



Phase II Data on Lilly's Antibody Show It Affects Amyloid Beta, a Protein Believed To Be Associated with Alzheimer's Disease

Findings lead to decision to start Phase III pivotal study of LY2062430 in 2009

CHICAGO, July 30, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY) today announced interim results of its Phase II study of LY2062430, an investigational anti-amyloid beta monoclonal antibody for the treatment of mild to moderate Alzheimer's disease. In this study, intravenously administered LY2062430 bound to the amyloid beta protein, resulting in increased amounts of amyloid beta in participants' blood and cerebrospinal fluid. These and other results suggest that by binding to soluble amyloid beta proteins, LY2062430 may begin to dissolve the amyloid plaques that are present in the brains of patients with Alzheimer's disease. While the precise cause of Alzheimer's disease is not known, it has been shown that people with this disorder have an excess of amyloid beta plaque in the brain, particularly in the regions associated with memory. It is theorized that decreasing the total amount of amyloid plaque and other forms of the amyloid beta protein in the brain may result in slowing of the disease progression. Importantly, LY2062430 was well tolerated with no evidence of treatment-related brain inflammation, bleeding or other side effects. The findings from this Phase II study were presented today at the Alzheimer's Association's 2008 International Conference on Alzheimer's Disease (ICAD) in Chicago.

In this randomized, controlled trial, researchers evaluated the safety and tolerability of LY2062430 administered intravenously in patients with Alzheimer's disease and in healthy volunteers. They assessed the effects of the antibody on levels of amyloid beta in the blood and cerebrospinal fluid, as an indirect measure of the effect of the antibody on amyloid beta present in the brain. Cerebrospinal fluid, which surrounds the brain and spinal cord, is thought to provide important biomarker data in addition to that obtained from blood. Amyloid plaques, the pathological hallmark of Alzheimer's disease, are composed largely of aggregated amyloid beta proteins. Amyloid plaques or other types of the amyloid beta protein are thought ultimately to disrupt normal nerve cell function in the brain, leading to the dementia that characterizes Alzheimer's disease.

"We are encouraged that in this study, we saw increased amyloid beta which is thought to be bound to LY2062430, in both the blood and cerebrospinal fluid. We hypothesize that this effect may lead to reduced formation of amyloid plaques in the brain after long-term treatment," said Eric Siemers, M.D., Medical Director, Alzheimer's disease research for Eli Lilly and Company. "Alzheimer's disease is complex, and there's a real need for new treatments that might be shown ultimately to slow disease progression. In addition to the biomarker results, we are particularly encouraged by the finding that patients who received the monoclonal antibody treatment over 12 weeks appeared to have no treatment-related side effects."

In this 12-week Phase II study, researchers gave 52 mild to moderate Alzheimer's disease patients infusions of placebo or LY2062430 in varying doses: 100mg or 400mg once a week, or 100mg or 400mg every four weeks. Alzheimer's disease symptom severity was also evaluated. In addition, 16 volunteers each received a single dose of 100mg of LY2062430 or placebo. For all study participants, safety assessments included magnetic resonance imaging (MRI) and cerebrospinal fluid examinations. A sub-study of 24 patients and 13 volunteers underwent single photon emission tomography (SPECT) scanning using an experimental tracer to assess levels of amyloid beta plaque in the brain.

The interim analysis showed that weekly infusions of LY2062430 up to 400mg per dose was well tolerated, with no side effects related to treatment. An evaluation of MRI brain imaging and an assessment of cerebrospinal fluid showed no evidence of brain inflammation or bleeding. As expected for a study of this duration, no change in patients' cognitive scores was observed and there was no change in levels of brain amyloid beta plaque as measured by the SPECT tracer. In addition to the increase in the two major forms of the amyloid beta protein seen in blood and cerebrospinal fluid, an increase in the two other types of the amyloid beta protein thought to be present only in amyloid plaques was observed in participants' blood and cerebrospinal fluid. The biomarker effects lasted for several weeks. These biomarker findings suggest that longer term treatment with LY2062430 may slow the clinical progression of Alzheimer's disease, thus providing a rationale for additional trials of LY2062430.

"Results from this Phase II study are promising, and we are pleased to announce our intention to commence a Phase III pivotal study of LY2062430 beginning in 2009," said Steven M. Paul, M.D., Executive Vice President, Science and Technology, President of Lilly Research Laboratories. "Additionally we are currently enrolling patients into the Phase III study called IDENTITY, which examines treatment with LY450139, an investigational gamma secretase inhibitor believed to slow the rate of formation of amyloid beta, potentially slowing disease progression. These two neuroscience pipeline candidates represent potentially important advances in the effort to slow the progression of this fatal disease, and demonstrate our longstanding commitment to developing treatments for devastating brain illnesses."

About Alzheimer's Disease

Alzheimer's disease is a progressive neurodegenerative condition that is the most common cause of dementia in patients over 65 years of age. Estimates show that 6-8 percent of people older than age 65 are affected by Alzheimer's disease(1), totaling approximately 5 million people in the United States alone(2). Every 72 seconds, an American is developing Alzheimer's disease (3), and it is the seventh-leading cause of death in the United States(4). The direct and indirect health care costs associated with Alzheimer's disease in the U.S. are estimated to be about \$150 billion(5). In 2005, the total cost worldwide was estimated at \$315.4 billion(6).

Given the aging population, without the availability of medicines that delay or prevent the onset of Alzheimer's disease, the number of affected people worldwide is expected to quadruple by the year 2050(7). The average duration between onset of symptoms and death due to complications of Alzheimer's disease is about 8-10 years(8). The burden to caregivers and health care costs can increase dramatically in the late stages of Alzheimer's disease, when patients cannot maintain independent function and are frequently bedridden.

About LY2062430

LY2062430 binds specifically to soluble amyloid beta and thereby alters the sticky characteristics of this peptide. Alzheimer's disease theory suggests that amyloid beta kills brain cells. Clinical studies have examined the ability of LY2062430 to impact amyloid beta in blood and cerebrospinal fluid and found significant dose-dependent changes. To date, the most frequently occurring side effect experienced in clinical studies with LY2062430 has been mild chills consistent with an infusion reaction. For a more complete listing of potential side effects, prospective clinical trial participants should refer to the informed consent document.

About Lilly

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

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This press release contains forward-looking statements about the potential of the investigational compound LY2062430 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.

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(2) Alzheimer's Association. "2008 Alzheimer's Disease Facts and Figures." Available at: http://www.alz.org/national/documents/report_alzfactsfigures2008.pdf . Accessed July 1, 2008.

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(4) Centers for Disease Control and Prevention. "National Vital Statistics Reports." Available at: http://www.cdc.gov/nchs/data/nvsr/nvsr55/nvsr55_19.pdf . Accessed July 1, 2008.

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(6) Wimoa, Anders, Bengt Winblada, and Linus J. Jonssonb. An estimate of the total worldwide societal costs of dementia in 2005. Alzheimer's & Dementia (2007) 3: 81-91.

(7) Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi M. Forecasting the Global Burden of Alzheimer's disease. Alzheimer's

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(8) National Institute on Aging. "Alzheimer's Disease Fact Sheet." Available at <http://www.nia.nih.gov/Alzheimers/Publications/adfact.htm> . Accessed July 1, 2008.

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