New Data from KEYNOTE-028, Merck’s Trial Evaluating KEYTRUDA® (pembrolizumab) Across a Range of Cancer Types, Presented at 2015 European Cancer Congress

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Findings Show Anti-Tumor Activity for KEYTRUDA in Two Gastrointestinal Cancers

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced new findings from the KEYNOTE-028 Phase 1b study, the clinical trial investigating the use of the company’s anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) in multiple, difficult-to-treat cancers. Data from this trial, to be presented at the European Cancer Congress (ECC) in Vienna, Austria, Sept. 25-29, include the first-time findings for KEYTRUDA in two gastrointestinal cancers, advanced anal cancer and advanced biliary tract cancer, and add to Merck’s growing body of clinical data for KEYTRUDA.

KEYNOTE-028 is an ongoing multi-cohort, non-randomized Phase 1b basket trial – a trial design that allows for the study of multiple sub-populations of different tumor or histological types within one study. The study is evaluating the safety, tolerability, and anti-tumor activity of KEYTRUDA monotherapy (10 mg/kg dosed every two weeks) in more than 450 patients across 20 different types of cancer. The study was designed to evaluate patients with advanced solid tumors that express PD-L1 and which have not responded to current therapy or for which current therapy is not appropriate.

“Through innovative trials like KEYNOTE-028, we are advancing our understanding of the potential benefit of KEYTRUDA in a wide range of difficult-to-treat cancers,” said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories. “Merck is committed to evaluating KEYTRUDA across as many tumor types as possible and the expansion of our clinical development program over the years reflects this. We are encouraged by these early stage data, and will continue to advance KEYTRUDA in order to deliver on our goal of helping as many people with cancer as possible.”

The KEYTRUDA clinical development program has rapidly expanded to encompass more than 30 tumor types in more than 130 clinical trials, of which more than 70 trials combine KEYTRUDA with other cancer treatments. Registration-enabling trials of KEYTRUDA monotherapy are currently enrolling patients in melanoma, non-small cell lung cancer (NSCLC), head and neck cancer, bladder cancer, gastric cancer, colorectal cancer, and Hodgkin Lymphoma, with further trials in planning for other cancers.

Early Findings from Advanced Squamous Cell Carcinoma (SCC) of the Anal Canal (Abstract #500)

Early findings from 25 heavily pre-treated patients with advanced anal cancer – to be presented in an oral session on Sunday, Sept. 27 by Dr. Patrick Ott, Dana-Farber Cancer Institute – demonstrated an overall response rate (ORR) of 20 percent (confirmed and unconfirmed) (95% CI, 6.8-40.7) and a disease control rate (DCR) of 64 percent (95% CI, 42.5-82.0). Five partial responses (95% CI, 6.8-40.7) were observed, and 44 percent of patients (n=11/25) had stable disease (95% CI, 24.4-65.1). Additionally, the 6-month progression-free survival (PFS) rate was 31.6 percent and the 12-month PFS rate was 19.7 percent. At the time of the analysis, response duration ranged from 0.1+ to 9.2+ months, with the median not yet reached. The median stable disease duration was 3.6 months (range, 1.8+ to 11.0+).

Adverse events were generally consistent with previously reported safety data for KEYTRUDA. Grade 3-4 investigator-assessed, treatment-related adverse events were thyroid-stimulating hormone increased (n=1), colitis (n=1), diarrhea (n=1), and general physical health deterioration (n=1). Immune-mediated adverse events were hypothyroidism (n=3) and colitis (n=1). There were no treatment-related deaths.

Early Findings from Advanced Biliary Tract Cancer (Abstract #525)

Early findings from 24 heavily pre-treated patients with advanced biliary tract cancer – presented in a poster session on
Saturday, Sept. 26 by Dr. Yung-Jue Bang, Seoul National University Hospital, Seoul, Korea – demonstrated an ORR of 17.4 percent (confirmed and unconfirmed) (95% CI 5.0-38.8) (n=4/23); 17.4 percent of patients had stable disease (95% CI 5.0-38.8) (n=4/23). As the time of the analysis, three of four responses were ongoing, and the median response duration had not yet been reached (range, 5.4+ to 9.3+ weeks).

Adverse events were generally consistent with previously reported safety data for KEYTRUDA. Grade 3-4 investigator-assessed, treatment-related adverse events were anemia (n=1), autoimmune hemolytic anemia (n=1), colitis (n=1) and dermatitis (n=1). Immune-mediated adverse events were autoimmune hemolytic anemia (n=1), colitis (n=1), hypothyroidism (n=1), and hypophysitis (n=1). There were no treatment-related deaths.

About KEYTRUDA® (pembrolizumab)

KEYTRUDA 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 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.

Selected Important Safety Information for KEYTRUDA

Pneumonitis occurred in 12 (2.9%) of 411 patients, including Grade 2 or 3 cases in 8 (1.9%) and 1 (0.2%) patients, respectively, 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 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 patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). 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.

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. Hyperthyroidism 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.

Type 1 diabetes mellitus, including diabetic ketoacidosis, has occurred in patients receiving KEYTRUDA. Monitor patients for hyperglycemia and other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA in cases of severe hyperglycemia until metabolic control is achieved.

Nephritis occurred in 3 (0.7%) patients, 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.

Other clinically important immune-mediated adverse reactions can occur. The following clinically significant immune-mediated adverse reactions occurred in patients treated with KEYTRUDA: exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, hemolytic anemia, partial seizures arising in a patient with inflammatory foci in brain parenchyma, severe dermatitis including bullous pemphigoid, 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.

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 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.
KEYTRUDA was discontinued for adverse reactions in 9% of 411 patients. Adverse reactions, reported in at least two patients, that led to discontinuation of KEYTRUDA were: pneumonitis, renal failure, and pain. Serious adverse reactions occurred in 36% of patients. The most frequent serious adverse reactions, reported in 2% or more of patients, were renal failure, dyspnea, pneumonia, and cellulitis.

The most common adverse reactions (reported in at least 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 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 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).


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