



NEWS RELEASE

New Findings Show Durable Anti-Tumor Activity with KEYTRUDA® (pembrolizumab), Merck's Anti-PD-1 Therapy, in Patients with Advanced Head and Neck Cancer, Regardless of PD-L1 Expression Status

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Results from KEYNOTE-012, the First and Largest Study to Date of an Anti-PD-1 Therapy in Head and Neck Cancer, to be Presented at 2015 ASCO Annual Meeting

KEYTRUDA Monotherapy Achieved Overall Response Rate of 25 Percent in Heavily Pre-treated Patients

Merck is Advancing a Broad Head and Neck Clinical Program for KEYTRUDA with Five Clinical Trials, Across Multiple Lines of Therapy and in Combination with Other Agents

KENILWORTH, N.J.--**(BUSINESS WIRE)**--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced new investigational data evaluating KEYTRUDA® (pembrolizumab), the company's anti-PD-1 therapy, as a monotherapy from the KEYNOTE-012 Phase 1b study in 132 pre-treated patients with recurrent or metastatic head and neck cancer, regardless of PD-L1 expression status. In the evaluable patients, the overall response rate (ORR) (confirmed and unconfirmed) was 24.8 percent for KEYTRUDA (200 mg fixed dose every three weeks) (n=29/117) (95% CI, 17.3-33.6). When looking at HPV status, the ORR was similar among HPV-positive and HPV-negative disease (20.6 percent [n=7/34] and 27.2 percent [n=22/81], respectively) (95% CI, 8.7-37.9 and 17.9-38.2). These data, featured in the ASCO Press Program today, will be presented in an oral session by Dr. Tanguy Seiwert, The University of Chicago, on Monday, June 1 at the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago (Abstract #LBA6008).

Merck has initiated a comprehensive clinical development program for KEYTRUDA evaluating a fixed dosing regimen (200 mg every three weeks) in head and neck cancer across multiple lines of therapy as monotherapy and in combination with chemotherapy and other agents. Results from KEYNOTE-012 were first presented at the 2014 ASCO Annual Meeting and showed 19.6 percent ORR for KEYTRUDA (10 mg/kg every two weeks) in heavily pre-treated patients with advanced head and neck cancer with tumor cells positive for PD-L1 expression.

"Advanced head and neck cancer is a severe and life-altering condition. Unfortunately we have few effective treatment options, particularly for patients whose disease is not responding to current therapies," said Dr. Seiwert. "As a practicing oncologist, I am very encouraged by the durable responses demonstrated with pembrolizumab in this study, and look forward to data being shared in the future from the additional confirmatory studies now being conducted in advanced head and neck cancer."

"The totality of the data presented at ASCO furthers our understanding of the clinical potential of KEYTRUDA in head and neck cancer, regardless of PD-L1 expression or HPV status," said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories. "Based on the results observed to date, we are advancing multiple registrational studies in head and neck cancer including randomized evaluations of overall survival and progression-free survival with KEYTRUDA, as monotherapy and in combination with chemotherapy, compared to standard of care."

Additional Results from KEYNOTE-012 in Advanced Head and Neck Cancer

Additional findings from KEYNOTE-012, the first and largest Phase 1b study of an anti-PD-1 therapy in advanced head and neck cancer, showed tumor shrinkage was achieved in 56 percent of total evaluable patients who had measurable disease with one post baseline scan (n=59/106). The median duration of response was not reached (7.3+ - 25.1+ weeks among patients with a confirmed response), with a median follow up duration of 5.7 months (0.2 – 8.7 months). At the time of the analysis, 86 percent of patients who responded continued to respond to treatment (n=25/29). The data are based on an analysis conducted with a cut-off of March 23, 2015.

Adverse events in the study were consistent with previously reported safety data for KEYTRUDA (n=132). The most common treatment-related adverse events (occurring in greater than or equal to 5% of patients) included: fatigue (15.2%), hypothyroidism (9.1%), decreased appetite (7.6%), rash (7.6%), dry skin (6.8%), and pyrexia (6.8%). Some patients experienced adverse events of special interest, including hypothyroidism (10.6%), pneumonitis (3.0%), thyroiditis (2.3%), colitis (0.8%), interstitial lung disease (0.8%), acquired epidermolysis bullosa (0.8%), drug induced liver injury (0.8%), epidermolysis (0.8%), and diabetic ketoacidosis (0.8%). Four patients experienced adverse events of special interest that resulted in treatment discontinuation. There were no treatment-related deaths.

About the KEYNOTE-012 Study

KEYNOTE-012 is an ongoing multi-center, non-randomized Phase 1b trial evaluating the safety, tolerability and anti-tumor activity of KEYTRUDA monotherapy (10 mg/kg every two weeks or 200 mg IV every three weeks) in patients with advanced triple negative breast cancer (TNBC), advanced head and neck cancer, advanced urothelial cancer, or advanced gastric cancer. The primary endpoints of the study include overall safety, tolerability, and anti-tumor activity (as measured by RECIST v1.1); secondary endpoints include progression-free survival (PFS), overall survival (OS), and duration of response.

About Head and Neck Cancer

Head and neck cancer describes a number of different tumors that develop in or around the throat, larynx, nose, sinuses and mouth. Most head and neck cancers are squamous cell carcinomas that begin in the flat, squamous cells that make up the thin surface layer of the structures in the head and neck. The leading modifiable risk factors for head and neck cancer include tobacco and heavy alcohol use. Other non-modifiable risk factors include infection with certain types of HPV, also called **human papillomaviruses**. Each year there are approximately 400,000 cases of cancer of the oral cavity and pharynx, in addition to approximately 160,000 cancers of the larynx, resulting in approximately 300,000 deaths.

About KEYTRUDA® (pembrolizumab)

KEYTRUDA (pembrolizumab) is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. By binding to the PD-1 receptor and blocking the interaction with the receptor ligands, KEYTRUDA releases the PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response.

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 unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. 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.

Merck is advancing a broad and fast-growing clinical development program for KEYTRUDA with more than 100 clinical trials – across more than 30 tumor types and enrolling more than 16,000 patients – both as a monotherapy and in combination with other therapies.

Selected Important Safety Information for KEYTRUDA

Pneumonitis occurred in 12 (2.9%) of 411 patients with advanced melanoma receiving KEYTRUDA (the approved indication in the United States), including Grade 2 or 3 cases in 8 (1.9%) and 1 (0.2%) patients, respectively. 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 pneumonitis.

Colitis (including microscopic colitis) occurred in 4 (1%) of 411 patients, including Grade 2 or 3 cases in 1 (0.2%) and 2 (0.5%) patients respectively, 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 (including autoimmune hepatitis) occurred in 2 (0.5%) of 411 patients, including a Grade 4 case in 1 (0.2%) patient, 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 2 (0.5%) of 411 patients, including a Grade 2 case in 1 and a Grade 4 case in 1 (0.2% each) patient, receiving KEYTRUDA. Monitor for signs and symptoms of hypophysitis. Administer corticosteroids for Grade 2 or greater hypophysitis. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3; and permanently discontinue KEYTRUDA for Grade 4 hypophysitis.

Nephritis occurred in 3 (0.7%) patients receiving KEYTRUDA, consisting of one case of Grade 2 autoimmune nephritis (0.2%) and two cases of interstitial nephritis with renal failure (0.5%), one Grade 3 and one Grade 4. 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.

Hyperthyroidism occurred in 5 (1.2%) of 411 patients, including Grade 2 or 3 cases in 2 (0.5%) and 1 (0.2%) patients respectively, receiving KEYTRUDA. Hypothyroidism occurred in 34 (8.3%) of 411 patients, including a Grade 3 case in 1 (0.2%) patient, receiving KEYTRUDA. 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 corticosteroids for Grade 3 or greater hyperthyroidism. Withhold KEYTRUDA for Grade 3; permanently discontinue KEYTRUDA for Grade 4 hyperthyroidism. Isolated hypothyroidism may be managed with replacement therapy without treatment interruption and without corticosteroids.

Other clinically important immune-mediated adverse reactions can occur. The following clinically significant, immune-mediated adverse reactions occurred in less than 1% of patients treated with KEYTRUDA: exfoliative

dermatitis, uveitis, arthritis, myositis, pancreatitis, hemolytic anemia, partial seizures arising in a patient with inflammatory foci in brain parenchyma, adrenal insufficiency, myasthenic syndrome, optic neuritis, and rhabdomyolysis.

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. Restart KEYTRUDA if the adverse reaction remains at Grade 1 or less. Permanently discontinue KEYTRUDA for any severe or Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

Based on its mechanism of action, KEYTRUDA may 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.

For the treatment of advanced melanoma, KEYTRUDA was discontinued for adverse reactions in 6% of 89 patients who received the recommended dose of 2 mg/kg and 9% of 411 patients across all doses studied. Serious adverse reactions occurred in 36% of patients receiving KEYTRUDA. The most frequent serious adverse drug reactions reported in 2% or more of patients were renal failure, dyspnea, pneumonia, and cellulitis.

The most common adverse reactions (reported in $\geq 20\%$ of patients) were fatigue (47%), cough (30%), nausea (30%), pruritus (30%), rash (29%), decreased appetite (26%), constipation (21%), arthralgia (20%), and diarrhea (20%).

The recommended dose of KEYTRUDA is 2 mg/kg administered as an intravenous infusion over 30 minutes every three weeks until disease progression or unacceptable toxicity. 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. 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

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

This news release 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 Merck’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; Merck’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 Merck’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

Merck 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 Merck’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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