



NEWS RELEASE

Merck Receives Breakthrough Therapy Designation from U.S. Food and Drug Administration for KEYTRUDA® (pembrolizumab) in Classical Hodgkin Lymphoma (cHL)

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Fourth Designation for KEYTRUDA Follows Breakthrough Status in Advanced Melanoma, Non-Small Cell Lung Cancer, and Colorectal Cancer

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation to KEYTRUDA® (pembrolizumab), the company's anti-PD-1 therapy, for the treatment of patients with relapsed or refractory classical Hodgkin lymphoma (cHL). This is the fourth Breakthrough Therapy Designation granted for KEYTRUDA.

"Merck has launched an ambitious clinical development program examining the efficacy of KEYTRUDA in a broad range of solid and blood cancers, and our studies of relapsed or refractory classical Hodgkin lymphoma are quite promising," said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. "The FDA's Breakthrough Designation for this blood cancer provides an important mechanism to assist us in bringing this immunotherapy to patients who could benefit from its use."

The FDA's Breakthrough Therapy Designation is intended to expedite the development and review of a candidate that is planned for use, alone or in combination, to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. KEYTRUDA was previously granted breakthrough status

for specific patients with advanced melanoma, advanced non-small cell lung cancer (NSCLC), and advanced colorectal cancer.

The Breakthrough Therapy Designation in cHL is based on data from the ongoing Phase 1b KEYNOTE-013 and Phase 2 KEYNOTE-087 studies evaluating single agent KEYTRUDA in patients with cHL. Findings from the KEYNOTE-013 study were presented at the 2015 American Society of Hematology (ASH) Annual Meeting and data from KEYNOTE-087 will be presented at an upcoming medical meeting.

The KEYTRUDA clinical development program includes patients with more than 30 tumor types in more than 250 clinical trials, including more than 100 trials that combine KEYTRUDA with other cancer treatments. Registration-enabling trials of KEYTRUDA are currently enrolling patients in melanoma, NSCLC, head and neck cancer, bladder cancer, gastric cancer, colorectal cancer, esophageal cancer, breast cancer, ovarian cancer, Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and other tumors, with further trials in planning for other cancers.

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.

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. 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.

About Hodgkin Lymphoma

Lymphoma is a type of blood cancer that affects the lymphatic system, which removes excess fluids from the body and produces immune cells. Lymphoma cells are abnormal lymphocytes which multiply and collect in the lymph

nodes and other tissues. Normal lymphocytes are a type of white blood cell that fight infection. Hodgkin lymphoma (also called Hodgkin disease) is a specific type of lymphoma and includes two subtypes: classical Hodgkin lymphoma (cHL) and nodular lymphocyte predominant Hodgkin lymphoma. In 2016, it is estimated that more than 8,500 people will be diagnosed with Hodgkin lymphoma in the U.S. alone and cHL accounts for 95 percent of all Hodgkin lymphoma cases.

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 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. 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 (pembrolizumab) 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. 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 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% (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 (pembrolizumab).

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 Trial 6, 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 ($\geq 1\%$) 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 Trial 2, KEYTRUDA was discontinued due to adverse reactions in 12% of 357 patients with advanced melanoma; the most common ($\geq 1\%$) 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 ($\geq 1\%$) were dyspnea (1%), diarrhea (1%), and maculo-papular 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 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 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. 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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