



## NEWS RELEASE

# New KEYTRUDA® (pembrolizumab) Data from KEYNOTE-006 and KEYNOTE-001 in Advanced Melanoma, Including Updated Survival Data, To Be Presented at 2016 ASCO Annual Meeting

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Final Overall Survival Data from KEYNOTE-006 To Be Presented at ASCO; KEYTRUDA, the First Anti-PD-1 Monotherapy to Demonstrate Overall Survival Compared to Ipilimumab, Shows Continued Benefit with Longer Follow-Up

KEYNOTE-001 Findings Show Continued Benefit in Response Rates, Duration of Response, and Include New Three-Year Overall Survival Data for KEYTRUDA

Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced final overall survival (OS) data from KEYNOTE-006 and new findings from KEYNOTE-001, including updated response rates, duration of response data and three-year OS data with KEYTRUDA® (pembrolizumab), the company's anti-PD-1 therapy, in patients with unresectable or metastatic melanoma. Findings from the final OS analysis from KEYNOTE-006, a phase 3 study evaluating KEYTRUDA as monotherapy compared to ipilimumab, continue to show a significant survival benefit compared to ipilimumab in the first-line setting for advanced melanoma. These data will be presented at the 52nd Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, June 3 – 7, 2016.

Long-term OS data from KEYNOTE-006 to be presented at ASCO showed that with KEYTRUDA, 55.1 percent and 55.3 percent of patients were alive two years after starting treatment (10 mg/kg every two weeks and three weeks, respectively), compared to 43 percent of patients receiving ipilimumab (hazard ratio: 0.68 [95% CI, 0.53-0.87;

p=0.0008] and hazard ratio: 0.68 [95% CI, 0.53-0.86; p=0.0008], respectively). These data will be presented by Dr. Jacob Schachter, Ella Institute for Research and Treatment of Melanoma, Sheba Medical Center, in an oral session on Monday, June 6, from 2:27 to 2:39 p.m. CDT (Location: Arie Crown Theater) (Abstract #9504).

Additionally, data from KEYNOTE-001, including the long-term, three-year OS analysis, were featured in the official ASCO Press Program today and will be presented at ASCO in Chicago. The primary efficacy measure in KEYNOTE-001 was overall response rate (ORR), and secondary outcome measures included duration of response, progression-free survival (PFS) and OS. The data from KEYNOTE-001 discussed today will be presented along with additional findings in an oral session by Dr. Caroline Robert, Institut Gustave-Roussy, on Monday, June 6, from 2:15 to 2:27 p.m. CDT (Location: Arie Crown Theater) (Abstract #9503).

"With longer-term follow-up from two studies, including a head-to-head trial demonstrating superior survival compared to another immunotherapy, we are continuing to see durability of response with KEYTRUDA as monotherapy," said Dr. Roger Dansey, senior vice president and therapeutic area head, oncology late-stage development, Merck Research Laboratories. "These results add to the growing body of data supporting the use of KEYTRUDA as first-line treatment in advanced melanoma, and serve as an important reminder for what we are aiming to achieve through our immuno-oncology development program – enhanced survival for people with cancer."

Findings from the melanoma cohorts of the phase 1b KEYNOTE-001 trial, which included 655 patients, showed an ORR of 33 percent (per RECIST v1.1). At the time of the analysis, a response duration of two years or more was observed in 73 percent of patients. Long-term OS data showed an estimated 40 percent of patients were alive three years after starting treatment with

KEYTRUDA (pembrolizumab), with a median survival of 24.4 months (95% CI, 20.2-29.0). Median duration of response has not yet been reached (range, 1.3+ to 38.8+).

Data from KEYNOTE-001 served as the basis for the U.S. Food and Drug Administration's accelerated approval of KEYTRUDA in September 2014. The label was subsequently updated to reflect data from the KEYNOTE-006 (phase 3) and KEYNOTE-002 (phase 2) trials, expanding the indication to include treatment of first-line advanced melanoma regardless of BRAF status. Today, KEYTRUDA is approved for the treatment of advanced melanoma in more than 50 countries, including the United States and throughout Europe.

The KEYTRUDA clinical development program includes more than 30 tumor types in more than 270 clinical trials, including more than 100 trials that combine KEYTRUDA with other cancer treatments.

## Key Findings from the KEYNOTE-006 Study

KEYNOTE-006 is a global, open-label, randomized, pivotal, phase 3 study evaluating KEYTRUDA (pembrolizumab) compared to ipilimumab in patients with unresectable stage III or IV advanced melanoma with no more than one prior systemic therapy. The study randomized 834 patients to receive KEYTRUDA 10 mg/kg every three weeks, KEYTRUDA 10 mg/kg every two weeks, or four cycles of ipilimumab 3 mg/kg every three weeks. The co-primary endpoints were PFS and OS; secondary endpoints were ORR, duration of response and safety, with an exploratory analysis for health-related quality of life (QoL). Tumor response was assessed at week 12, then every 6 weeks thereafter per RECIST v1.1 by independent, central, blinded radiographic review and investigator-assessed, immune-related response criteria.

Based on data to be presented at ASCO, KEYTRUDA (10 mg/kg every two or three weeks) continued to provide superior OS, PFS and ORR compared to ipilimumab. Specifically, long-term OS data showed 55.1 percent and 55.3 percent of patients were alive two years after starting treatment with KEYTRUDA (every two weeks and three weeks, respectively) compared to 43 percent of patients receiving ipilimumab (hazard ratio: 0.68 [95% CI, 0.53-0.87; p=0.0008] and hazard ratio: 0.68 [95% CI, 0.53-0.86; p=0.0008], respectively). Median OS was not reached for KEYTRUDA; for ipilimumab, median OS was 16 months.

Additionally, an estimated 31.2 percent and 27.8 percent of patients receiving KEYTRUDA (every two weeks and three weeks, respectively) were alive and were disease progression-free at two years compared to 13.5 percent of patients receiving ipilimumab (hazard ratio: 0.61 [95% CI, 0.50-0.75; p<0.0001] for both). For patients receiving KEYTRUDA, ORR was 36.9 percent and 36.1 percent (every two weeks and three weeks, respectively) compared to 13.3 percent for patients receiving ipilimumab (p<0.0001 for both groups).

With longer follow-up, adverse events have remained consistent with previously reported safety data. There was one treatment-related death (due to sepsis) in the KEYTRUDA every two week group.

## Key Findings from the KEYNOTE-001 Study

KEYNOTE-001 is a phase 1b multicenter, open-label, multi-cohort trial evaluating KEYTRUDA in various advanced cancers, including advanced melanoma. Patients in the melanoma cohorts received 2 mg/kg or 10 mg/kg of KEYTRUDA every three weeks or 10 mg/kg of KEYTRUDA every two weeks until unacceptable toxicity or disease progression. The major efficacy outcome measure was confirmed ORR as assessed by blinded independent central review using RECIST v1.1. Tumor response was assessed every 12 weeks. The secondary outcome measures included PFS, OS and duration of response.

The findings to be presented at ASCO include updated response rates and duration of response data, as well as three-year OS data from the 655 patients with unresectable or metastatic melanoma and progression of disease. All

patients were followed for at least two years, with some being followed for almost four years (with median follow-up duration of 32 months).

Of those patients who responded to treatment with KEYTRUDA (pembrolizumab), a complete response (CR) was observed in 10 percent of patients. Among the 61 patients who stopped treatment once a complete response had occurred, the response duration ranged from 17+ to 44+ months (median duration not reached). Only two patients who had a complete response experienced disease progression after stopping treatment. In addition, long-term survival data showed that 40 percent of patients survived three years after starting treatment with KEYTRUDA (n=655).

With longer follow-up, adverse events have remained consistent with previously reported safety data. Immune-mediated treatment-related adverse events observed in this trial were hypothyroidism (9.6%), pneumonitis (4.3%), hyperthyroidism (2.3%), colitis (2.3%), uveitis (1.5%), hepatitis (0.9%), and nephritis (0.5%).

## 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 also 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.

## 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, including Grade 1 (0.8%), 2 (0.8%), and 3 (0.4%) pneumonitis. 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, including Grade 2 (0.5%), 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.

Immune-mediated hepatitis occurred in 16 (1%) of 1567 patients, 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, including Grade 2 (0.3%), 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.

Hyperthyroidism occurred in 51 (3.3%) of 1567 patients, including Grade 2 (0.6%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 127 (8.1%) of 1567 patients, including Grade 3 (0.1%) 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 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 7 (0.4%) of 1567 patients, 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 (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 1567 patients: 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.

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.

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; 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; 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 (pembrolizumab) 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 (pembrolizumab) 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.

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.

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 270 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](http://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](http://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](http://www.sec.gov)).

Please see Prescribing Information for KEYTRUDA (pembrolizumab) at [http://www.merck.com/product/usa/pi\\_circulars/k/keytruda/keytruda\\_pi.pdf](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](http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf).

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