Updated KEYTRUDA® (pembrolizumab) Data in Small Cell Lung Cancer and Mesothelioma Presented at 17th World Conference on Lung Cancer

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Findings in Small Cell Lung Cancer and Malignant Pleural Mesothelioma Show Overall Response Rates of 33.3 Percent and 20.0 Percent, Respectively, in KEYNOTE-028

Long-Term Data Demonstrate Durable Responses in Difficult-to-Treat Cancers

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that updated findings from the phase 1b KEYNOTE-028 study investigating the use of KEYTRUDA® (pembrolizumab), the company's anti-PD-1 therapy, in previously treated patients with advanced small cell lung cancer (SCLC) and malignant pleural mesothelioma, showed clinical activity and durable responses in some patients. These data were featured in oral presentations at the 17th World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer.

“As data from our initial trials exploring KEYTRUDA mature, we are encouraged to see durable clinical activity in difficult-to-treat cancers such as small cell lung cancer and malignant pleural mesothelioma, where new treatments are clearly needed,” said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories. “With our extensive immuno-oncology research program, we are developing KEYTRUDA across a range of thoracic malignancies, and we have additional studies underway in these two cancer types.”

KEYNOTE-028 is an ongoing multi-cohort, non-randomized Phase 1b basket trial evaluating the safety, tolerability,
and anti-tumor activity of KEYTRUDA monotherapy (10 mg/kg dosed every two weeks) in more than 450 patients with PD-L1 positive tumors across 20 different types of cancer. PD-L1 positivity was defined as expression in one percent or more of tumor and associated inflammatory cells or positive staining in stroma. The primary outcome measure is overall response rate (ORR), with secondary outcome measures of progression-free survival (PFS), overall survival (OS), and duration of response.

The KEYTRUDA (pembrolizumab) clinical development program includes more than 30 tumor types in nearly 400 clinical trials, including more than 200 trials that combine KEYTRUDA with other cancer treatments. Merck has initiated a phase 2 trial, KEYNOTE-158, to further evaluate KEYTRUDA in advanced solid tumors including SCLC and malignant pleural mesothelioma.

**Results from KEYNOTE-028 SCLC Cohort (Abstract #OA05.01)**

Data from the SCLC cohort of the KEYNOTE-028 trial were presented in an oral presentation on Dec. 5 by Dr. Patrick Ott, Dana-Farber Cancer Institute.

Updated findings from 24 heavily pre-treated patients with advanced SCLC demonstrated a confirmed ORR of 33.3 percent (n=8/24) (95% CI, 15.6%-55.3%), including one complete response and seven partial responses. One patient had stable disease and 13 patients had progressive disease. Responses were durable, with a median duration of response of 19.4 months (95% CI, range: 3.6+ to 20.0+).

Additionally, the median PFS was 1.9 months (95% CI, 1.7-5.9), with a six-month PFS rate of 28.6 percent and 12-month PFS rate of 23.8 percent. The median OS was 9.7 months (95% CI, 4.1-NR), with a six-month OS rate of 66.0 percent and a 12-month OS rate of 37.7 percent.

The safety profile of KEYTRUDA was consistent with that observed in previously reported studies. Grade 3-5 treatment-related adverse events were asthenia, blood bilirubin increased, colitis and intestinal ischemia (n=1 for all). Some patients experienced adverse events of special interest, including autoimmune thyroiditis, infusion site reaction, cytokine release syndrome and colitis (n=1 for all).

“These long-term data, which show meaningful response rates and durable responses in certain patients with small cell lung cancer, are encouraging,” said Dr. Ott. “With these findings, we are advancing understanding of the potential for immunotherapy to make a difference for these patients.”

**Results from KEYNOTE-028 Malignant Pleural Mesothelioma Cohort (Abstract #OA13.03)**

Data from the malignant pleural mesothelioma cohort of the KEYNOTE-028 trial were presented in an oral
presentation on Dec. 6 by Dr. Evan Alley, Abramson Cancer Center, University of Pennsylvania.

Results showed a confirmed ORR of 20.0 percent (n=5/25) (95% CI, 6.8-40.7). All responses were partial responses and 13 patients had stable disease. The median duration of response was 12.0 months (range, 3.7-20.5+). In total, 60.9 percent of evaluable patients experienced a decrease in tumor size.

Additionally, the median PFS was 5.4 months (95% CI, 3.4-7.5), with a six-month PFS rate of 45.8 percent and a 12-month PFS rate of 20.8 percent. Median OS was 18.0 months (95% CI, 9.4-NR), with a six-month OS rate of 83.5 percent and a 12-month OS rate of 62.6 percent.

The safety profile of KEYTRUDA (pembrolizumab) was consistent with that observed in previously reported studies. Grade 3 treatment-related adverse events were ALT increase, appetite decrease, dyspnea, iridocyclitis, neutrophil count decreased, pyrexia and thrombocytopenia (n=1 for all). Some patients experienced adverse events of special interest, including erythema/erythema multiforme, hypothyroidism, infusion-related reaction, iridocyclitis and rhabdomyolysis (n=1 for all). There were no Grade 4 or 5 treatment-related adverse events and no treatment-related deaths.

About KEYTRUDA ® (pembrolizumab)

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 administered as an intravenous infusion over 30 minutes every three weeks for the approved indications. KEYTRUDA for injection is supplied in a 100 mg single use vial.

KEYTRUDA (pembrolizumab) Indications and Dosing

Melanoma

KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma at a dose of 2 mg/kg every three weeks until disease progression or unacceptable toxicity.

Lung Cancer

KEYTRUDA is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS) ≥50%] as determined by an FDA-approved
test, with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA (pembrolizumab) is also indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) 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.

In metastatic NSCLC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Head and Neck Cancer

KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. In HNSCC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Selected Important Safety Information for KEYTRUDA® (pembrolizumab)

KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 94 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 1 (0.8%), 2 (1.3%), 3 (0.9%), 4 (0.3%), and 5 (0.1%) pneumonitis, and occurred more frequently in patients with a history of prior thoracic radiation (6.9%) compared to those without (2.9%). 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.

KEYTRUDA can cause immune-mediated colitis. Colitis occurred in 48 (1.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.4%), 3 (1.1%), and 4 (<0.1%) 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.

KEYTRUDA (pembrolizumab) can cause immune-mediated hepatitis. Hepatitis occurred in 19 (0.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.4%), 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.
KEYTRUDA can cause hypophysitis. Hypophysitis occurred in 17 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.2%), 3 (0.3%), and 4 (<0.1%) hypophysitis. 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.

KEYTRUDA can cause thyroid disorders, including hyperthyroidism, hypothyroidism, and thyroiditis. Hyperthyroidism occurred in 96 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.8%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 237 (8.5%) of 2799 patients receiving KEYTRUDA, including Grade 2 (6.2%) and 3 (0.1%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in patients with HNSCC occurring in 28 (15%) of 192 patients with HNSCC, including Grade 3 (0.5%) hypothyroidism. Thyroiditis occurred in 16 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.3%) thyroiditis. 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.

KEYTRUDA can cause type 1 diabetes mellitus, including diabetic ketoacidosis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer antihyperglycemics in patients with severe hyperglycemia.

KEYTRUDA can cause immune-mediated nephritis. Nephritis occurred in 9 (0.3%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.1%), 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.

KEYTRUDA can cause other clinically important immune-mediated adverse reactions. 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 (pembrolizumab) 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 2799 patients: arthritis (1.5%), exfoliative dermatitis, bullous pemphigoid, rash (1.4%), uveitis, myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, and partial seizures arising in a patient with inflammatory foci in brain parenchyma.

KEYTRUDA can cause severe or life-threatening infusion-related reactions, which have been reported in 6 (0.2%) of 2799 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.

In KEYNOTE-006, 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 (≥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 KEYNOTE-002, KEYTRUDA was discontinued due to adverse reactions in 12% of 357 patients with advanced melanoma; the most common (≥1%) were general physical health deterioration (1%), asthenia (1%), dyspnea (1%), pneumonitis (1%), and generalized edema (1%). Adverse reactions leading to interruption of KEYTRUDA (pembrolizumab) occurred in 14% of patients; the most common (≥1%) were dyspnea (1%), diarrhea (1%), and maculopapular 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 8% of 682 patients with metastatic NSCLC. The most common adverse event resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.8%). Adverse reactions leading to interruption of KEYTRUDA occurred in 23% of patients; the most common (≥1%) were diarrhea (1%), fatigue (1.3%), pneumonia (1%), liver enzyme elevation (1.2%), decreased appetite (1.3%), and pneumonitis
The most common adverse reactions (occurring in at least 20% of patients and at a higher incidence than with docetaxel) were decreased appetite (25% vs 23%), dyspnea (23% vs 20%), and nausea (20% vs 18%).

KEYTRUDA was discontinued due to adverse reactions in 17% of 192 patients with HNSCC. Serious adverse reactions occurred in 45% of patients. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia, dyspnea, confusional state, vomiting, pleural effusion, and respiratory failure. The most common adverse reactions (reported in at least 20% of patients) were fatigue, decreased appetite, and dyspnea. Adverse reactions occurring in patients with HNSCC were generally similar to those occurring in patients with melanoma or NSCLC, with the exception of increased incidences of facial edema (10% all Grades; 2.1% Grades 3 or 4) and new or worsening hypothyroidism.

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, 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 nearly 400 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.

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).


Media:
Pamela Eisele, 267-305-3558
or
Courtney Ronaldo, 908-236-1108
or
Investors
Teri Loxam, 908-740-1986
or
Amy Klug, 908-740-1898