Lilly Halts Development of Semagacestat for Alzheimer's Disease Based on Preliminary Results of Phase III Clinical Trials

Decision does not affect other Lilly Alzheimer's compounds in development

INDIANAPOLIS, Aug 17, 2010 /PRNewswire via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY) will halt development of semagacestat, a gamma secretase inhibitor being studied as a potential treatment for Alzheimer's disease, because preliminary results from two ongoing long-term Phase III studies showed it did not slow disease progression and was associated with worsening of clinical measures of cognition and the ability to perform activities of daily living.

The company's decision does not affect the ongoing clinical trials of solanezumab, Lilly's other compound in Phase III trials as a potential Alzheimer's treatment. While both drugs focus on amyloid-beta proteins, which are believed to play a critical role in Alzheimer's disease, they have different mechanisms of action. Lilly also has two other compounds in earlier stages of clinical development; those studies are not affected by today's announcement.

In two pivotal Phase III trials, semagacestat was compared with placebo in more than 2,600 patients with mild-to-moderate Alzheimer's disease. Lilly has now reviewed data from a pre-planned interim analysis of semagacestat studies. This interim analysis showed that, as expected, cognition and the ability to complete activities of daily living of placebo-treated patients worsened. However, by these same measures, patients treated with semagacestat worsened to a statistically significantly greater degree than those treated with placebo. In addition, data showed semagacestat is associated with an increased risk of skin cancer compared with those who received placebo.

"This is disappointing news for the millions of Alzheimer's patients and their families worldwide who anxiously await a successful treatment for this devastating illness," said Jan M. Lundberg, Ph.D., Executive Vice President, Science and Technology, and President, Lilly Research Laboratories. "This is a setback, but Lilly's commitment to beating Alzheimer's will not waver."

Lilly is instructing clinical trial investigators for all semagacestat studies to contact study participants as soon as possible and tell them to immediately stop taking the study drug they have received. Study participants or caregivers should call their study physician to schedule their next appointment. Lilly has appropriately informed regulatory agencies and is providing instructions to investigators outlining the process for finalizing the studies.

Lilly's clinical team will continue to gather and evaluate data from these studies, and will publish the results for the benefit of future Alzheimer's research. Although dosing with semagacestat is being stopped, Lilly plans to continue collecting safety data, including cognitive scores, for at least six months through regularly scheduled follow-up visits with study physicians and modifications of the existing Phase III protocols. These additional follow-up visits will help to answer a number of important questions, including whether the differences between patients who received semagacestat and those who received placebo will continue after semagacestat has been discontinued. Other smaller short-term studies will be stopped and participants will receive appropriate follow-up.

The decision to halt development of semagacestat is expected to result in a third-quarter charge to earnings of approximately $.03 to $.04 per share. The company confirmed its previous 2010 earnings per share guidance range of $4.44 to $4.59 on a reported basis, or $4.50 to $4.65 on a non-GAAP basis.

"We are clearly disappointed by the results we are announcing today. However, Lilly's innovation strategy, based on advancing a pipeline of nearly 70 molecules currently in clinical development, does not rest on the success or failure of any single compound," said John C. Lechleiter Ph.D., Lilly's chairman and chief executive officer. "Pharmaceutical research always carries risk, as these results show. But it offers as well the potential for tremendous reward for millions of patients who await new medicines. Despite this and other recent setbacks, Eli Lilly and Company remains financially strong and is even more determined to prevail in our quest to provide new treatments for Alzheimer's and other serious diseases."

About Alzheimer's disease

Alzheimer's disease is a fatal form of dementia that causes progressive decline in memory and other aspects of cognition. It occurs when billions of neurons in the brain begin dying prematurely. Researchers don't know exactly what causes it, but the leading hypothesis is that amyloid beta plaques play an important role.

About semagacestat

Semagacestat is an oral agent designed to reduce the body's production of amyloid beta plaques, which scientists believe play an important role in causing Alzheimer's disease. Semagacestat is believed to block the activity of gamma secretase, an enzyme that is essential to the body's production of amyloid beta plaques. The compound's safety and efficacy are being tested in two Phase III clinical trials called IDENTITY and IDENTITY-2.

About the IDENTITY trials

IDENTITY (Interrupting Alzheimer's Dementia by EvaluatiNg Treatment of AmyloId PaThologY) and IDENTITY-2 are Lilly's Phase III placebo-controlled trials studying semagacestat, a gamma-secretase inhibitor being investigated as a potential treatment to slow the progression of mild to moderate Alzheimer's disease. Both Phase III trials are fully enrolled, with more than 2,600 patients from 31 countries, and include a treatment period of approximately 21 months. An open-label extension study (IDENTITY-XT) is available to all participants completing either study.

All study participants had to be at least 55 years old and meet the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria for probable Alzheimer's disease, with certain assessment scores indicating mild to moderate Alzheimer's disease. Patients with more advanced Alzheimer's disease were not included in the studies.

Use of approved treatments for Alzheimer's disease (including donepezil (Aricept), rivastigmine (Exelon), galantamine (Razadyne, RazadyneER), tacrine (Cognex) and memantine (Namenda)) is permitted during the study, provided that such medications had been given for at least 4 months and the dose had been unchanged for 2 months before study participants first received their study drug.

The primary objective of both IDENTITY trials was to determine whether semagacestat given orally would slow the decline associated with Alzheimer 's disease as compared with placebo. The study protocol calls for this to be evaluated periodically for 21 months after initiation of treatment for most patients. A participant's cognition and function are assessed using two 2 co-primary endpoints:

- the Alzheimer's disease Assessment Scale - Cognitive subscore (referred to as the ADAS-Cog11); and
- the Alzheimer's disease Cooperative Study - Activities of Daily Living Inventory (Referred to as the ADCS-ADL).

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.

This press release contains forward-looking statements that are based on management's current expectations, but actual results may differ materially due to various factors. There are significant risks and uncertainties in pharmaceutical research and development. There can be no guarantees with respect to pipeline products that the products will receive the necessary clinical and manufacturing regulatory approvals or that they will prove to be commercially successful. The company's results may also be affected by such factors as competitive developments affecting current products; rate of sales growth of recently launched products; the timing of anticipated regulatory approvals and launches of new products; regulatory actions regarding currently marketed products; other regulatory developments and government investigations; patent disputes and other litigation involving current and future products; the impact of governmental actions regarding pricing, importation, and reimbursement for pharmaceuticals, including U.S. health care reform; changes in tax law; asset impairments and restructuring charges; acquisitions and business development transactions; and the impact of exchange rates and global macroeconomic conditions. For additional information about the factors that affect the company's business, please see the company's latest Forms 10-Q and 10-K filed with the U.S. Securities and Exchange Commission. The company undertakes no duty to update forward-looking statements.

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