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Lilly Announces Detailed Results of Solanezumab Phase 3 EXPEDITION3 Study at the Clinical Trials on Alzheimer's Disease (CTAD) 2016 Meeting

INDIANAPOLIS, Dec. 8, 2016 /CNW/ -- Eli Lilly and Company (NYSE:LLY) today presented detailed results of its phase 3 EXPEDITION3 trial at the 9th Clinical Trials on Alzheimer's Disease (CTAD) meeting. As previously disclosed, solanezumab did not meet the primary endpoint in the EXPEDITION3 clinical trial, a study of solanezumab initiated in people with mild dementia due to Alzheimer's disease (AD), and Lilly will not pursue regulatory submissions for solanezumab for the treatment of mild dementia due to AD.

"The results of EXPEDTION3 are without question disappointing," said Eric Siemers, M.D., distinguished medical fellow at Lilly. "However, Lilly remains committed to finding solutions for this devastating disease. We will continue to analyze study results and work with the external scientific community in the hopes of uncovering findings that will help shape and advance future Alzheimer's disease research."

Lawrence S. Honig, M.D., Ph.D., professor of neurology at Columbia University Medical Center and principal investigator of the EXPEDITION3 study, presented the data at the meeting.

"Alzheimer's is a challenging disease that researchers have been committed to studying for some years," Dr. Honig said. "Now is not the time to give up. While the outcome of this study is not what we had hoped for, it is reasonable to believe that disease modifying therapies to slow down the progression of Alzheimer's disease will be discovered."

A Summary of Key Results

While the study results, including many secondary clinical endpoints, directionally favored solanezumab, the magnitudes of treatment differences were small.

Primary Endpoint

- Patients treated with solanezumab did not experience a statistically significant slowing in cognitive decline compared to patients treated with placebo. This finding represented an 11 percent reduction in decline (p=.095), as measured by the Alzheimer's Disease Assessment Scale-Cognitive ($ADAS\text{-}Cog_{14}$) subscale. The $ADAS\text{-}Cog_{14}$ measures a person's cognitive functions, including memory, attention and language abilities.[1]

Key Secondary Clinical Endpoints

As the primary endpoint was not met in this study, the p-values for the efficacy secondary statistical analyses were not adjusted for multiple comparisons.

- Patients treated with solanezumab had a 13 percent slowing of cognitive decline (p=0.014) compared to patients treated with placebo as measured by the Mini-Mental State Examination (MMSE). The MMSE is the most commonly used test for complaints of problems with memory or other mental abilities and can be used by clinicians to help diagnose dementia and to help assess its progression and severity. It consists of a series of questions and tests, each of which scores points if answered correctly. The MMSE tests a number of different mental abilities, including a person's memory, attention and language.[2]
- The Clinical Dementia Rating-Sum of Boxes (CDR-SB) scale showed a 15 percent slowing in decline (p=0.004) between patients treated with solanezumab and patients treated with placebo. The CDR-SB scale measures cognitive and functional performance — in areas such as memory, orientation and personal care — through semi-structured interviews of patients and their family members or other reliable informants.[3]
- Patients treated with solanezumab had a slowing of decline in complex activities of daily living compared to patients treated with placebo. This finding represented a 14 percent slowing of decline (p=.019) as measured by the Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-iADL). The ADCS-iADL scale measures a person's independent performance in complex activities of daily living such as participating in a conversation, preparing a meal or shopping.[4]
- A different functional measure, the FAQ (Functional Activities Questionnaire), did not show a statistically significant difference between patients treated with solanezumab and patients treated with placebo (7 percent reduction in

decline, p=0.140). The FAQ scale is a different informant-based measure of functional abilities. Informants provide performance ratings of the patient on ten complex higher-order activities.[5]

Biomarkers

Changes in plasma a-beta were similar to those seen in previous studies, and the differences between treatment and placebo groups were statistically significant. Changes in amyloid deposition as measured by positron emission tomography (PET) imaging did not reach statistical significance between treatment and placebo groups.

Adverse events

- Events more frequent in the solanezumab treatment group that were statistically significant include: spinal osteoarthritis (1.1 percent in the solanezumab group, 0.4 percent in the placebo group), dysuria (0.9 percent in the solanezumab group, 0.2 percent in the placebo group), vitamin D deficiency (1.4 percent in the solanezumab group, 0.6 percent in the placebo group), and nasal congestion (1.2 percent in the solanezumab group, 0.4 percent in the placebo group).
- The incidence of vasogenic edema (ARIA-E or amyloid-related imaging abnormality-edema/effusions) was approximately 0.1 percent of patients treated with solanezumab and 0.3 percent of patients on placebo.

About Solanezumab

Solanezumab is Lilly's phase 3 monoclonal antibody being studied as a potential therapy for people with mild cognitive impairment due to Alzheimer's disease (EXPEDITION-PRO), preclinical Alzheimer's disease (Anti-Amyloid Treatment in Asymptomatic Alzheimer's "A4"), and Dominantly Inherited Alzheimer's Disease ("DIAN").

About EXPEDITION3

EXPEDITION3 is a multinational, phase 3 trial of solanezumab in more than 2,100 patients diagnosed with mild dementia due to Alzheimer's disease. The study includes an 18-month placebo-controlled period followed by an open label extension. Enrollment was completed in 2015 and the last patient visit for the placebo-controlled period occurred in October 2016. EXPEDITION3 is the first phase 3 trial to evaluate only people with mild dementia due to Alzheimer's disease.

About Alzheimer's Disease

Alzheimer's disease is a fatal illness that is believed to start with changes in the brain that may begin 20 years or more before symptoms appear.[6] Those changes cause a progressive decline in memory and other aspects of cognition that eventually lead to dementia.

Dementia due to Alzheimer's disease is the most common form of dementia, accounting for 60 to 80 percent of dementia cases.[6] There are currently an estimated 47 million people living with dementia worldwide.[7] The number of people affected by dementia is expected to be nearly 75 million in 2030 and 131 million in 2050.[7] Estimates vary, but experts suggest that as many as 5.4 million Americans may have Alzheimer's disease.[6]

About Eli Lilly and Company
Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and newsroom.lilly.com/social-channels. **P-LLY**

This press release contains certain forward-looking statements about solanezumab, an anti-amyloid monoclonal antibody in clinical testing for treatment of Alzheimer's disease, and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there is no guarantee that future study results and patient experience will be consistent with study findings to date or that solanezumab will receive regulatory approvals or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

[1] Liu-Seifert H., et al. Cognitive and Functional Decline and Their Relationship in Patients with Mild Alzheimer's Dementia. *Journal of Alzheimer's Disease*. 43 (2015) 949-955

[2] Alzheimer's Society. The Mini Mental State Examination. https://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=121. Accessed November 2016

[3] The Washington University Knight ADRC. http://alzheimer.wustl.edu/CDR/CDR.htm. Accessed November 2016.

[4] Liu-Seifert H., et al. Cognitive and Functional Decline and Their Relationship in Patients with Mild Alzheimer's Dementia. *Journal of Alzheimer's Disease*. 43 (2015) 949-955

[5] Alzheimer's Association. Tools for Early Identification, Assessment, and Treatment for People with Alzheimer's Disease and Dementia. https://www.alz.org/national/documents/brochure_toolsforidassesstreat.pdf. Accessed November 2016.

[6] Alzheimer's Association. 2016 Alzheimer's Disease Facts and Figures. http://www.alz.org/documents_custom/2016-facts-and-figures.pdf. Accessed November 2016.

[7] Alzheimer's Disease International. Dementia statistics. http://www.alz.co.uk/research/statistics. Accessed November 2016.

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