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Lilly Announces Detailed Results of the Phase 3 Solanezumab EXPEDITION Studies Following a Presentation of the Independent Analyses by the Alzheimer's Disease Cooperative Study (ADCS)

INDIANAPOLIS, Oct. 8, 2012 /PRNewswire/ --

- Lilly's analysis, as previously reported, showed primary endpoints, both cognitive and functional, were not met in the two Phase 3, double-blind, placebo-controlled solanezumab EXPEDITION trials in patients with mild-to-moderate Alzheimer's disease
- In Lilly's pre-specified secondary analysis of pooled data in patients with mild Alzheimer's disease, a statistically significant slowing of cognitive decline was shown; this finding represented a 34 percent reduction in decline
- Independent analyses of EXPEDITION studies conducted by the ADCS were generally similar to Lilly's top-line results reported on August 24, 2012
- Next steps for solanezumab will be determined after discussions with regulators

Eli Lilly and Company (NYSE: LLY) today announced its detailed results for the Phase 3, double-blind, placebo-controlled EXPEDITION studies in patients with mild-to-moderate Alzheimer's disease. This announcement follows the presentation of results from independent analyses of the EXPEDITION study data conducted by the Alzheimer's Disease Cooperative Study (ADCS), an academic research consortium, at the annual meeting of the American Neurological Association (ANA) by Rachelle Doody, M.D., Ph.D., professor of Neurology and the Effie Marie Cain Chair in Alzheimer's Disease Research, Baylor College of Medicine. Dr. Doody is a member of the steering committee for the ADCS.

Lilly provided the raw data (the full data set collected from the EXPEDITION studies) to the ADCS. The ADCS statisticians then performed independent analyses of these data. These results were presented at today's meeting.

"Alzheimer's disease research has been extremely challenging," said Dr. Doody. "The data results from the solanezumab Phase 3 trials were encouraging to the ADCS team. These results represent an important step for the medical, academic, and scientific communities in understanding brain amyloid as a target of AD therapies."

Lilly's relationship with the ADCS is longstanding and the decision to have them conduct independent analyses of the Phase 3 solanezumab data was made prior to seeing the top-line results from either of the EXPEDITION studies.

Lilly Results from EXPEDITION1

The EXPEDITION1 study was designed with co-primary cognitive and functional endpoints (the Alzheimer's Disease Assessment Scale- Cognitive subscale [ADAS-Cog_{11}] and the Alzheimer's Disease Cooperative Study-Activities of Daily Living [ADCS-ADL], respectively) in patients with mild-to-moderate Alzeimer's disease.

Lilly's pre-specified secondary analyses showed that results in patients with mild Alzheimer's disease taking solanezumab demonstrated a slowing of cognitive decline compared with placebo (p=.008), as measured by the ADAS- Cog_{11}. This finding represented a 42 percent reduction in decline at the endpoint of the 18-month study. The difference in functional decline (ADCS-ADL) was not statistically significant.

Lilly Results from EXPEDITION2

Based on the results of EXPEDITION1, Lilly modified the statistical analysis plan (SAP) for EXPEDITION2, prior to database lock, to specify a single primary endpoint of cognition in patients with mild Alzheimer's disease as measured by the ADAS-Cog_{14}, a 14-item scale, which includes three additional items considered relevant for patients with mild Alzheimer's disease.[1] At the conclusion of EXPEDITION2, there was a 20 percent reduction in cognitive decline in patients with mild Alzheimer's disease taking solanezumab; however, the treatment difference was not statistically significant (p=.120). In the pre-specified secondary endpoint of ADCS-ADL, there was a 19 percent reduction in functional decline in patients with mild Alzheimer's disease treated with solanezumab, as compared with placebo; this difference was not statistically significant (p=.076).

Lilly Results from Pooled Analyses of EXPEDITION1 and EXPEDITION2

A pre-specified secondary analysis of pooled data in patients with mild Alzheimer's disease showed a slowing of cognitive decline (p=.001) compared with placebo, as measured by the ADAS-Cog$_{14}$; this finding represented a 34 percent reduction in decline. In addition, the secondary analysis of the pooled data in patients with mild Alzheimer's disease showed a 17 percent reduction of functional decline as measured by the ADCS-ADL; however, the treatment difference was not statistically significant compared with placebo (p=.057).

A number of different biomarkers were assessed in the EXPEDITION studies. Some, but not all, of these biomarkers showed an effect of solanezumab. These additional data will be presented by the ADCS at the Clinical Trials on Alzheimer's Disease (CTAD) meeting in Monte Carlo, Monaco, on October 29, 2012, or at subsequent medical meetings and in appropriate scientific venues.

In the EXPEDITION studies, the only adverse event with an incidence of at least 1 percent that occurred statistically significantly more in the solanezumab group than in the placebo group was angina (1.1 percent versus 0.2 percent). The incidence of vasogenic edema (ARIA-E) was approximately 1 percent, occurring in 11 patients treated with solanezumab and 5 patients on placebo, which was not statistically significant.

"This is a complex disease that touches millions of people worldwide," said David Ricks, senior vice president and president, Lilly Bio-Medicines. "Alzheimer's disease causes significant burden on patients, caregivers and our society. While the path forward has not been determined, we believe these data in patients with mild disease may provide a step toward a potential treatment option."

About the Primary Endpoint Scales[2]

The ADAS-Cog is a standard tool used in pivotal clinical trials to detect therapeutic efficacy in cognition. It consists of subtests related to memory, praxis, and language. Higher scores on the ADAS-Cog indicate more cognitive impairment. The ADCS-ADL measures activities of daily living, such as reading books or magazines, pastime activities, or household chores. Higher scores on the ADCS-ADL indicate less functional impairment.

About the EXPEDITION Trials

The EXPEDITION trials consisted of two Phase 3, double-blind, placebo-controlled solanezumab trials in patients with mild-to-moderate Alzheimer's disease in 16 countries around the world. In both of the EXPEDITION study protocols, mild Alzheimer's disease was defined as a baseline Mini-Mental Status Examination (MMSE) score of 20 to 26 and moderate Alzheimer's disease was defined as a baseline MMSE score of 16 to 19.

The designs of EXPEDITION1 and EXPEDITION2 were the same. Patients aged 55-94 years were eligible to enroll in these studies; EXPEDITION1 enrolled 1,012 patients and EXPEDITION2 enrolled 1,040 patients. Patients received either 400mg of solanezumab infused intravenously (IV) or placebo every four weeks for approximately 18 months. Both EXPEDITION trials allowed patients to remain on stable standard of care (defined as their existing treatment regimen) during these studies. More than 85 percent of the patients in these trials were taking an acetycholinesterase inhibitor and / or memantine.

About Alzheimer's disease

Alzheimer's disease, the most common form of dementia, causes progressive decline in memory and other aspects of cognition.[3,4] Researchers do not know exactly what causes Alzheimer's disease and there are currently no approved treatments shown to slow the progression of this devastating disease, only treatment options that reduce certain symptoms of the disease.[2,3,5] Alzheimer's Disease International (ADI) estimates that there are currently 35.6 million people with dementia worldwide, with 7.7 million new cases each year (which implies one new case every four seconds).[6] The number of people affected is estimated to be over 115 million by 2050.[4] Estimates vary, but experts suggest that as many as 5.4 million Americans may have Alzheimer's disease.[3]

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. P-LLY

This press release contains certain forward-looking statements about solanezumab. This release 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 study results and patient experience will be consistent with study findings to date, or that solanezumab will be approved as a product or will 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.

[1] Mohs R, Knopman D, Petersen RC, Ferris SH, Ernesto C, Grundman M, Sano M, Bieliauskas L, Geldmacher D, Clark C, Thal LJ, and the Alzheimer's Disease Cooperative Study. Development of cognitive instruments for use in clinical trials of antidementia drugs: additions to the Alzheimer's Disease Assessment Scale that broadens its scope. Alzheimer Dis Assoc Disord 1997;11(Suppl 2):S13-S21.

[2] Robert P, Ferris S, Gauthier S, Ihl R, Winblad B, Tennigkeit F. Review of Alzheimer's disease Scales: Is There a Need for a New Multi-domain Scale for Therapy Evaluation in Medical Practice?. *Alzheimer's Research & Therapy*. 2010; 2(24): 1-13.

[3] National Institute of Neurological Disorders and Stroke. "Dementia: Hope Through Research." Available at: http://www.ninds.nih.gov/disorders/dementias/detail_dementia.htm#1908919213. Accessed on August 13, 2012.

[4] Alzheimer's Association. "2012 Alzheimer's Disease Facts and Figures." Available at: http://www.alz.org/downloads/facts_figures_2012.pdf. Accessed on August 13, 2012.

[5] Perrin, R., et al. "Multimodal techniques for diagnosis and prognosis of Alzheimer's disease." *Nature* 2009 (461); 916-922.

[6] Alzheimer's Disease International. "Dementia Statistics." Available at: http://www.alz.co.uk/research/statistics. Accessed on August 13, 2012.

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