Pembrolizumab (KEYTRUDA) Checkpoint Inhibitor for the treatment of patients with metastatic non-small cell lung cancer (NSCLC)

Silver Springs, MD, USA (October 25, 2016) - On October 24, 2016, the U.S. Food and Drug Administration approved pembrolizumab (KEYTRUDA, Merck & Co., Inc.) 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.

This is the first FDA approval of a checkpoint inhibitor for first-line treatment of lung cancer. This approval also expands the indication in second-line treatment of lung cancer to include all patients with PD-L1-expressing NSCLC.

The FDA approval added the following indications for pembrolizumab:

- Patients with metastatic NSCLC whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] greater than or equal to 50%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC.
- Patients with metastatic NSCLC whose tumors express PD-L1 (TPS greater than or equal to 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 pembrolizumab.

Approval was based on results of two randomized, controlled trials that demonstrated statistically significant improvements in progression-free survival (PFS) and overall survival (OS) for patients randomized to pembrolizumab compared with chemotherapy.

In a trial of 305 patients who had no prior treatment for metastatic NSCLC and

TPS greater than or equal to 50%, those who received pembrolizumab (200 mg every 3 weeks) had a significant improvement in PFS (HR 0.50 [95% CI: 0.37, 0.68]; p<0.001) with a median PFS of 10.3 months versus 6.0 months for those receiving platinum-based chemotherapy. A pre-specified interim analysis demonstrated a statistically significant improvement in OS for patients randomized to pembrolizumab as compared with chemotherapy (HR 0.60 [95% CI: 0.41, 0.89]; p<0.005).

In a three-arm trial of 1033 patients who were previously treated for metastatic NSCLC with a TPS greater than or equal to 1%, those randomized to pembrolizumab 2 mg/kg every 3 weeks (HR 0.71 (95% CI: 0.58, 0.88]; p<0.001) or pembrolizumab 10 mg/kg every 3 weeks (HR 0.61 [95% CI: 0.49, 0.75]; p<0.001) had an improved OS compared with patients receiving docetaxel. The median survival was 10.4 months in the pembrolizumab 2 mg/kg arm, 12.7 months in the pembrolizumab 10 mg/kg arm, and 8.5 months in the docetaxel arm.

The most common side effects of treatment with pembrolizumab included decreased appetite, fatigue, nausea, dyspnea, cough, and constipation. Rare but serious adverse events included immune-mediated pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis.

The recommended dose and schedule of pembrolizumab for NSCLC is 200 mg intravenously every three weeks.

- FDA granted pembrolizumab breakthrough therapy designation and priority review status, and previously granted accelerated approval. The current approval converts the prior accelerated approval in second-line treatment of metastatic NSCLC patients to regular approval. The application for the first-line indication was approved nearly three months before the PDUFA goal date. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics, available at:

http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformati

on/guidances/ucm358301.pdf

- Full prescribing information is available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125514s012lbl.pdf

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System by completing a form online at http://www.fda.gov/medwatch/report.ht by faxing (1-800-FDA-0178) or mailing the postage-paid address form provided online, or by telephone (1-800-FDA-1088).

U.S. Food and Drug Administration , 25.10.2016 (tB).