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ALIMTA® Extends Survival in Continuation Maintenance Setting for Specific Lung Cancer Patients

FDA Approves New Use of ALIMTA (pemetrexed for injection) in the Continuation Maintenance Setting for Advanced Nonsquamous Non-Small Cell Lung Cancer

INDIANAPOLIS, Oct. 17, 2012 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that patients may receive ALIMTA® (pemetrexed for injection) as a maintenance therapy following first-line ALIMTA plus cisplatin for locally advanced or metastatic nonsquamous non-small cell lung cancer (NS NSCLC). The FDA approved the label inclusion of Phase III data that demonstrated progression-free and overall survival advantages in the continuation maintenance setting for these patients.

Appropriate patients can now start with ALIMTA plus cisplatin and continue with ALIMTA in the maintenance setting in advanced or metastatic NS NSCLC. ALIMTA is indicated for the maintenance treatment of patients with locally advanced or metastatic NS NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. ALIMTA is not indicated for patients with squamous-cell NSCLC. Myelosuppression is usually the dose-limiting toxicity with ALIMTA therapy.

"Continuation maintenance" involves continuing one of the same medicines prescribed in first-line treatment as maintenance therapy, in an effort to extend survival. It is the most recent addition to a new paradigm of maintenance treatment for advanced nonsquamous non-small cell lung cancer. Prior to the use of maintenance treatment, physicians typically treated a patient with four to six cycles of chemotherapy and then waited until the disease returned or worsened before resuming treatment.

"The approval provides patients and physicians with a new regimen that has demonstrated an improvement in overall survival. A survival benefit was previously established for ALIMTA for the first-line treatment of advanced nonsquamous non-small cell lung cancer in combination with cisplatin, and now as a single-agent for continuation maintenance treatment," said Richard Gaynor, M.D., vice president, product development and medical affairs for Lilly Oncology. "This is the first study to show a survival advantage for continuation maintenance, and it reinforces the role of ALIMTA in treating patients with advanced nonsquamous NSCLC."

In October 2011, the European Commission granted approval for the use of ALIMTA as a single agent for continuation maintenance in patients with advanced NS NSCLC based on progression-free survival and preliminary overall survival. On September 21, 2012, theCommittee for Medicinal Products for Human Use (CHMP) in the European Union issued a positive opinion for a label update for ALIMTA in the continuation maintenance setting for certain patients with advanced nonsquamous non-small cell lung cancer after initial treatment with ALIMTA plus cisplatin.

The FDA and European Commission approvals were based on results from PARAMOUNT, a global, multicenter, double-blind Phase III trial, the final results of which were shared in an oral presentation at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago, Ill. on June 4, 2012. PARAMOUNT was the first study to evaluate the first-line use of ALIMTA plus cisplatin therapy followed immediately by the use of ALIMTA as a single-agent in the continuation maintenance setting.

A total of 939 patients with advanced nonsquamous NSCLC were enrolled in the study and received ALIMTA (500 mg/m^2 on day one of a 21-day cycle) in combination with cisplatin (75 mg/m^2) induction therapy. All patients received vitamin B_{12}, folic acid and dexamethasone. Patients whose disease had not progressed during the ALIMTA plus cisplatin induction and who had an ECOG performance status of 0-1 (n=539) were randomized two-to-one to receive ALIMTA maintenance (500 mg/m^2 on day one of a 21-day cycle) plus best supportive care (n=359) or placebo plus best supportive care (n=180) until disease progression. Of the patients whose disease had not progressed during ALIMTA plus cisplatin induction therapy and who were randomized to receive maintenance therapy, 44% versus 42% achieved a complete or partial response to induction therapy and 53% versus 53% had stable disease after induction treatment in the ALIMTA and placebo arms, respectively.

Final results of the PARAMOUNT trial demonstrated a statistically significant 22 percent reduction in the risk of death (HR=0.78; 95% CI: 0.64—0.96; p=0.02) with ALIMTA, compared to placebo. This reduction in the risk of death resulted in an improved median overall survival from the time patients were randomized of 13.9 months median for patients receiving ALIMTA, compared to 11.0 months median for patients on the placebo arm.

Median progression-free survival measured from randomization was 4.1 months on the ALIMTA arm as compared to 2.8 months on the placebo arm with a hazard ratio of 0.62. Stated another way, the study showed that patients on the ALIMTA continuation maintenance arm had a 38 percent improvement of survival without disease worsening, compared to the placebo arm.

The most severe adverse reactions (grades 3-4) with ALIMTA as a single agent versus placebo, respectively, for these patients in the maintenance setting were anemia (4.8% vs 0.6%); neutropenia (3.9% vs 0%); fatigue (4.5% vs 0.6%).

Common adverse reactions (all grades) with ALIMTA as a single agent versus placebo, respectively, were anemia (15% vs 4.8%); neutropenia (9% vs 0.6%); fatigue (18% vs 11%); nausea (12% vs 2.4%); vomiting (6% vs 1.8%); mucositis/stomatitis (5% vs 2.4%); edema (5% vs 3.6%).

U.S. ALIMTA Approvals
In 2004, ALIMTA received consecutive approvals: it was the first agent to be approved in combination with cisplatin as a treatment for patients with malignant pleural mesothelioma, whose disease is unresectable or who are otherwise not candidates for curative surgery, and then as a single agent for the second-line treatment of patients with locally advanced or metastatic NSCLC after prior chemotherapy treatment.[1]

In 2008, ALIMTA, in combination with cisplatin, was approved as a first-line treatment for locally advanced or metastatic NSCLC for patients with nonsquamous histology. At the time of the first-line approval, the FDA also approved a change to the second-line indication. ALIMTA is now indicated as a single agent for the treatment of patients with locally advanced or metastatic, nonsquamous NSCLC after prior chemotherapy.

In 2009, ALIMTA was approved as a maintenance therapy for locally advanced or metastatic NSCLC, specifically for patients with a nonsquamous histology whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.

ALIMTA is not indicated for treatment of patients with squamous cell NSCLC. Myelosuppression is usually the dose-limiting toxicity with ALIMTA therapy.

About Non-Small Cell Lung Cancer (NSCLC)
Lung cancer has long been the most common cancer in the world, representing nearly 13 percent of all new cancers and causing nearly 1.4 million deaths annually.[2] About 85 percent of all lung cancers are NSCLC.[3] The liver, bones and brain are potential targets if the cancerous cells spread to other areas in the body.

NSCLC comprises a group of histologies or tumor types differentiated by cellular structure. Nonsquamous histology includes adenocarcinoma and large cell carcinoma, which account for more than half of all NSCLC diagnoses,[4] as well as histologies classified as "other."

About Lilly Oncology
For more than four decades, Lilly Oncology, a division of Eli Lilly and Company, has been dedicated to delivering innovative solutions that improve the care of people living with cancer. Because no two cancer patients are alike, Lilly Oncology is committed to developing novel treatment approaches. To learn more about Lilly's commitment to cancer, please visit www.LillyOncology.com.

About Eli Lilly and Company
Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers — through medicines and information — for some of the world's most urgent medical needs.

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Consumer Important Safety Information (ISI)

Important Safety Information for ALIMTA® (pemetrexed for injection)

What is the most important information that I should know about ALIMTA?
ALIMTA can suppress bone marrow function, which may cause low blood cell counts.

ALIMTA may not be appropriate for some patients.

If you are allergic to ALIMTA, tell your doctor because you should not receive it.

If you have liver or kidney problems, be sure to tell your doctor. Your dose of ALIMTA may have to be changed, or ALIMTA may not be right for you.

It is very important to take the following medications prior to and during your treatment with ALIMTA to lower your chances of harmful side effects:

- You must take folic acid every day by mouth beginning 7 days before your first dose of ALIMTA. You must keep taking folic acid every day during the time you are being treated with ALIMTA, and every day for 21 days after you receive your last dose of ALIMTA.
- Your doctor will give you vitamin B_{12} injections while you are getting treatment with ALIMTA. You will get your first vitamin B_{12} injection one week before your first dose of ALIMTA, and then about every 9 weeks during treatment.
- Your doctor will prescribe a medicine called a "corticosteroid" which you must take the day before, the day of, and the day after each treatment with ALIMTA to reduce rash.

You will have regular blood tests before and during your treatment with ALIMTA. Your doctor may adjust your dose of ALIMTA or delay your treatment based on the results of your blood test and on your general condition.

What should I tell my doctor before receiving ALIMTA?
If you think you are pregnant, are planning to become pregnant, or are nursing, please tell your healthcare team. ALIMTA may harm your unborn or nursing baby. Your physician may advise you to use effective contraception (birth control) to prevent pregnancy while you are being treated with ALIMTA.

Tell your doctor if you are taking other medicines, including prescription and nonprescription medicines, vitamins, and herbal supplements. ALIMTA and other medicines may affect each other, causing serious side effects. Especially, tell your doctor if you are taking medicines called "nonsteroidal anti-inflammatory drugs" (NSAIDs) for pain or swelling.

What are the possible side effects of ALIMTA?
Most patients taking ALIMTA will have side effects. Sometimes it is not always possible to tell whether ALIMTA, another medicine, or the cancer itself is causing these side effects.

Call your doctor right away if you have a fever, chills, diarrhea, or mouth sores. These symptoms could mean you have an infection, which may be severe and could lead to death.

The most common side effects of ALIMTA when given alone or in combination with cisplatin are:

- **Stomach upset, including nausea, vomiting, diarrhea, or constipation.** You can obtain medicines to help control some of these symptoms. Call your doctor if you get any of these symptoms.
- **Low blood cell counts:**
  - **Low red blood cells.** Low red blood cells may make you feel tired, get tired easily, appear pale, and become short of breath.
  - **Low white blood cells.** Low white blood cells may give you a greater chance for infection. If you have a fever (temperature above 100.4°F) or other signs of infection, call your doctor right away.
  - **Low platelets.** Low platelets give you a greater chance for bleeding. Your doctor will do blood tests to check your blood counts before and during treatment with ALIMTA.
- **Tiredness.** You may feel tired or weak for a few days after your ALIMTA treatments. If you have severe weakness or tiredness, call your doctor.
- **Redness or sores in your mouth, throat, on your lips or in the tube that connects your throat and stomach (esophagus).** You may get redness or sores in your mouth, throat, on your lips, or in your esophagus (stomatitis, pharyngitis, esophagitis) or you may feel pain or have difficulty when drinking or swallowing food. These symptoms may happen a few days after ALIMTA treatment. Talk with your doctor if you get any of these symptoms.
- **Loss of appetite.** You may lose your appetite and lose weight during your treatment. Talk to your doctor if this is a problem for you.
- **Rash.** You may get a rash or itching during treatment. These reactions usually appear between treatments with ALIMTA and usually go away before the next treatment. Skin reactions or rashes that include blistering or peeling may be severe and could lead to death. Call your doctor if you have any of these symptoms.

Talk with your doctor, nurse, or pharmacist about any side effect that bothers you or that doesn't go away.

These are not all the side effects of ALIMTA. For more information, ask your doctor, nurse, or pharmacist.

How is ALIMTA given?
ALIMTA is slowly infused (injected) into a vein. The injection or infusion will last about 10 minutes. You will usually receive ALIMTA once every 21 days (3 weeks).

For more information about all of the side effects of ALIMTA, please see the Patient Prescribing Information at http://pi.lilly.com/us/alimta-ppi.pdf, the full Prescribing Information at http://pi.lilly.com/us/alimta-pi.pdf, visit www.ALIMTA.com, or call 1-800-545-5979.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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This press release contains forward-looking statements about the potential of ALIMTA for the treatment of non-small cell lung cancer and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development, commercialization, and regulatory review. There is no guarantee that the product will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

[1] NOTE: The second-line NSCLC indication was approved under 21 CFR 314.500 et seq (Subpart H — Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) using a surrogate endpoint.

[2] World Health Organization International Agency for Research in Cancer, GLOBOCAN 2008, Section of Cancer Information, http://globocan.iarc.fr/factsheets/cancers/lung.asp, (Accessed June 20, 2012).

[3] American Cancer Society, "What Is Non-Small Cell Lung Cancer?," February 17, 2012, American Cancer Society, http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer, (Accessed June 20, 2012).

[4] American Cancer Society, "What Is Non-Small Cell Lung Cancer?," February 17, 2012, American Cancer Society, http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer, (Accessed June 20, 2012).

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