Lilly Presents Follow-Up Data on Semagacestat to Assist Future Alzheimer's Disease Research

INDIANAPOLIS, July 19, 2011 /PRNewswire/ -- Data were presented today from the first of two Phase III trials of semagacestat, including data from a 32 week follow-up period after dosing was halted in August 2010. Semagacestat is a gamma secretase inhibitor that had been studied as a potential treatment for Alzheimer's disease. Results shown today provided patient outcomes from the active treatment portion of the study and from a modified portion of the study conducted after dosing with semagacestat was stopped. Lilly presented the data during a plenary session at the Alzheimer's Association International Conference 2011 (AAIC 2011) in Paris, France.

The dosing in both semagacestat trials was halted in August 2010 because preliminary results from the two Phase III trials showed semagacestat did not slow Alzheimer's disease progression and was associated with worsening of clinical measures of cognition and the ability to perform activities of daily living. Lilly continued to gather data, including cognitive scores, for 32 weeks after dosing was stopped.

"When we made the decision to halt dosing in the trials, we committed to collecting this data in an effort to benefit future Alzheimer's research and to provide safety follow-up for the patients," said Eric Siemers, M.D., senior medical director for the Alzheimer's Disease Team at Eli Lilly and Company. "We have a great deal of appreciation and respect for the dedication of the patients and caregivers who remained committed to the semagacestat trials from the beginning until these follow-up data were collected. By obtaining this information, future research efforts can be guided much more effectively."

The study data confirmed preliminary results that showed that during the period of dosing, patients receiving semagacestat declined at a greater rate than patients taking placebo. During the follow-up period after dosing was halted, the cognitive and functional deficits of the patients initially treated with semagacestat remained worse than the deficits of patients initially treated with placebo. However, the course of the decline over time in the two groups did not diverge further after dosing was stopped.

Alzheimer's disease is a fatal form of dementia that causes progressive decline in memory and other aspects of cognition.(1) Researchers do not know exactly what causes Alzheimer's, but one hypothesis is that beta-amyloid protein plays an important role.(1,2)

"Although today we focused on what happened with semagacestat, the broader important point is that Lilly remains committed to Alzheimer's research and the Alzheimer's disease community," said Dr. Siemers. "We continue to move forward with the development of other molecules in our pipeline aimed at slowing the progression of Alzheimer's disease."

Study Methods

An external Data Monitoring Committee (DMC) was established prior to beginning the semagacestat IDENTITY studies so that they could monitor safety during the trials; unlike the patients and investigators, the DMC knew which patients were taking semagacestat and which patients were taking placebo. A planned analysis of the cognitive data by the DMC partway through the trial showed the increased rate of worsening, leading to the decision to discontinue dosing of semagacestat. The IDENTITY trials were then modified substantially in order to obtain more data for approximately seven months while the patients were no longer taking semagacestat. By studying the patients after stopping dosing, some of the factors that may have led to the increased cognitive decline could be more fully understood.

Study Findings

After 76 weeks of treatment with semagacestat or placebo, patients taking placebo (501 patients) worsened by 6.19 points on the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog11), which is approximately the amount of change expected for placebo-treated patients over this time period. Patients taking 100 mg semagacestat daily (506 patients) worsened by 7.29 points; patients taking 140 mg semagacestat (527 patients) worsened by 7.68 points. Over the seven months after stopping dosing of semagacestat, the differences between placebo- and semagacestat-treated patients were largely unchanged. The adverse effects seen in the IDENTITY trial were similar to those seen during Phase II studies. As disclosed previously and communicated to investigators, patients and regulators earlier in the trials, an increased rate of skin cancer was seen in patients taking semagacestat; this adverse effect was not seen in Phase II studies. The adverse events and laboratory abnormalities seen in the semagacestat-treated subjects resolved shortly after stopping dosing.

About Semagacestat

Semagacestat was an oral agent designed to reduce the body's production of beta-amyloid, 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 beta-amyloid.

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 about compounds currently in clinical development for Alzheimer's disease. It reflects Lilly's current beliefs; however, as with any such undertaking, there are substantial risks and uncertainties in the process of drug development and commercialization. There is no guarantee that any of these compounds will be approved by the relevant regulatory authorities or be commercially successful. For further discussion of these and other risks and uncertainties, please see Lilly's latest Forms 10-Q and 10-K filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

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(1)"Dementia: Hope Through Research." National Institute of Neurological Disorders and Stroke, National Institutes of Health. Available at: http://www.ninds.nih.gov/disorders/dementias/detail_dementia.htm. Accessed on June 28, 2011.

(2)Hardy, John & Selkoe, Dennis. "The Amyloid Hypothesis of Alzheimer's Disease: Progress and Problems on the Road to Therapeutics." Science 2002 (297); 353-356.

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