July 21, 2016

Diversity of Lilly's Alzheimer's Disease Pipeline Showcased at the Alzheimer's Association International Conference® 2016 (AAIC® 2016)

Data highlights include two phase 2 analyses of tau imaging agent

INDIANAPOLIS, July 21, 2016 /PRNewswire/ -- Eli Lilly and Company (NYSE:LLY) today announced it will present findings from more than 25 research studies at the upcoming Alzheimer's Association International Conference® 2016 (AAIC® 2016) in Toronto, Canada, July 24 - 28. The data highlight a broad research program that targets beta-amyloid and tau, two known hallmarks of Alzheimer's disease, along with positron emission tomography (PET) imaging diagnostics that allow researchers to estimate both pathologies in the living brain.

"Our current pipeline is shaped by the discoveries we've made over nearly three decades of research and development," said J. Anthony Ware, M.D., senior vice president, product development, Lilly Bio-Medicines. "We recognize the significant burden this devastating illness has on patients, caregivers and our society, and we remain deeply committed to finding ways to disrupt the course of this disease."

Of particular interest are two oral presentations which may inform Lilly's future clinical research in Alzheimer's disease:

- **The Relationship of [18F] AV-1451 PET Tau Images to Changes in Cognition over Time** *(Oral presentation, Wed., July 27, 3:00 p.m. - 3:15 p.m. EDT. Presenting author: Devous, M.)*
- **Evolution of [18F] AV-1451 PET Tau Signal: Interim Analysis of an 18-Month Phase 2 Study** *(Oral presentation, Wed., July 27, 4:15 p.m. - 4:30 p.m. EDT. Presenting author: Mintun, M.)*

Additional studies being presented include:

Solanezumab Data

- **Exposure-Adjusted Analysis of TEAEs from EXPEDITION and EXPEDITION2 Trials of Solanezumab for Tx of AD** *(Poster, Mon., July 25, 9:30 a.m. - 10:30 a.m. EDT)*

LY3002813 Data (N3pG)

- **Safety, Pharmacokinetics (PK), and Florbetapir F-18 Positron Emission Tomography (PET) After Multiple Dose Administration of LY3002813, a b-amyloid Plaque-Specific Antibody, in Alzheimer's Disease** *(Oral presentation, Wed., July 27, 5:30 p.m. - 5:45 p.m. EDT)*

Florbetapir Data

- **Conversion of Florbetapir SUVr to the Centiloid Scale** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Tues., July 26, noon - 1:00 p.m. EDT)*

Flortaucipir [18F] AV-1451 Data

- **Quantification of Tau Load Using [18F] AV-1451 and PET** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Wed., July 27, noon - 1:00 p.m. EDT)*
- **Association of [18F] AV-1451 with Cognitive and Neurodegeneration Measures: Prelim Analysis - ADNI Cohort** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Sun., July 24, 9:30 a.m. - 4:15 p.m. EDT)*
- **Functional Connectivity with Anterior Temporal Lobe Regions Ordered According to the Braak Progression Scheme Reveals Sequential Coupling to Default Mode and then Sensory Networks** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Tues., July 26, 9:30 a.m. - 4:15 p.m. EDT)*
- **Image Patterns & Clinical Phenotypes Associated with Fastest Increase of Tau Burden Measured by Longitudinal [18F] AV-1451 (T807) PET Studies** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Sun., July 24, 4:15 p.m. - 5:45 p.m. EDT)*

- **Relationship Between [18F] AV-1451 Binding & Antecedent Amyloid Deposition, Glucose Hypometabolism & Atrophy Msrs** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Tues., July 26, 2:00 p.m. - 3:30 p.m. EDT)*

AZD3293/LY3314814 Data (BACE Inhibitor)

- **PK/PD Modeling of AZD3293, a Novel BACE1 Inhibitor for AD in Healthy Subjects and Patients with AD** *(Poster, Mon., July 25, 9:30 a.m. - 4:15 p.m. EDT)*
- **Assessment of the Safety, Tolerability, Pharmacokinetics, and Effects on Plasma and Cerebrospinal Fluid Aβ Peptides of AZD3293, a Novel BACE1 Inhibitor, in Healthy Japanese Adults** *(Poster, Mon., July 25, 9:30 a.m. - 10:30 a.m. EDT)*

LY3202626 Data (BACE Inhibitor)

- **Nonclinical Pharmacological Characterization of the BACE1 Inhibitor LY3202626** *(Poster, Sun., July 24, 9:30 a.m. - 10:30 a.m. EDT)*
- **Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of LY3202626, a Novel BACE1 Inhibitor, in Healthy Subjects and Patients with AD** *(Poster, Sun., July 24, 9:30 a.m. - 10:30 a.m. EDT)*
- **Correlational Analysis of In Vitro BACE1 Inhibitory Activity with In Vivo PK/PD Relationship in Cerebrospinal Fluid of Dog** *(Poster, Mon., July 25, 1:00 p.m. - 2:00 p.m. EDT)*
- **Correlational Analysis of Exposure and Pharmacodynamic Effects of BACE1 Inhibitor LY3202626 in PDAPP Mice Following Acute Oral Dosing** *(Poster, Tues., July 26, 9:30 a.m. - 10:30 a.m. EDT)*

LY2811376 Data (BACE Inhibitor)

- **Combination Therapy with a Plaque-Specific Abeta Antibody and a BACE Inhibitor Used to Evaluate Plaque Reduction in a Dose-Dependent Manner in Aged PDAPP Transgenic Mice** *(Poster, Wed., July 27, 1:00 p.m. - 2:00 p.m. EDT)*

m266 Fab Data

- **Optimization of the Pharmacokinetic (PK) and Pharmacodynamic (PD) Properties of an Anti-Abeta Antibody m266 Fab Fragment Variant By Site-Specific Pegylation** *(Poster, Sun., July 24, 9:30 a.m. - 10:30 a.m. EDT)*

General Alzheimer's Disease Data

- **Comparative Longitudinal Change of Functional Connectivity, Diffusion and Structural MRI Markers in a Prodromal/Mild AD Population** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Wed., July 27, 9:30 a.m. - 4:15 p.m. EDT)*
- **The Relationship Between Ratio of Cortical and Hippocampal Volumes and Rate of Clinical Decline in Alzheimer's Disease** *(Poster, Sat., July 23, 12:15 p.m. - 2:00 p.m. EDT and Sun., July 24, 9:30 a.m. - 4:15 p.m. EDT)*
- **Cognitive & Functional Decline During Usual Care of Patients with Mild AD Dementia with and without Diabetes** *(Poster, Mon., July 25, 9:30 a.m. - 4:15 p.m. EDT)*
- **Patient Characteristics and Outcomes Associated with Receiving an Early Versus Late Diagnosis of Alzheimer's Disease** *(Poster, Mon., July 25, noon - 1:00 p.m. EDT)*
- **TREM2-Mediated Early Response by Resident Microglia Limits Diffusion and Toxicity of Amyloid Plaques** *(Oral presentation, Mon., July 25, 2:15 - 2:30 p.m. EDT)*
- **Levels of Tau Protein in Plasma are Associated with Neurodegeneration and Cognitive Function in a Population Based Elderly Cohort** (*Poster, Tues., July 26, noon - 1:00 p.m. EDT)*
- **Exploring the Utility of CSF Neurogranin Levels in an AD CT** *(Poster, Wed., July 27, 9:30 a.m. - 10:30 a.m. EDT)*
- **Dependence Levels as Interim Clinical Milestones Along the Continuum of AD: 18-Month Results from GERAS Study** *(Oral Presentation, Thurs., July 28, 11:45 a.m. - 1:15 p.m. EDT)*
- **In-Vivo Processing of Carboxyl-Terminus of Aβ: Conversion from Aβ42 to Aβ40** *(Oral presentation, Thurs., July 28, 11:45 a.m. - 1:15 p.m. EDT)*

About Alzheimer's Disease

Alzheimer's disease is a fatal illness that causes progressive decline in memory and other aspects of cognition. It is the most common form of dementia, accounting for 60 to 80 percent of dementia cases.[1,2] It is estimated that there are nearly 47 million people living with dementia worldwide.[1] The number of people affected by dementia is expected to reach nearly 75 million in 2030 and 132 million in 2050.[1] Estimates vary, but experts suggest that as many as 5.4 million Americans may

have Alzheimer's disease.[3]

About Amyvid™ (Florbetapir F 18 Injection)[4]

Amyvid is a radioactive diagnostic agent for Positron Emission Tomography (PET) imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD) and other causes of cognitive decline.

A negative Amyvid scan indicates sparse to no neuritic plaques and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to AD. A positive Amyvid scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of amyloid neuritic plaque is present in patients with AD, but may also be present in patients with other types of neurologic conditions as well as older people with normal cognition. Amyvid is an adjunct to other diagnostic evaluations.

Limitations of Use:

- A positive Amyvid scan does not establish a diagnosis of AD or other cognitive disorder
- Safety and effectiveness of Amyvid have not been established for:
  - Predicting development of dementia or other neurologic condition
  - Monitoring responses to therapies

Amyvid for intravenous use is supplied in 10 mL, 30 mL or 50 mL multidose vials containing 500-1900 MBq/mL Florbetapir F 18

WARNINGS AND PRECAUTIONS

Risk for Image Misinterpretation and Other Errors

- Errors may occur in the Amyvid estimation of brain neuritic plaque density during image interpretation
- Image interpretation should be performed independently of the patient's clinical information. The use of clinical information in the interpretation of Amyvid images has not been evaluated and may lead to errors. Other errors may be due to extensive brain atrophy that limits the ability to distinguish gray and white matter on the Amyvid scan as well as motion artifacts that distort the image
- Amyvid scan results are indicative of the brain neuritic amyloid plaque content only at the time of image acquisition and a negative scan result does not preclude the development of brain amyloid in the future

Radiation Risk

- Amyvid, similar to other radiopharmaceuticals, contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling to protect patients and health care workers from unintentional radiation exposure

MOST COMMON ADVERSE REACTIONS

- The most common adverse reactions reported in clinical trials were headache (1.8%), musculoskeletal pain (0.7%), blood pressure increased (0.7%), nausea (0.7%), fatigue (0.5%), and injection site reaction (0.5%)

For more information about florbetapir F 18, please see the Prescribing Information at http://pi.lilly.com/us/amyvid-uspi.pdf.

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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.

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This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about investigational treatments and diagnostics for 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 can be no guarantee that future study results will be consistent with study findings to-date, or that these investigational compounds or diagnostics will receive regulatory approvals or prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent 10-K and 10-Q filings with the United States Securities and Exchange Commission. Except as may be required by law, Lilly undertakes no duty to update forward-looking statements for events occurring after the date of this release.

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

[2] Alzheimer's Association. What Is Dementia? http://www.alz.org/what-is-dementia.asp. Published January 2016. Accessed May 2016.

[3] Alzheimer's Association. 2016 Alzheimer's Disease Facts and Figures. *Alzheimer's & Dementia*. Available at http://www.alz.org/documents_custom/2016-facts-and-figures.pdf. Accessed May 2016.

[4] Amyvid [package insert]. Indianapolis, IN: Lilly USA, LLC; 2014.

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