Lilly Receives U.S. FDA Approval of TAUVID™ (flortaucipir F 18 injection) for Use in Patients Being Evaluated for Alzheimer's Disease

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The first and only approved diagnostic agent to image tau neurofibrillary tangles in the brain

INDIANAPOLIS, May 28, 2020 /PRNewswire/ -- TAUVID ™, a radioactive diagnostic agent, has been approved by the FDA for positron emission tomography (PET) imaging of the brain to estimate the density and distribution of aggregated tau neurofibrillary tangles (NFTs) in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD).[1] A neuropathological diagnosis of AD requires the demonstration of the presence of both beta-amyloid neuritic plaques and tau NFTs in the brain. TAUVID is the first and only approved diagnostic agent to image tau NFTs in the brain. Avid Radiopharmaceuticals, Inc., a wholly owned subsidiary of Eli Lilly and Company (NYSE: LLY), developed TAUVID and AMYVID® (Florbetapir F 18 Injection) to provide physicians with meaningful information on the presence of both pathologies to aid the evaluation of patients suspected of having AD.[1,2]

"The use of diagnostic imaging can help patients and their families plan for the future and make informed choices about their health and well-being, in addition to facilitating appropriate patient management for physicians," said Reisa Sperling, M.D., Professor of Neurology of Harvard Medical School, and Director of the Center for Alzheimer Research and Treatment at Brigham and Women's Hospital and Massachusetts General Hospital. "Determining the anatomic distribution and density of tau NFTs in the brain was previously possible only at autopsy. Now we have a way to obtain this important information in patients."

TAUVID was evaluated in two clinical studies. In Study 1, reader interpretations of premortem TAUVID scans from 64 cognitively normal and impaired terminally ill patients who agreed to undergo TAUVID imaging and to participate in a postmortem brain donation program were compared to tau pathology at autopsy based on scoring provided by independent pathologists blinded to scan results. This study met its pre-specified success criteria, with reader sensitivity (95% CI) ranging from 92% (80, 97) to 100% (91, 100) and specificity (95% CI) from 52% (34, 70) to 92% (75, 98) in the primary efficacy cohort. In Study 2, images from the same terminally ill patients as in Study 1 (plus 18 additional terminally ill patients) and 159 patients with cognitive impairment being evaluated for AD (the indicated population) were evaluated by 5 new readers. This study also met the prespecified success criteria for comparison of TAUVID reads to NFT pathology. In addition, inter-reader agreement was evaluated using Fleiss' kappa statistic and found to be 0.87 (95% CI: 0.83, 0.91) across 241 patients in Study 2. The most common adverse reactions reported in clinical trials were headache (1.4%), injection site pain (1.2%), and increased blood pressure (0.8%).[1,3]

"The fight against AD requires precise and reliable assessments of the two key pathologies of the disease because clinical assessments alone are limited in their ability to accurately diagnose patients," said Mark Mintun, M.D., vice president of Lilly's pain and neurodegeneration research and development. "History was made with the FDA approval of AMYVID to demonstrate the presence of one of those two pathologies, beta-amyloid plaques. I am excited that TAUVID has now been approved to image tau NFTs, which is the other key pathology, allowing a more comprehensive evaluation of patients. Lilly and Avid Radiopharmaceuticals are committed to bringing innovative AD diagnostics to the patients who need them most."

Availability of TAUVID will initially be limited and will expand in response to commercial demand and payor reimbursement. Lilly remains committed to patients with cognitive impairment associated with Alzheimer's disease and to ensuring patient access to this innovative diagnostic tool. Lilly is supportive of policies that will provide access and coverage for beta-amyloid PET and tau PET imaging agents.

For more than 30 years, Lilly has been engaged in bringing innovative Alzheimer's disease therapies and diagnostics to patients and continues to lead the field in research, which also includes identifying biomarkers to support early detection of the disease.

Indication and Important Safety Information for TAUVID

Indication
TAUVID is indicated for use with positron emission tomography (PET) imaging of the brain to estimate the density and distribution of aggregated tau neurofibrillary tangles (NFTs) in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease (AD).

Limitations of Use
TAUVID is not indicated for use in the evaluation of patients for chronic traumatic encephalopathy (CTE).

Important Safety Information

Warnings and Precautions

Risk of Misdiagnosis in Patients Evaluated for Alzheimer's disease
TAUVID does not target β-amyloid, one of two required components of the neuropathological diagnosis of AD. TAUVID performance for detecting tau pathology was assessed in terminally ill patients, the majority of whom had AD dementia with B3 level NFT pathology. TAUVID performance for detecting tau pathology may be lower in patients in earlier stages of the pathological spectrum.

Negative TAUVID Scan

NFTs may be present at levels that qualify for the neuropathological diagnosis of AD (B2 tau pathology in the presence of at least moderate levels of cortical amyloid pathology) in patients with a negative TAUVID scan. Consider additional evaluation to confirm the absence of AD pathology in patients with a negative TAUVID scan.

False Positive TAUVID Scan
Small foci of noncontiguous tracer uptake may lead to a false positive TAUVID scan. Only uptake of tracer in the neocortex should contribute to the interpretation of a positive TAUVID scan.

Risk of Chronic Traumatic Encephalopathy Misdiagnosis
The safety and effectiveness of TAUVID have not been established for patients being evaluated for CTE. Preliminary non-clinical and clinical investigations suggest differences in tau conformation and distribution may limit flortaucipir F 18 binding. Therefore, TAUVID is not indicated for detection of CTE.

Radiation Risk
Diagnostic radiopharmaceuticals, including TAUVID, expose patients to radiation. Radiation exposure is associated with a dose-dependent increased risk of cancer. Ensure safe handling and preparation procedures to protect patients and health care workers from unintentional radiation exposure.

Adverse Reactions
The most common adverse reactions reported in clinical trials were headache (1.4%), injection site pain (1.2%), and increased blood pressure (0.8%).

For Full Prescribing Information, visit http://pi.lilly.com/us/tauvid-uspi.pdf.

Indication and Important Safety Information for AMYVID
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 and other causes of cognitive decline. A negative AMYVID scan indicates sparse to no neuritic plaques and is inconsistent with a neuropathological diagnosis of Alzheimer's Disease at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to Alzheimer's Disease. 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 Alzheimer's Disease, 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 Alzheimer's Disease or other cognitive disorder. Additionally, the safety and effectiveness of AMYVID have not been established for predicting development of dementia or other neurologic condition, or monitoring responses to therapies.

AMYVID is supplied in 30 mL or 50 mL multidose vials containing 500-1900 MBq/mL Florbetapir F 18.

Important Safety Information

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 Full Prescribing Information, visit http://pi.lilly.com/us/amyvid-uspi.pdf.

About Avid Radiopharmaceuticals
The mission of Avid Radiopharmaceuticals, a wholly owned subsidiary of Lilly, is to discover and develop radiopharmaceuticals and imaging methods that improve global health by accelerating the development of new medicines and enabling a tailored approach to healthcare.

About Eli Lilly and Company
Lilly is a global health care leader that unites caring with discovery to create medicines that 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 lilly.com and lilly.com/newsroom. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about TAUVID, a radioactive diagnostic agent indicated for positron emission tomography (PET) imaging of the brain to estimate the density and distribution of aggregated tau neurofibrillary tangles (NFTs) in adult patients with cognitive impairment who are being evaluated for Alzheimer's disease. 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 the product 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.

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[1] TAUVID™ Prescribing Information May 2020.

[2] AMYVID® Prescribing Information. December 2019.

[3] Fleisher AS, Pontecorvo MJ, Devous MD, et al. Positron Emission Tomography Imaging With [^{18}F]flortaucipir and Postmortem Assessment of Alzheimer Disease Neuropathologic Changes. *JAMA Neurol.* Published online April 27, 2020. doi:10.1001/jamaneurol.2020.0528.

Refer to: Gina Goodenough; demayo_gina_maria@lilly.com; 646-221-3022 – Media
Kevin Hern; hern_kevin_r@lilly.com; 317-277-1838 – Investor Relations

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