New Data Show Durability of Response for Merck’s KEYTRUDA® (pembrolizumab) in Advanced Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Solid Tumors, Regardless of Tumor Type

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First-Time Findings from KEYNOTE-164 and KEYNOTE-158, to Be Presented at ASCO, Further Support the Utility of MSI-H and dMMR as Predictive Biomarkers for Tumor-Agnostic Treatment Approach with KEYTRUDA

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced the first presentation of findings from KEYNOTE-164 and KEYNOTE-158, two phase 2 studies evaluating KEYTRUDA® (pembrolizumab), the company’s anti-PD-1 therapy, in patients with advanced microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors. The studies showed overall response rates (ORR), regardless of histology, with ORR between 28 percent (95% CI, 17-41) and 38 percent (95% CI, 27-49) across patients with MSI-H/dMMR colorectal cancer (CRC) and other advanced MSI-H/dMMR solid tumors, respectively. These findings will be presented on Monday, June 5 at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago (Abstract #3071).

“These important data build on the research to date showing clinically meaningful responses with pembrolizumab (KEYTRUDA) monotherapy across a wide range of tumors with MSI-H or dMMR status in patients whose disease is locally advanced or metastatic,” said Dr. Luis A. Diaz, Jr., head of the division of solid tumor oncology, Memorial Sloan Kettering Cancer Center. “Moreover, these data confirm the initial findings we made demonstrating the value of MSI-H or dMMR tumor status as a predictive biomarker for KEYTRUDA for these difficult-to-treat cancers.”

“These data exemplify our commitment to advancing the use of biomarkers to help identify patients most likely to benefit from KEYTRUDA,” said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories.

The KEYTRUDA (pembrolizumab) clinical development program includes more than 30 tumor types in more than 500 clinical trials, including more than 300 trials that combine KEYTRUDA with other cancer treatments. Merck’s immuno-oncology clinical development program includes multiple registration-enabling studies investigating KEYTRUDA as a monotherapy in MSI-H and dMMR cancers.

Key Findings from KEYNOTE-164 and KEYNOTE-158 Studies

KEYNOTE-164 and KEYNOTE-158 are ongoing global, open-label, non-randomized, multi-cohort, multi-center phase 2 studies evaluating KEYTRUDA (200 mg every three weeks) in patients with advanced MSI-H or dMMR solid tumors. KEYNOTE-164 is enrolling patients with previously treated, unresectable locally advanced or metastatic MSI-H or dMMR CRC who received two or more prior therapies that included fluoropyrimidine, irinotecan, and oxaliplatin. KEYNOTE-158 is enrolling patients with any advanced MSI-H solid tumor, with the exception of CRC, who had received one or more prior therapies. MSI-H or dMMR tumor status is determined using local laboratory-developed, polymerase chain reaction (PCR) tests for MSI-H status or immunohistochemistry (IHC) tests for dMMR. Tumor response is assessed every nine weeks per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 by independent, central, blinded radiographic review. The primary endpoint of the studies is ORR; secondary endpoints include duration of response, progression-free survival (PFS), overall survival (OS) and safety.

Of the 61 patients with advanced CRC who were enrolled in KEYNOTE-164 (as of Feb. 10, 2017), the ORR was 28 percent (n=17/61) (95% CI, 17-41) – with zero complete responses and 17 partial responses; fourteen had stable disease and 28 had progressive disease – for an overall disease control rate of 51 percent (n=31/61) (95% CI, 38-64). Median time to response...
Lung Cancer
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 (pembrolizumab), in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.
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.
When administering KEYTRUDA in combination with chemotherapy, KEYTRUDA should be administered prior to chemotherapy when given on the same day. See also the Prescribing Information for pemetrexed and carboplatin.

About KEYTRUDA® (pembrolizumab) Injection
KEYTRUDA is an anti-PD-1 therapy that works by increasing the ability of T lymphocytes to attack and treat a variety of cancers across all stages. This indicates that KEYTRUDA should be administered prior to chemotherapy when given on the same day. See also the Prescribing Information for pemetrexed and carboplatin.

About Microsatellite Instability and DNA Mismatch Repair
Microsatellites are short repetitive sequences of DNA found throughout the genome. Microsatellite instability – or MSI – is caused by a deficiency in the cell’s ability to repair errors in the DNA sequence (DNA mismatch repair) that occur during cell division, leading to a characteristic change in microsatellite repeats. MSI is detected indirectly by demonstrating absence of expression of mismatch repair proteins by IHC, or more directly by PCR-based amplification of specific microsatellite repeats. MSI-H (microsatellite instability-high) is already an established biomarker in certain types of cancer. Patients determined to have mismatch repair deficiency (dMMR) are biologically similar to those with MSI-H status. MSI-H/dMMR occurs in a variety of cancers across all stages.

About KEYTRUDA® (pembrolizumab) Indications and Dosing
Melanoma
KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity.

Lung Cancer
KEYTRUDA, as a single agent, 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, as a single agent, 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.

KEYTRUDA (pembrolizumab) Injection
KEYTRUDA is an anti-PD-1 therapy that works by increasing the ability of the body’s immune system to help detect and fight tumor cells. KEYTRUDA is a humanized monoclonal antibody that 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.

Studies of KEYTRUDA – from the largest immuno-oncology program in the industry with more than 500 trials – include a wide variety of cancers and treatment settings. The KEYTRUDA clinical program seeks to understand factors that predict a patient’s likelihood of benefiting from treatment with KEYTRUDA, including the exploration of several different biomarkers across a broad range of tumors.

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-dose vial.

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KEYTRUDA (pembrolizumab), in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

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For the PFS analysis, in patients with CRC the estimated 6-month rate was 43 percent and the 12-month rate was 34 percent – with a median PFS of 2.3 months (95% CI 2.1-8.1); in patients with any advanced solid tumor, excluding CRC, the estimated 6-month rate was 45 percent – with a median PFS of 4.3 months (95% CI 3.1-not reached). For the OS analysis, in patients with CRC the estimated 6-month rate was 87 percent and the 12-month rate was 72 percent – with a median OS not yet reached; in patients with any advanced solid tumor, excluding CRC, the estimated 6-month rate was 73 percent – with a median OS not yet reached (95% CI 9.2-not reached). Median follow-up was 13.2 months (range: 0-17) and 6.1 months (range: 1-12), respectively. At the time of analysis, median duration of response had not been reached in either study (range: 2.9+/-12.5+ and range: 2.4+/-9.2+,

The safety profile of KEYTRUDA (pembrolizumab) was consistent with that observed in previously reported studies. In patients with CRC, the treatment-related adverse events observed to date (any grade occurring in 10% or more of patients) were arthralgia (n=10), nausea (n=9), diarrhea (n=8), anemia (n=7), pruritus (n=7) and fatigue (n=6); these included Grade 3-4 treatment-related fatigue (n=2) and anemia (n=1). Immune-mediated adverse events of Grade 3-4 were pancreatitis (n=3), hepatitis (n=1) and severe skin toxicity (n=1). There were no treatment-related deaths.

In patients with any advanced solid tumor, excluding CRC, the treatment-related adverse events observed to date (any grade occurring in 10% or more of patients) were fatigue (n=8), pruritus (n=7), anemia (n=7), diarrhea (n=7), nausea (n=6) and arthralgia (n=2); these include Grade 3-4 anemia (n=1) and diarrhea (n=1). Immune-mediated adverse events of Grade 3-4 toxicity were severe skin toxicity (n=2), hyperthyroidism (n=1), pneumonitis (n=1), fulminant type 1 diabetes mellitus (n=1) and Guillain-Barre Syndrome (n=1). There was one death attributed to treatment-related pneumonia by investigator.

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KEYTRUDA, as a single agent, 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.

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Microsatellites are short repetitive sequences of DNA found throughout the genome. Microsatellite instability – or MSI – is caused by a deficiency in the cell’s ability to repair errors in the DNA sequence (DNA mismatch repair) that occur during cell division, leading to a characteristic change in microsatellite repeats. MSI is detected indirectly by demonstrating absence of expression of mismatch repair proteins by IHC, or more directly by PCR-based amplification of specific microsatellite repeats. MSI-H (microsatellite instability-high) is already an established biomarker in certain types of cancer. Patients determined to have mismatch repair deficiency (dMMR) are biologically similar to those with MSI-H status. MSI-H/dMMR occurs in a variety of cancers across all stages.

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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-dose vial.
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 locally advanced or metastatic urothelial carcinoma, 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.

KEYTRUDA is also indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

In adult patients with MSI-H cancer, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

KEYTRUDA (pembrolizumab) is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

KEYTRUDA is also indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with 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. The safety and effectiveness of KEYTRUDA in pediatric patients with MSI-H central nervous system cancers have not been established.

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 (pembrolizumab) 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 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
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
more than 500 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 more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world’s most challenging diseases. 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. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world – including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer’s disease and infectious diseases including HIV and Ebola. For more information, visit www.merck.com and connect with us on Twitter, Facebook, Instagram, 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 2016 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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