Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with KEYTRUDA® (pembrolizumab) Presented at AACR Annual Meeting and Published in the New England Journal of Medicine

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Data Formed the Basis for KEYTRUDA U.S. FDA Submission and Breakthrough Therapy Designation in Advanced NSCLC

KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced new data from KEYNOTE-001, a Phase 1b study evaluating KEYTRUDA® (pembrolizumab), the company's anti-PD-1 therapy, in naïve and previously-treated patients with advanced non-small cell lung cancer (NSCLC). In an analysis of 313 patients from a validation data set for tumor PD-L1 expression, overall-response rate (ORR) was 45.2 percent (95% CI, 33.5-57.3) in patients with greater than or equal to (≥) 50 percent of tumor cells positive for PD-L1 expression (n=73). In the other PD-L1 subgroups, ORR was 16.5 percent (95% CI, 9.9-25.1) in patients with 1-49 percent tumor cells positive (n=103) and 10.7 percent (95% CI, 2.3-28.2) in patients with less than 1 percent tumor cells positive (n=28) for PD-L1 expression. In the total study population, ORR was 19.4 percent (95% CI, 16.0-23.2) (n=495), which was consistent with data previously presented from this study. These data from KEYNOTE-001 will be presented today by Dr. Edward Garon, Jonsson Comprehensive Cancer Center, University of California, Los Angeles at the American Association for Cancer Research (AACR) Annual Meeting (abstract #CT104), were part of the AACR press program, and were also published today in the New England Journal of Medicine.

The efficacy findings demonstrated that tumor PD-L1 expression may be a relevant biomarker for the identification of NSCLC patients with an enhanced likelihood of experiencing improved efficacy with an anti-PD-1 therapy. PD-L1 is a protein that may be overexpressed in the tumor and may contribute mechanistically to an inhibited immune response.

"In this study, NSCLC patients whose tumors express PD-L1 in the majority of their cells experienced the highest response rates to KEYTRUDA treatment," said Dr. Roger Perlmutter, president, Merck Research Laboratories. "The results from this study formed the basis for our Breakthrough Therapy designation and our recent FDA submission for advanced NSCLC, and indicate that tumor PD-L1 expression may be a relevant biomarker to identify patients more likely to have higher rates of response to KEYTRUDA in this tumor type."

Merck recently announced that the company submitted a supplemental Biologics License Application (sBLA) for KEYTRUDA in advanced NSCLC with the U.S. Food and Drug Administration (FDA). Under PDUFA, the FDA has 60 days from submission of the sBLA to determine if the application will be accepted for review. KEYTRUDA was granted Breakthrough Therapy designation in advanced NSCLC by the U.S Food and Drug Administration (FDA) in October 2014.

Additional Findings from KEYNOTE-001 for the Total Evaluable Population

Data for progression-free survival (PFS) and overall survival (OS) based on tumor PD-L1 expression was also presented in 356 naïve and previously-treated patients with advanced NSCLC (total evaluable for PD-L1 staining). In the ≥50 percent PD-L1 sub-group, median PFS (95% CI) was 6.3 months (2.9-12.5) (n=119); within this group, PFS was 6.1 months (2.1-12.5) for previously-treated patients (n=294) and 12.5 months (2.4-12.5) for naïve patients (n=62). PFS was 3.3 months (95% CI, 2.1-4.1) in the 1-49 percent PD-L1 sub-group (n=161), and 2.3 months (95% CI, 2.1-4.0) in less than 1 percent PD-L1 sub-group (n=76). Median OS had not yet been reached in the ≥50 percent PD-L1 sub-group, regardless of prior treatment. Median OS was 8.8 months for the other PD-L1 subgroups (95% CI, 6.8-12.4 for 1-49% sub-group and 5.5-12 for less than 1% sub-group, respectively), and was similar regardless of prior treatment.

Median duration of response was similar across tumor PD-L1 expression subgroups; 12.5 months (2.1+ to 23.3) for the ≥50 percent sub-group, 7.2 months (1.4+ to 8.3+) for the 1-49 percent sub-group, and not reached (1.0+ to 10.8+) in the less than 1 percent sub-group. At the time of analysis, median follow-up duration was 10.9 months (range, 5.2-27.5).

“These results represent the largest data set of an anti-PD-1 therapy in naïve and previously-treated patients with
advanced non-small cell lung cancer. We are advancing a broad Phase 3 program that will further characterize the potential benefit of KEYTRUDA compared to the standard of care in these patients,” said Roger Dansey, therapeutic area head and senior vice president, oncology late-stage development, Merck Research Laboratories.

Adverse events evaluated in the total study population were consistent with previously reported safety data for KEYTRUDA. The most common treatment-related adverse events were fatigue, pruritus, and decreased appetite. Grade 3-5 treatment-related adverse events occurred in 9.5 percent of patients (n=47). Treatment-related adverse events of an inflammatory or immune-mediated nature that occurred in more than 2 percent of patients were infusion-related reactions (n=15; 3.0%), hypothyroidism (n=34; 6.9%), and pneumonitis (n=18; 3.6%). One infusion reaction led to treatment discontinuation and all hypothyroidism cases were successfully managed with medical therapy. There was one treatment-related death (pneumonitis) and grade 3-5 pneumonitis was observed in 1.8 percent of patients (n=9). At the time of analysis, two pneumonitis cases were ongoing (both grade 1-2).

About the KEYNOTE-001 Study and tumor PD-L1 Validation Data Set

KEYNOTE-001 is an ongoing multi-center, single-arm, open-label phase 1b study evaluating KEYTRUDA in more than 1,000 patients with diverse late-stage cancers – predominantly lung and melanoma. Three dosing regimens were evaluated; 10mg/kg every two weeks, 10mg/kg every three weeks or 2mg/kg every three weeks. The primary endpoints include ORR and safety; the secondary endpoints include PFS, OS and duration of response. Tumor response was assessed every 9 weeks per RECIST 1.1 by independent, central, blinded radiographic review. For the tumor PD-L1 expression validation data set, tumor samples were contemporaneously collected within six months of staining and tumor PD-L1 expression was measured by Dako’s immunohistochemistry companion diagnostic test PD-L1™HC 22C3 PharmDx. The training data set for tumor PD-L1 expression from KEYNOTE-001 was presented at the AACR Annual Meeting in April 2014.

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 85 clinical trials – across more than 30 tumor types and more than 14,000 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.

Hyphophysitis 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 hyphophysitis. Administer corticosteroids for Grade 2 or greater hyphophysitis. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3; and permanently discontinue KEYTRUDA for Grade 4 hyphophysitis.

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. 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 hyperthyroidism 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, arthrits, 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 cellullitis.

The most common adverse reactions (reported in ≥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.

### About Lung Cancer

Lung cancer, which forms in the tissues of the lungs, usually within cells lining the air passages, is the leading cause of cancer death worldwide. Each year, more people die of lung cancer than die of colon, breast, and prostate cancers combined. The two main types of lung cancer are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC is the most common type of lung cancer, accounting for about 85 percent of all cases. The five-year relative survival rate for all advanced or metastatic (Stage IV) lung cancers combined is estimated to be four percent.

### About PD-L1 and PD-L1 Expression

PD-L1, also called programmed death-ligand 1, is a protein expressed on many types of cells, including some cancer cells. Under normal conditions, the interaction of PD-L1 with another protein, called programmed death receptor-1 (PD-1), serves as an important immune system checkpoint, keeping the immune system in balance and preventing the body from attacking its own cells when inflammation or an infection is present. When cancerous tumors express PD-L1, however, they are able to escape detection and destruction by cytotoxic T-cells – a type of cancer-killing immune cell – allowing the tumor to survive and grow. Tumor PD-L1 expression has been observed at varying levels across many tumor types, including breast, lung and bladder cancer. High levels of PD-L1 expression, called overexpression, are under investigation for potential use as a way to help identify patients with an enhanced likelihood to respond to certain immune-based treatment approaches.

### Our Focus on Cancer

Our goal is to translate breakthrough science into biomedical innovations to help people with cancer worldwide. For Merck Oncology, helping people fight cancer is our passion, supporting accessibility to our cancer medicines is our commitment, and pursuing research in immuno-oncology is our focus to potentially bring new hope to people with cancer. For more information about our oncology clinical trials, visit [www.merck.com/clinicaltrials](http://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](http://www.merck.com) and connect with us on [Twitter](https://twitter.com/merck), [Facebook](https://www.facebook.com/merck) and [YouTube](https://www.youtube.com/user/merck).

### 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).

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1 Original release distributed on Sunday, April 19, 2015 listed ORR as 45.4 percent; Release corrected on Wednesday, May 20, 2015 to reflect ORR of 45.2 percent

2 Original release distributed on Sunday, April 19, 2015 listed median duration of response for the ≥50 percent PD-L1 expression sub-group as 12.4 months (2+ to 22.8+); Release corrected on Wednesday, May 20, 2015 to reflect median duration of response for the ≥50 percent PD-L1 expression sub-group as 12.5 months (2.1+ to 23.3)

3 Original release distributed on Sunday, April 19, 2015 listed median duration of response for the 1-49 percent PD-L1 expression sub-group as 10.3 months (1.4+ to 10.3+); Release corrected on Wednesday, May 20, 2015 to reflect median duration of response for the 1-49 percent PD-L1 expression sub-group as 7.2 months (1.4+ to 8.3+)

4 Original release distributed on Sunday, April 19, 2015 listed median duration of response for the less than 1 percent PD-L1 expression sub-group as not reached (0.9+ to 10.8+); Release corrected on Wednesday, May 20, 2015 to reflect median duration of response for the less than 1 percent PD-L1 expression sub-group as not reached (1.0+ to 10.8+)

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