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Lilly Targeted Agent Shows Promise in Treating Primary Brain Cancer

Investigational Oral, Targeted Agent Shrinks Tumor with Minimal Side Effects in Glioblastoma

INDIANAPOLIS, May 17, 2005 /PRNewswire-FirstCall via COMTEX/ -- Preliminary results from a Phase II clinical trial show patients with recurrent glioblastoma multiforme, a form of primary brain cancer, experienced a significant tumor response rate with minimal side effects when treated with enzastaurin, an oral, targeted agent under development at Eli Lilly and Company (LLY).(1) Enzastaurin is the first targeted agent of Lilly Oncology to enter into late stage clinical development heralding a new phase of innovation for the group, which has produced Gemzar(R) (gemcitabine HCl) and Alimta(R) (pemetrexed), two of the world's leading chemotherapy agents.

"Recurring glioblastoma is a desperate disease for which there are very few adequate treatments," said Howard Fine, M.D., chief of Neuro-Oncology at the National Cancer Institute and lead author of the study, which was presented today at the annual meeting of the American Society of Clinical Oncology (ASCO).

Glioblastoma, a type of brain cancer, is part of the larger group of tumors that impact the central nervous system, known as gliomas. Patients with highly recurrent glioblastoma are usually at a more advanced stage of the disease and correspondingly may face altered brain function or death due to the tumor's rapid growth rate. Radiation therapy is the most effective treatment following surgery. Almost all patients receive some form of radiation therapy. Gliomas -- tumors of the brain -- are among the most angiogenic of all tumors, meaning the tumor has the ability to grow by drawing on blood from surrounding vessels at a very rapid rate. The inhibition of tumor angiogenesis may offer the potential as a highly effective form of therapy.

The Phase II study presented at ASCO included 92 patients with recurrent glioblastoma who had failed more than one prior regimen of chemotherapy. Patients' treatment consisted of an oral fixed dose of 500 mg of enzastaurin, administered daily. Treatment was allowed to continue indefinitely depending upon the patient's response to the drug.

Results show that tumor shrinkage was evident in patients who received enzastaurin, with a corresponding response rate of 20 - 25 percent. Overall, enzastaurin was well tolerated in this patient population and clinical results show that patients experienced minimal side effects while administered enzastaurin. The most common side effect was thrombocytopenia, which is a low platelet count.

"Enzastaurin's mode of action is unique because it impacts tumor cells in multiple ways, while other targeted agents act on one pathway," said Richard Gaynor, M.D., vice president of cancer research and clinical investigation at Lilly.

Gaynor said that in the trial enzastaurin stopped the flow of blood to patients' tumors, resulting in disruption of tumor growth and -- in most cases -- tumor shrinkage. In addition to prohibiting angiogenesis of tumor cells, enzastaurin inhibits the cell pathway signaling through the PKC-beta and PI3 kinase/AKT pathways, two of the pathways that are vital to the survival of tumor cells.(2) These pathways are frequently activated in glioblastoma and because cancer cells don't follow the checks and balances seen in normal cells, the tumors grow unchecked. Furthermore, tumor-induced angiogenesis requires activation of these pathways. Enzastaurin causes tumor cells to turn off those survival signals. Consequently, enzastaurin has both direct tumor cell killing effects (apoptosis) and indirect, tumor-starving effects (antiangiogenesis) said Gaynor.

Gaynor said final results from the Phase II study are expected by 2006 and Lilly is currently designing the protocol for the Phase III study of enzastaurin in recurrent glioblastoma. The Phase III study will further verify the efficacy and safety of the drug in a larger patient population.

About Glioblastoma

Glioblastoma is the most aggressive and malignant form of glioma, a type of primary brain cancer. Surgery is often used to treat gliomas, along with radiation. However, since surgery and radiation fail to cure the disease, doctors may turn to additional radiation or chemotherapy. In early stages glioblastoma tumors often grow without symptoms and therefore can become quite large before symptoms arise. When the tumor becomes symptomatic, tumor growth is usually very rapid and is accompanied by altered brain function, and if left untreated the disease becomes lethal. Although primary treatment is often successful in temporarily stopping the progression of the tumor, glioblastomas almost always recur and become lethal.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class 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 . P-LLY

This press release contains forward-looking statements about the potential of the investigational compound enzastaurin (LY-317615) and reflects Lilly's current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development and regulatory review. There is no guarantee that the product will receive regulatory approvals, or that the regulatory approval will be for the indication(s) anticipated by the company. There is also no guarantee that the product will prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filing with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

Enzastaurin (LY-317615, Lilly)
Gemzar(R) (gemcitabine HCl), Lilly
Alimta(R) (pemetrexed), Lilly

(1) Results from a phase II trial of Enzastaurin HCl (LY317615) in patients with recurrent high grade gliomas; H. Fine, L. Kim, C. Royce, D. Draper, I. Haggarty, H. Elinzano, D. Thorton

(2) Results from clinical trial: The PKC-Beta selective inhibitor, Enzastaurin HCl (LY317615), suppresses GSK3Beta phosphorylation, induces apoptosis and suppresses growth of human colon cancer and glioblastoma xenografts; J. Graff, A. McNulty, K. Hanna, B. Konicek, R. Lynch, S. Bailey

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