responses of six months or longer. Immune-mediated adverse reactions occurred with KEYTRUDA including pneumonitis, colitis, hepatitis, hypophysitis, hyperthyroidism, hypothyroidism, type 1 diabetes mellitus, and nephritis. Based on the severity of the adverse reaction, KEYTRUDA (pembrolizumab) should be withheld or discontinued and corticosteroids administered. Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised of the potential hazard to a fetus. For more information regarding immune-mediated adverse reactions and use in pregnancy, see “Selected Important Safety Information” below.

“Today’s approval of KEYTRUDA is the result of our deep commitment to bring the benefits of immunotherapy to cancer patients,” said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. “Together with scientists and physicians around the world, we endeavor to improve the lives of patients suffering from these grievous illnesses.”

“This important news means that we now have a new immunotherapy option to help patients with squamous and non-squamous metastatic non-small cell lung cancer with disease progression on or after platinum-containing chemotherapy and whose tumors express PD-L1. The durability of response with immune checkpoint inhibitors is exciting and has given new options for our patients,” said Dr. Naiyer Rizvi, director of thoracic oncology and director of immunotherapeutics, New York Presbyterian Hospital, Columbia University Medical Center, and a principal investigator for the KEYTRUDA lung cancer clinical program. “And, with the approval of the first PD-L1 companion diagnostic, we can identify patients who are more likely to experience benefit from KEYTRUDA.”

KEYTRUDA is an immunotherapy that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby helping the immune system do what it is meant to do: help detect and fight cancer cells. KEYTRUDA can also cause the immune system to attack normal organs and tissues.

“We are pleased that today’s approval of KEYTRUDA provides physicians and patients with a new anti-PD-1 immunotherapy option to help fight this deadly disease,” said Andrea Ferris, president and chairman, LUNGeVity Foundation. “It is an exciting time as more treatment options are becoming available that help to combat cancer by harnessing the power of the body’s own immune system.”

Data Supporting FDA Accelerated Approval in Advanced NSCLC

The accelerated FDA approval was based on a multicenter, open-label multi-cohort, activity-estimating study

(KEYNOTE-001), which evaluated KEYTRUDA in a cohort of 280 patients with metastatic NSCLC that had progressed following platinum-containing chemotherapy, and if appropriate, targeted therapy for EGFR (epidermal growth factor receptor) or ALK (anaplastic lymphoma kinase) mutations and any evidence of PD-L1 expression by a clinical trial immunohistochemistry assay. A prospectively defined subgroup was retrospectively analyzed to evaluate PD-L1 as a biomarker among 61 patients with a PD-L1 TPS greater than or equal to 50 percent. Patients received KEYTRUDA monotherapy [10 mg/kg every two (n=27) or three (n=34) weeks] until unacceptable toxicity or disease progression. Primary endpoints were overall response rate (ORR) per RECIST 1.1 and duration of response. In the study, ORR for KEYTRUDA (pembrolizumab) was 41 percent (n=25/61) in patients with a PD-L1 TPS greater than or equal to 50 percent; all responses were partial responses (95% CI, 29, 54). Of the patients who responded, 84 percent (n=21/25) continued to respond to treatment with KEYTRUDA, including 11 patients with ongoing responses of six months or longer. The ORR and duration of response were similar regardless of dosing schedule (every 2 weeks or every 3 weeks). In a separate subgroup of 25 patients with limited follow-up with PD-L1 TPS greater than or equal to 50% receiving KEYTRUDA at a dose of 2 mg/kg every 3 weeks in KEYNOTE-001, activity was also observed.

The most common adverse reactions (reported in at least 20% of study patients) were fatigue (44%), cough (29%), decreased appetite (25%), and dyspnea (23%).

Merck is conducting multiple Phase 3 clinical studies in advanced NSCLC.

Approval of PD-L1 Companion Diagnostic for Patients with Advanced NSCLC

In parallel with the approval of KEYTRUDA, the FDA has also given Pre-Market Approval (PMA) to the first predictive companion diagnostic for use in detecting PD-L1, an immune-related biomarker expressed on some tumor cells: the PD-L1 IHC 22C3 pharmDx kit made by Dako North America, Inc., an Agilent Technologies Company. The data supporting the approval of KEYTRUDA for metastatic NSCLC showed that 22 percent of patients (n=61/280) had a PD-L1 TPS greater than or equal to 50 percent. This companion diagnostic will be available commercially to laboratories in the U.S. through Dako and testing using the assay will be available at U.S. reference laboratories including Laboratory Corporation of America® Holdings (LabCorp®), Quest Diagnostics, and GE Healthcare Clariant Diagnostic Services. These national reference laboratories do not represent an exclusive network of accredited pathology laboratories offering PD-L1 testing and PD-L1 testing may be offered by other accredited pathology laboratories.

Selected Safety Information for KEYTRUDA (pembrolizumab) Injection 100 mg

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 in patients receiving KEYTRUDA. 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.

Colitis occurred in 4 (0.7%) of 550 patients, including Grade 2 (0.2%) or 3 (0.4%) colitis in patients receiving KEYTRUDA. 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.

Hepatitis occurred in patients receiving KEYTRUDA (pembrolizumab). 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 indicated. Withhold KEYTRUDA for Grade 2 and withhold or discontinue for Grade 3 or Grade 4 hypophysitis.

Hyperthyroidism occurred in 10 (1.8%) of 550 patients, including Grade 2 (0.7%) or 3 (0.3%). Hypothyroidism occurred in 38 (6.9%) of 550 patients, including Grade 2 (5.5%) or 3 (0.2%). 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 Grade 4 hyperthyroidism.

Type 1 diabetes mellitus, including diabetic ketoacidosis, has occurred in patients receiving KEYTRUDA. 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.

Nephritis occurred in patients receiving KEYTRUDA. 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.

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 of the adverse reaction to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Resume KEYTRUDA when the adverse reaction remains at Grade 1 or less following steroid taper. Permanently discontinue KEYTRUDA for any severe or 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 patients treated with KEYTRUDA: rash, vasculitis, hemolytic anemia, serum sickness, myasthenia gravis, bullous pemphigoid, and Guillain-Barre syndrome.

Infusion-related reactions, including severe and life-threatening reactions, have occurred in patients receiving KEYTRUDA. Monitor patients for signs and symptoms of infusion-related reactions including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For severe or life-threatening reactions, stop infusion and permanently discontinue KEYTRUDA.

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.

KEYTRUDA was discontinued due to adverse reactions in 14% of patients. Serious adverse reactions occurred in 38% of patients. The most frequent serious adverse reactions reported in 2% or more 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%), decreased appetite (25%), dyspnea (23%), and cough (29%).

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

Merck's Commitment to Access for KEYTRUDA

Merck provides multiple programs to help ensure patients who are prescribed KEYTRUDA have access to our anti-PD-1 therapy. The **Merck Access Program** provides reimbursement support for eligible patients receiving KEYTRUDA, including help with out-of-pocket costs and co-pay assistance. Merck also offers financial assistance for eligible patients who are uninsured through our patient assistance program. More information is available by calling 1-855-257-3932 or visiting www.merckaccessprogram-keytruda.com.

About KEYTRUDA® (pembrolizumab)

KEYTRUDA is indicated in the United States at a dose of 2 mg/kg administered as an intravenous infusion over 30 minutes every three weeks 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. KEYTRUDA is also indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. These indications are 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.

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

About Merck

Today's Merck is a global healthcare 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 healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on **Twitter**, **Facebook** and **YouTube**.

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

This news release of Merck & Co., Inc., Kenilworth, NJ, USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the United States 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 healthcare legislation in the United States and internationally; global trends toward healthcare 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 2014 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 the Medication Guide for KEYTRUDA at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf

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