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Lilly Announces Phase III Necitumumab Study Meets Primary Endpoint of Overall Survival

Study found improved overall survival in patients with stage IV squamous NSCLC

INDIANAPOLIS, Aug. 13, 2013 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that SQUIRE, a recently completed Phase III study, met its primary endpoint, finding that patients with stage IV metastatic squamous non-small cell lung cancer (NSCLC) experienced increased overall survival (OS) when administered necitumumab (IMC-11F8) in combination with gemcitabine and cisplatin as a first-line treatment, as compared to chemotherapy alone.

The most common adverse events occurring more frequently in patients on the necitumumab arm were rash and hypomagnesemia. Serious, but less frequent, adverse events occurring more often on the necitumumab arm included thromboembolism.

"We are pleased with these data which represent a potential advance in treatment for patients with squamous non-small cell lung cancer, which is a difficult cancer to treat," said Richard Gaynor, M.D., vice president, product development and medical affairs for Lilly Oncology. "If approved, necitumumab could be the first biologic therapy indicated to treat patients with squamous lung cancer."

Lung cancer is the leading cause of cancer death in the US and most other countries.[1] Non-small cell lung cancer (NSCLC) is much more common than other types of lung cancer, and accounts for 85 percent of all lung cancer cases.[2] Patients with squamous cell carcinoma represent about 30% of all patients affected by NSCLC.[1]

Lilly plans to present results from this study at a scientific meeting in 2014, and currently anticipates submitting to regulatory authorities before the end of 2014.

About the Study

SQUIRE enrolled 1093 patients (age greater than or equal to 18 years, ECOG PS 0-2) with histologically- or cytologically-confirmed, stage IV squamous NSCLC, who had received no prior therapy for metastatic disease. Patients were randomized to receive first-line necitumumab plus chemotherapy consisting of gemcitabine and cisplatin in study Arm A, or gemcitabine-cisplatin chemotherapy alone in study Arm B. Patients underwent radiographic assessment of disease status (computed tomography or magnetic resonance imaging) every six weeks (+/- 3 days), until radiographic documentation of progressive disease (PD). Chemotherapy continued for a maximum of six cycles in each arm (or until there was radiographic documentation of PD, toxicity requiring cessation, or withdrawal of consent); patients in Arm A continued to receive necitumumab (IMC-11F8) until there was radiographic documentation of PD, toxicity requiring cessation, or withdrawal of consent.

About Necitumumab

Necitumumab is a fully human IgG1 monoclonal antibody that is designed to block the ligand binding site of the human epidermal growth factor receptor (EGFR). Activation of EGFR has been correlated with malignant progression, induction of angiogenesis and inhibition of apoptosis or cell death.

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. Additional information about Lilly is available at www.lilly.com.

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This press release contains forward-looking statements about the potential of necitumumab as a treatment for patients with squamous 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 and commercialization. There is no guarantee that future studies will be positive or that necitumumab will receive regulatory approvals or prove 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.

Important Safety Information for GEMZAR® (gemcitabine for injection)

Myelosuppression is usually the dose-limiting toxicity with GEMZAR therapy.

Contraindication
GEMZAR is contraindicated in patients with a known hypersensitivity to gemcitabine.

Warnings and Precautions
Patients receiving therapy with GEMZAR should be monitored closely by a physician experienced in the use of cancer chemotherapeutic agents.

Infusions of GEMZAR longer than 60 minutes or dosing more frequently than weekly resulted in an increased incidence of clinically significant hypotension, severe flu-like symptoms, myelosuppression, and asthenia. The half-life of GEMZAR is influenced by the length of the infusion.

Myelosuppression manifested by neutropenia, thrombocytopenia, and anemia occurs with GEMZAR as a single agent, and the risks are increased when GEMZAR is combined with other cytotoxic drugs. Patients should be monitored for myelosuppression during therapy including a complete blood count with differential prior to each dose.

Pulmonary toxicity, sometimes fatal, including interstitial pneumonitis, pulmonary fibrosis, pulmonary edema, and adult respiratory distress syndrome (ARDS), has been reported. The onset of pulmonary symptoms may occur up to 2 weeks after the last dose of GEMZAR. Discontinue GEMZAR in patients who develop unexplained dyspnea, with or without bronchospasm, or have any evidence of pulmonary toxicity. In some cases, these pulmonary events can lead to fatal respiratory failure despite discontinuation of therapy.

Hemolytic Uremic Syndrome (HUS), including fatalities from renal failure or the requirement of dialysis, can occur in patients treated with GEMZAR. Always monitor renal function prior to initiation of GEMZAR therapy and periodically during treatment. Use GEMZAR with caution in patients with renal impairment. Permanently discontinue GEMZAR in patients with HUS or severe renal impairment. Renal failure may not be reversible even with discontinuation of therapy.

Drug-induced liver injury, including liver failure and death, has been reported in patients receiving GEMZAR alone or in combination with other potentially hepatotoxic drugs. Administration of GEMZAR in patients with concurrent liver metastases or a preexisting medical history of hepatitis, alcoholism, or liver cirrhosis can lead to exacerbation of hepatic insufficiency. Assess hepatic function prior to initiation of GEMZAR and periodically during treatment. Discontinue GEMZAR in patients that develop severe liver injury.

GEMZAR can cause fetal harm when administered to a pregnant woman. Advise women of potential risks to the fetus.

GEMZAR is not indicated for use in combination with radiation therapy. When GEMZAR was administered within 7 days of receiving radiation therapy or concurrent with radiation therapy, toxicity of radiation therapy was increased. In a clinical trial, life-threatening mucositis, especially esophagitis and pneumonitis, occurred. Excessive toxicity has not been observed when GEMZAR is administered more than 7 days before or after radiation (nonconcurrent). Radiation recall has been reported in patients who receive GEMZAR after prior radiation.

Capillary Leak Syndrome (CLS) with severe consequences has been reported in patients receiving GEMZAR as a single agent or in combination with other chemotherapeutic agents. Discontinue GEMZAR if CLS develops during therapy.

Use in Specific Populations

GEMZAR is Pregnancy Category D. GEMZAR can cause fetal harm when administered to a pregnant woman. Based on its mechanism of action, GEMZAR is expected to result in adverse reproductive effects. It is not known whether GEMZAR is

excreted in human milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

The safety and efficacy of GEMZAR in pediatric patients have not been established.

No clinical studies have been conducted with gemcitabine in patients with decreased renal or hepatic function.

GEMZAR clearance is affected by age as well as gender.

Dose Modifications and Administration Guidelines

GEMZAR is for intravenous use only. Immediately and permanently discontinue GEMZAR for any of the following: unexplained dyspnea or other evidence of severe pulmonary toxicity, severe hepatic toxicity, Hemolytic Uremic Syndrome, or Capillary Leak Syndrome. Consider immediate discontinuation or dose modifications for severe nonhematologic toxicity according to the Dosage and Administration guidelines in the full Prescribing Information.

Serum creatinine, potassium, calcium, and magnesium should be monitored during combination therapy with cisplatin. See the manufacturers' prescribing information for more information on any drug indicated in combination with GEMZAR.

Abbreviated Adverse Reactions (%-incidence) — Patients receiving single-agent GEMZAR across 5 trials

The most severe adverse reactions (grades 3/4) in all patients receiving single-agent GEMZAR across five clinical trials were anemia (8), neutropenia (25), thrombocytopenia (5), hepatic transaminitis (increased ALT, 10; increased AST, 8), increased alkaline phosphatase (9), hyperbilirubinemia (3), nausea and vomiting (14), fever (2), and dyspnea (3).

The most common adverse reactions (all grades) in the same patient population were anemia (68), neutropenia (63), thrombocytopenia (24), increased ALT (68), increased AST (67), increased alkaline phosphatase (55), hyperbilirubinemia (13), proteinuria (45), hematuria (35), increased BUN (16), increased creatinine (8), nausea and vomiting (69), fever (41), rash (30), dyspnea (23), diarrhea (19), hemorrhage (17), infection (16), alopecia (15), stomatitis (11), somnolence (11), and paresthesias (10).

Abbreviated Adverse Reactions (%-incidence) – 1st-line advanced NSCLC

The most severe adverse reactions (grades 3/4, with incidence of 5% or greater) with GEMZAR plus cisplatin for the first-line treatment of patients with NSCLC in comparative trials of a 28-day regimen (GEMZAR plus cisplatin versus cisplatin alone) and a 21-day regimen (GEMZAR plus cisplatin versus etoposide plus cisplatin), respectively, were neutropenia (57 vs 4, 64 vs 76); thrombocytopenia (50 vs 4, 55 vs 13); lymphopenia 28d (43 vs 17); anemia (25 vs 7, 22 vs 15); nausea and vomiting 21d (39 vs 26); nausea 28d (27 vs 21); vomiting 28d (23 vs 19); alopecia 21d (13 vs 51); neuromotor 28d (12 vs 3); hypomagnesemia 28d (7 vs 2); creatinine elevation 28d (5 vs 3); and infection (5 vs 1, 4 vs 8).

The most common adverse reactions (all grades, with incidence of 20% or greater) of the 28-day regimen (GEMZAR plus cisplatin versus cisplatin alone) and the 21-day regimen (GEMZAR plus cisplatin versus etoposide plus cisplatin), respectively, were anemia (89 vs 67, 88 vs 77); neutropenia (79 vs 20, 88 vs 87); thrombocytopenia (85 vs 13, 81 vs 45); lymphopenia 28d (75 vs 51); RBC transfusion (39 vs 13, 29 vs 21); platelet transfusions (21 vs 1, 3 vs 8); increased transaminases 28d (22 vs 10); nausea 28d (93 vs 87); vomiting 28d (78 vs 71); nausea and vomiting 21d (96 vs 86); alopecia (53 vs 33, 77 vs 92); creatinine elevation (38 vs 31, 2 vs 2); paresthesias 21d (38 vs 16); neuromotor 28d (35 vs 15); hyperglycemia 28d (30 vs 23); hypomagnesemia 28d (30 vs 17); infection (18 vs 12, 28 vs 21); neurohearing 28d (25 vs 21); diarrhea (24 vs 13, 14 vs 13); proteinuria (23 vs 18, 12 vs 5); neurosensory 28d (23 vs 18); hematuria (15 vs 13, 22 vs 10); and stomatitis (14 vs 5, 20 vs 18).

Abbreviated Adverse Reactions (%-incidence) – 1st-line metastatic breast cancer

The most severe adverse reactions (grades 3/4, with incidence of 5% or greater) with GEMZAR plus paclitaxel versus paclitaxel alone, respectively, for the treatment of patients with metastatic breast cancer were neutropenia (48 vs 11); anemia (7 vs 4); thrombocytopenia (6 vs 2); alopecia (18 vs 22); fatigue (7 vs 2); increased ALT (6 vs 1); and neuropathy-sensory (6 vs 3).

The most common adverse reactions (all grades, with incidence of 20% or greater) in the same patient population were anemia (69 vs 51); neutropenia (69 vs 31); thrombocytopenia (26 vs 7); leukopenia (21 vs 12); alopecia (90 vs 92); neuropathy-sensory (64 vs 58); nausea (50 vs 31); fatigue (40 vs 28); vomiting (29 vs 15); and diarrhea (20 vs 13).

Abbreviated Adverse Reactions (%-incidence) – Advanced recurrent ovarian cancer

The most severe adverse reactions (grades 3/4, with incidence of 5% or greater) with GEMZAR plus carboplatin versus carboplatin alone, respectively, for the treatment of patients with advanced ovarian cancer were neutropenia (71 vs 12);

thrombocytopenia (35 vs 11); anemia (28 vs 11); constipation (7 vs 3); nausea (6 vs 3); and vomiting (6 vs 3).

The most common adverse reactions (all grades, with incidence of 20% or greater) in the same patient population were neutropenia (90 vs 58); anemia (86 vs 75); thrombocytopenia (78 vs 57); RBC transfusion (38 vs 15); nausea (69 vs 61); alopecia (49 vs 17); vomiting (46 vs 36); constipation (42 vs 37); fatigue (40 vs 32); diarrhea (25 vs 14); and stomatitis/pharyngitis (22 vs 13).

For safety and dosing guidelines, see complete Warnings and Precautions, Adverse Reactions, and Dosage and Administration sections in the accompanying full Prescribing Information.

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[1] "Squamous cell carcinoma-similarities and differences among anatomical sites" - Am. J Cancer Re 2011;1(3):276)

[2] U.S. National Institutes of Health. National Cancer Institute: SEER Cancer Statistics Review, 1973-2006

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