News Release

FOR IMMEDIATE RELEASE

FDA Approves Expanded Indication for Merck's KEYTRUDA® (pembrolizumab) for the Treatment of Patients with Advanced Melanoma

KEYTRUDA is Now the First and Only Anti-PD-1 Therapy to Achieve Superior Overall Survival Compared to Ipilimumab

KENILWORTH, N.J., Dec. 18, 2015 – Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved an expanded indication for KEYTRUDA® (pembrolizumab), the company's anti-PD-1 (programmed death receptor-1) therapy, to include the first-line treatment of patients with unresectable or metastatic melanoma. This approval marks the second FDA-approved indication in advanced melanoma for KEYTRUDA, which is now the first anti-PD-1 therapy approved for previously untreated advanced melanoma patients regardless of BRAF status. The FDA-approved dose of KEYTRUDA is 2 mg/kg every three weeks.

In a Phase 3 trial, KEYNOTE-006, patients with unresectable or metastatic melanoma who were treated with KEYTRUDA experienced superior overall survival (OS) compared to those treated with ipilimumab. In this study supporting the first-line approval, patients given KEYTRUDA 10 mg/kg every two weeks demonstrated a 37 percent reduction in the risk of death and those given KEYTRUDA 10 mg/kg every three weeks demonstrated a 31 percent reduction in the risk of death, both compared to ipilimumab (hazard ratio: 0.63 [95% CI: 0.47, 0.83; p<0.001] and hazard ratio: 0.69 [95% CI: 0.52, 0.90; p=0.004], respectively).

Immune-mediated adverse reactions occurred with KEYTRUDA including pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis. Based on the severity of the adverse reaction, KEYTRUDA should be withheld or discontinued and corticosteroids administered. For more information regarding immune-mediated adverse reactions, see "Selected Important Safety Information" below.

"As recently as five years ago, there were few treatment options for patients suffering from advanced melanoma," said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. "Today's news is another exciting milestone for KEYTRUDA and for patients with this disease. Data supporting the approval emerged from a large and diverse patient population, including patients with very advanced disease and patients whose tumors carried BRAF mutations, thus demonstrating both

the breadth of our clinical development program for KEYTRUDA, and the potential of KEYTRUDA to extend the lives of those afflicted with this grievous malignancy."

KEYTRUDA (pembrolizumab) 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.

"This growing body of evidence in patients with advanced melanoma supports the expanded indication for KEYTRUDA," said Dr. Omid Hamid, Director of the Melanoma Center at The Angeles Clinic and Research Institute, and a principal investigator for the KEYTRUDA melanoma clinical program. "This approval highlights the importance of KEYTRUDA for advanced melanoma, where we are in need of additional treatment options."

Data Supporting First-Line Indication in Advanced Melanoma and KEYTRUDA Full Approval

The approval was based on data from a multicenter, controlled, Phase 3 study, KEYNOTE-006, which evaluated KEYTRUDA compared to ipilimumab in 834 patients with unresectable or metastatic melanoma with progression of disease; no prior therapy with ipilimumab; and prior therapy with at most one other systemic treatment. Patients were randomized (1:1:1) to receive KEYTRUDA at a dose of 10 mg/kg every two (n=279) or three weeks (n=277) until disease progression or unacceptable toxicity, or ipilimumab, the standard of care at the time of the study, at a dose of 3 mg/kg every three weeks for four doses unless discontinued earlier for disease progression or unacceptable toxicity (n=278). The primary efficacy outcome measures were OS and progression-free survival (PFS) (as assessed by Blinded Independent Central Review (BICR) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1). Secondary efficacy outcome measures were overall response rate (ORR) and response duration. KEYTRUDA 10 mg/kg every two or three weeks showed superior OS compared to ipilimumab (hazard ratio: 0.63 [95% CI: 0.47, 0.83; p<0.001] and hazard ratio: 0.69 [95% CI: 0.52, 0.90; p=0.004], respectively). Median PFS was 5.5 months (95% CI: 3.4, 6.9), 4.1 months (95% CI: 2.9, 6.9), and 2.8 months (95% CI: 2.8, 2.9) with KEYTRUDA 10 mg/kg every two weeks, KEYTRUDA 10 mg/kg every three weeks and ipilimumab, respectively. For PFS, both schedules for KEYTRUDA 10 mg/kg every two or three weeks resulted in superior outcomes compared to ipilimumab (hazard ratio: 0.58 [95% CI: 0.46, 0.72; p<0.001] and hazard ratio: 0.58 [95% CI: 0.47, 0.72; p<0.001], respectively). KEYTRUDA every two or three weeks demonstrated a 42 percent reduction in the risk of disease progression or death as compared to ipilimumab. The ORR was 34 percent (95% CI: 28, 40) with KEYTRUDA 10 mg/kg every two weeks and 33 percent (95% CI: 27, 39) with KEYTRUDA (pembrolizumab) 10 mg/kg every three weeks, as compared with 12 percent

(95% CI: 8, 16) with ipilimumab. KEYTRUDA 10 mg/kg every two weeks and three weeks achieved partial response rates of 29 percent and 27 percent, respectively, and complete response rates of 5 percent and 6 percent, respectively; there was a 10 percent partial response rate and 1 percent complete response rate for ipilimumab. Among the 94 patients randomized to KEYTRUDA 10 mg/kg every two weeks with an objective response, response durations ranged from 1.4+ to 8.2 months. Among the 91 patients randomized to KEYTRUDA 10 mg/kg every three weeks with an objective response, response durations ranged from 1.4+ to 8.1+ months.

Eighty percent of patients had PD-L1 positive melanoma, 18 percent had PD-L1 negative melanoma, and 2 percent had unknown PD-L1 status (positive: greater than or equal to 1 percent of tumor cells using an Investigational Use Only assay). BRAF mutations were reported in 36 percent of patients, of which 46 percent were previously treated with a BRAF-inhibitor. Patients with BRAF V600E mutated melanoma were not required to have received prior BRAF inhibitor therapy.

The most commonly reported adverse reactions were fatigue (28% with KEYTRUDA vs. 28% with ipilimumab), diarrhea (26% with KEYTRUDA), rash (24% with KEYTRUDA vs. 23% with ipilimumab), 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.

Severe and life-threatening infusion-related reactions have been reported in 3 (0.1%) of 2,117 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 four months after the last dose of KEYTRUDA.

FDA Approves Labeling Update in Advanced Melanoma: Supporting Data from KEYNOTE-002

Additionally, the FDA approved an update to the product labeling for KEYTRUDA for the treatment of patients with ipilimumab-refractory advanced melanoma. This update is based on results from the randomized Phase 2 trial, KEYNOTE-002, which demonstrated KEYTRUDA was superior to investigator’s choice chemotherapy.

KEYNOTE-002 is a multicenter, randomized controlled study of KEYTRUDA (pembrolizumab)

2 mg/kg every three weeks or 10 mg/kg every three weeks compared to investigator‘s choice chemotherapy (dacarbazine, temozolomide, carboplatin plus paclitaxel, paclitaxel, or carboplatin) in 540 patients with unresectable or metastatic melanoma with progression of disease; refractory to two or more doses of ipilimumab and, if BRAF V600 mutation positive, a BRAF or MEK inhibitor; and disease progression within 24 weeks following the last dose of ipilimumab. Patients on chemotherapy who experienced progression of disease were offered KEYTRUDA. Median PFS was 2.9 months (95% CI: 2.8, 3.8), 2.9 months (95% CI: 2.8, 4.7), and 2.7 months (95% CI: 2.5, 2.8) with KEYTRUDA 2 mg/kg every three weeks (n=180), KEYTRUDA 10 mg/kg every three weeks (n=181) and chemotherapy (n=179), respectively. Doses of KEYTRUDA 2 mg/kg or 10 mg/kg every three weeks were superior compared to chemotherapy for the PFS primary endpoint (hazard ratio: 0.57 [95% CI: 0.45, 0.73; p<0.001] and hazard ratio: 0.50 [95% CI: 0.39, 0.64; p<0.001], respectively). KEYTRUDA 2 mg/kg every three weeks demonstrated a 43 percent reduction in the risk of disease progression or death compared to chemotherapy. There was no statistically significant difference between KEYTRUDA and chemotherapy in the interim OS analysis. The ORR was 21 percent (95% CI: 15, 28) with KEYTRUDA 2 mg/kg every three weeks and 25 percent (95% CI: 19, 32) with KEYTRUDA 10 mg/kg every three weeks, as compared with 4 percent (95% CI: 2, 9) with chemotherapy. KEYTRUDA 2 mg/kg and 10 mg/kg every three weeks achieved partial response rates of 19 percent and 23 percent, respectively, and complete response rates of 2 percent and 3 percent, respectively; there was a 4 percent partial response rate and no complete responses for chemotherapy. Among the 38 patients randomized to KEYTRUDA 2 mg/kg with an objective response, response durations ranged from 1.3+ to 11.5+ months. Among the 46 patients randomized to KEYTRUDA 10 mg/kg with an objective response, response durations ranged from 1.1+ to 11.1+ months.

The most commonly reported adverse reactions were fatigue (43% with KEYTRUDA), pruritus (28% with KEYTRUDA vs. 8% with chemotherapy), rash (24% with KEYTRUDA vs. 8% with chemotherapy), constipation (22% with KEYTRUDA vs. 20% with chemotherapy), nausea (22% with KEYTRUDA), diarrhea (20% with KEYTRUDA vs. 20% with chemotherapy), 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 initially approved in 2014 under the FDA’s accelerated approval process for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. At the time of the initial approval, an improvement in survival or disease-related symptoms was not established. In accordance with the accelerated approval process, full approval was contingent upon verification and description of clinical benefit, which has now been demonstrated in KEYNOTE-002 and KEYNOTE-006.

Selected Important Safety Information for KEYTRUDA (pembrolizumab)

Immune-mediated pneumonitis, including fatal cases, occurred in patients receiving KEYTRUDA. Pneumonitis occurred in 32 (2%) of 1,567 patients with melanoma, including Grade 1 (0.8%), 2 (0.8%), and 3 (0.4%) pneumonitis. Pneumonitis occurred in 19 (3.5%) of 550 patients with non-small cell lung cancer (NSCLC), including Grade 2 (1.1%), 3 (1.3%), 4 (0.4%), or 5 (0.2%) 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 1,567 patients with melanoma, including Grade 2 (0.5%), 3 (1.1%), and 4 (0.1%) colitis. Immune-mediated colitis occurred in 4 (0.7%) of 550 patients with NSCLC, including Grade 2 (0.2%) or 3 (0.4%) 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 1,567 patients with melanoma, 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 1,567 patients with melanoma, including Grade 2 (0.3%), 3 (0.3%), and 4 (0.1%) hypophysitis. Hypophysitis occurred in 1 (0.2%) of 550 patients with NSCLC, which was Grade 3 in severity. 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 1,567 patients with melanoma, including Grade 2 (0.6%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 127 (8.1%) of 1,567 patients with melanoma, including Grade 3 (0.1%) hypothyroidism. Hyperthyroidism occurred in 10 (1.8%) of 550 patients with NSCLC, including Grade 2 (0.7%) or 3 (0.3%) hyperthyroidism. Hypothyroidism occurred in 38 (6.9%) of 550 patients with NSCLC, including Grade 2 (5.5%) or 3 (0.2%) 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 2,117 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA (pembrolizumab) and administer anti-hyperglycemics in patients with severe hyperglycemia.

Immune-mediated nephritis occurred in 7 (0.4%) of 1,567 patients with melanoma, including Grade 2 (0.2%), 3 (0.2%) and Grade 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 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 immune-mediated 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 with melanoma: 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. The following clinically significant, immune-mediated adverse reactions occurred in less than 1% of 550 patients with NSCLC: rash, vasculitis, hemolytic anemia, serum sickness, and myasthenia gravis.

Severe and life-threatening infusion-related reactions have been reported in 3 (0.1%) of 2,117 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 (pembrolizumab).

In Trial 6, 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 were fatigue (28% with KEYTRUDA vs. 28% with ipilimumab), diarrhea (26% with KEYTRUDA), rash (24% with KEYTRUDA vs. 23% with ipilimumab), 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 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 occurred in 14% of patients; the most common (≥1%) were dyspnea (1%), diarrhea (1%), and maculo-papular rash (1%). The most common adverse reactions were fatigue (43% with KEYTRUDA), pruritus (28% with KEYTRUDA vs. 8% with chemotherapy), rash (24% with KEYTRUDA vs. 8% with chemotherapy), constipation (22% with KEYTRUDA vs. 20% with chemotherapy), nausea (22% with KEYTRUDA), diarrhea (20% with KEYTRUDA vs. 20% with chemotherapy), 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 14% of 550 patients with NSCLC. Serious adverse reactions occurred in 38% of patients. The most frequent serious adverse reactions reported in 2% or more of patients were pleural effusion, pneumonia, dyspnea, pulmonary embolism, and pneumonitis. The most common adverse reactions (reported in at least 20% of patients) were fatigue (44%), decreased appetite (25%), cough (29%), and dyspnea (23%).

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.

Merck’s Commitment to Patients

Merck provides multiple programs to help ensure patients who are prescribed KEYTRUDA

have access to our anti-PD-1 therapy. The Merck Access Program provides reimbursement support for eligible patients receiving KEYTRUDA, including help with out-of-pocket costs and co-pay assistance. Merck also offers financial assistance for eligible patients who are uninsured through our patient assistance program. More information is available by calling 1-855-257-3932 or visiting www.merckaccessprogram-keytruda.com.

Merck also offers a 24/7 Patient Support program called KEY+YOU. The KEY+YOU program is staffed by compassionate nurses offering patients phone calls, email check-ins, wellness support, and referrals to community/peer groups as part of a comprehensive plan of support. A patient may enroll in the program by dialing 1-85-KEYTRUDA or visiting www.Keytruda.com.

About KEYTRUDA® (pembrolizumab) Injection 100 mg

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.

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. The NSCLC 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.

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 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 United States 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 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).

# # #

Please see Prescribing Information for KEYTRUDA (pembrolizumab) at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf and the Medication Guide for KEYTRUDA at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf

Media Contacts:	Pamela Eisele (267) 305-3558	Investor Contacts:	Teri Loxam (908) 740-1986
	An Phan (908) 255-6325		Justin Holko (908) 740-1879

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125514/S-4
BLA 125514/S-6

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Merck Sharp and Dohme Corp.
Attention: Ripal Shah, PharmD
Global Regulatory Affairs
126 East Lincoln Ave.
RY34-B292
P.O. Box 2000
Rahway, NJ 07065

Dear Dr. Shah:

Please refer to your Supplemental Biologics License Applications (sBLAs), dated March 25, 2015, received March 25, 2015, for Supplement #4 and dated June 19, 2015, received June 19, 2015, for Supplement #6 and to your amendments to both supplements, submitted under section 351(a) of the Public Health Service Act for Keytruda (pembrolizumab).

We acknowledge receipt of your major amendment dated June 25, 2015, for Supplement #4 which extended the goal date by three months.

These Prior Approval supplemental biologics applications provide for modifications of the approved indication for the treatment of patients with unresectable or metastatic melanoma approved on September 4, 2014, under the provisions of 21 CFR 601.70, to remove the following language (italicized) limiting the indication to patients with *disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor* and removing the statements that *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.* In addition, the WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS, and CLINICAL STUDIES sections of labeling have been revised with the results of the clinical trials verifying the clinical benefit of pembrolizumab in this population.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling text for the package insert and Medication Guide and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

SUBPART E FULFILLED

We approved this BLA under the regulations at 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of Supplements #4 and #6 fulfill the below postmarketing requirement (PMR #2770-1) made under 21 CFR 601.41.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENT

Approval of Supplements #4 and #6 fulfill the following postmarketing requirement listed in the September 4, 2014, approval letter for BLA 125514:

2770-1 Conduct and submit the results of a multicenter, randomized trial or trials establishing the superiority of pembrolizumab over standard therapy in adult patients with unresectable or metastatic melanoma who are refractory to ipilimumab or who have not been previously treated with ipilimumab.

You are no longer required to report on this requirement.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

3010-1 Submit the final clinical report and datasets at the time of the final analysis for overall survival (OS) for Trial P002, entitled "Randomized, Phase 2 Study of MK-3475 versus Chemotherapy in Patients with Advanced Melanoma", to revise the product label with mature OS data.

The timetable you submitted on December 2, 2015, states that you will submit the final clinical report and datasets according to the following schedule:

Final Report Submission: January 2017

3011-1 Submit the final clinical report and datasets at the time of the final analysis for overall survival (OS) for Trial P006, entitled "A Multicenter, Randomized, Controlled, Three-Arm, Phase III Study to Evaluate the Safety and Efficacy of Two Dosing Schedules of MK-3475 Compared to Ipilimumab in Patients with Advanced Melanoma", to revise the product label with mature OS data.

The timetable you submitted on December 2, 2015, states that you will submit the final clinical report and datasets according to the following schedule:

Final Report Submission: January 2017

Submit all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions,

including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, please call Ms. Sharon Sickafuse, Senior Regulatory Health Project Manager, at (301) 796-2320.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling