September 29, 2012

Lilly Releases Phase II Results for Monoclonal Antibody Ramucirumab in Lung Cancer

INDIANAPOLIS, Sept. 29, 2012 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced new data from two Phase II ramucirumab (IMC-1121B) trials in patients with non-small cell lung cancer (NSCLC). Results were presented today during the Lung Cancer — Metastatic Poster Session at the ESMO 2012 Congress (European Society for Medical Oncology), 1:00 p.m. — 2:00 p.m. CET, in Vienna, Austria.

Interim data for a study in chemotherapy-naive patients with advanced NSCLC treated with ramucirumab in combination with first-line ALIMTA® (pemetrexed for injection)/platinum-based chemotherapy (Abstract #1245) and final data for a study in patients treated with ramucirumab in combination with paclitaxel/carboplatinum chemotherapy (Abstract#1287) were presented. The pre-specified interim analysis of progression-free survival (PFS) (Abstract #1245) and final six-month PFS rate (Abstract #1287) support continued development of ramucirumab in lung cancer.

"We are encouraged by these results from two Phase II trials indicating ramucirumab may be beneficial to patients with non-small cell lung cancer," said Richard Gaynor, M.D., vice president, product development and medical affairs for Lilly Oncology. "These findings support our ongoing evaluation of ramucirumab for lung cancer patients and will need to be confirmed in larger pivotal studies."

Abstract # 1245
A randomized open-label Phase II study of 140 chemotherapy-naive patients investigated ramucirumab in combination with first-line chemotherapy in advanced nonsquamous NSCLC. Patients were randomized based on histology (nonsquamous [Arms A versus B]; squamous [Arms C versus D]). Enrollment of patients with squamous histology [Arms C versus D] is ongoing. Therapy in Arm A included Lilly's ALIMTA (500 mg/m^2) plus carboplatin (AUC=6) or cisplatin (75 mg/m^2) once every three weeks, while therapy in Arm B included ramucirumab (10 mg/kg), ALIMTA (500 mg/m^2) plus carboplatin (AUC=6) or cisplatin (75 mg/m^2) once every three weeks.

The primary endpoint for the interim analysis was PFS. Other interim endpoints included change in tumor size, disease control rate (DCR), and safety. Interim median PFS, based on a pre-specified analysis, was 4.3 months for Arm A, the control arm, and 6.3 months for Arm B, the experimental arm (hazard ratio, 0.48; 90% CI: 0.31-0.74). DCR was 72 percent for Arm A and 87 percent for Arm B.

The most frequently observed (> 10%) grade three or higher adverse events (AEs) on Arm B were thrombocytopenia (Arm B, 22% vs Arm A, 19%), neutropenia (18% vs 17%), fatigue (12% vs 17%), anemia (10% vs 16%), hypertension (10% vs 1%) and nausea (10% vs 7%).

Based on these interim analyses of PFS and acceptable tolerability and safety, investigators concluded that ramucirumab supports further study as a potential treatment with first-line platinum-based chemotherapy in nonsquamous NSCLC.

Abstract # 1287
An additional Phase II open-label study investigated ramucirumab in combination with paclitaxel and carboplatin as first-line therapy in patients with advanced NSCLC. Patients with squamous histology and treated brain metastases were allowed. Forty patients received treatment, receiving ramucirumab (10 mg/kg), paclitaxel (200mg/m^2) and carboplatin (AUC=6) on day one of a three-week cycle for up to six cycles, followed by maintenance ramucirumab.

The primary endpoint was PFS at six months. Secondary/exploratory endpoints were safety, overall response rate, overall survival rate at one year, pharmacokinetic and pharmacodynamic (PK/PD) profiles and immunogenicity. The overall DCR (CR+PR+SD) reached 90 percent and PFS at six months was 59.0 percent (95% CI = 41.3%-72.9%). Median PFS was 7.85 months.

The most frequently observed (> 5%) grade three or higher ramucirumab related AEs were neutropenia (13%), thrombocytopenia (10%), fatigue (8%) and febrile neutropenia (8%).

Investigators concluded that ramucirumab in combination with paclitaxel and carboplatin shows potential efficacy based on the overall DCR (CR+PR+SD) of 90 percent and PFS rate at 6 months of 59.0 percent, and is well tolerated by patients with

NSCLC in this Phase II study.

"Ramucirumab is one of the key molecules in Lilly's pipeline and represents one of the largest clinical programs currently underway at Lilly, with six Phase III trials ongoing around the globe including one in lung cancer," said Lilly's Gaynor. "With the breadth of ramucirumab trials we have underway, we have a tremendous opportunity to potentially affect how cancer patients across multiple tumors are being treated."

Notes to Editor

About Ramucirumab
Ramucirumab is a fully human IgG1 monoclonal antibody receptor antagonist designed to bind the extracellular domain of vascular endothelial growth factor (VEGF) receptor-2, thereby blocking the interaction of VEGF ligands (VEGF-A, VEGF-C, and VEGF-D) and inhibiting receptor activation. VEGF receptor 2 is considered a primary mediator of angiogenesis. When activated by VEGF ligands, VEGF receptor 2 promotes endothelial cell proliferation and survival, migration, and vascular permeability.

Ramucirumab, which Lilly gained through its 2008 acquisition of ImClone Systems, is being investigated in clinical trials as monotherapy and in combination with other anticancer therapies.

for the treatment of breast cancer, gastric cancer, non-small cell lung cancer, colorectal cancer, hepatocellular carcinoma, bladder cancer, urethra cancer, ureter cancer, renal pelvis carcinoma, prostate cancer, ovarian cancer and glioblastoma multiforme. It is in late-stage clinical evaluation for the treatment of breast, colorectal, gastric, hepatocellular and lung cancer.

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.[1] About 85 — 90 percent of all lung cancers are NSCLC.[2] The liver, bones and brain are potential targets if the cancerous cells enter the bloodstream.

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,[3] as well as histologies classified as 'other.'

For more information on NSCLC, please visit www.lillyoncologynewsroom.com.

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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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.

Your doctor will prescribe a medicine called a "corticosteroid" to take for 3 days during each treatment with ALIMTA. Corticosteroids lower your chances for getting skin reactions with ALIMTA.

It is very important to take folic acid and vitamin B_{12} prior to and during your treatment with ALIMTA to lower your chances of harmful side effects.

- You must take folic acid every day for at least 5 days out of the 7 days before your first dose of ALIMTA. You must keep taking folic acid every day during the time you are getting treatment with ALIMTA, and for 21 days after your last treatment.
- 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 during the week before your first dose of ALIMTA, and then about every 9 weeks during treatment.

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.
- **Mouth, throat, lip, or food pipe sores** (stomatitis, pharyngitis, esophagitis). You may get redness or sores in your mouth, throat, or on your lips, or you may feel pain or 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 talk with your healthcare team, see the Patient Prescribing Information and full Prescribing Information accompanying this booklet, 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.

This press release contains forward-looking statements about the potential of ramucirumab as a treatment of various cancers and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that the product will 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] 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).

[2] American Cancer Society, "What Is Non-Small Cell Lung Cancer?," December 16, 2010, American Cancer Society, http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer, (October 20, 2011).

[3] American Cancer Society, "What Is Non-Small Cell Lung Cancer?," October 20, 2009, American Cancer Society, http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer, (October 20, 2011)..

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