C-Path's Alzheimer's Consortium Unveils Seminal Methodology to Enhance Alzheimer's Clinical Trials Using Imaging Biomarkers

TUCSON, Ariz., July 28, 2024 — Critical Path Institute (C-Path) is proud to announce the publication of a new study in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* that was led by its Critical Path for Alzheimer's Disease (CPAD) consortium. The publication details a method that solves a major obstacle to comparing the findings of investigational tau imaging results across Alzheimer's disease (AD) clinical trials.

Alzheimer's disease is a progressive neurodegenerative condition that is a major cause of disability due to cognitive decline and behavioral changes. Every 67 seconds, someone in the U.S. develops Alzheimer's. It is estimated that nearly 500,000 new cases of Alzheimer's disease will be diagnosed this year. The disease is characterized by the presence of two pathogenic proteins, amyloid and tau, which lead to neurodegeneration through misfolding and dysfunction.

Recent advancements in AD therapeutics have led to the approval of the first disease-modifying treatments targeting amyloid "plaques." These drugs not only clear amyloid but also show promise in reducing tau levels, as evidenced by positron emission tomography (PET) scans. Tau PET imaging is increasingly used in the clinical research evaluation of AD patients and in clinical trials evaluating disease-modifying therapies for AD.

The field is rapidly evolving with the development of multiple PET imaging ligands capable of detecting tau protein in humans. To advance the utility of tau imaging in therapeutic trials, it is crucial to establish a standardized methodology for comparing tau outcomes across clinical trials that utilize different tau tracers. Recognizing the need for a tau PET standardization method, CPAD convened a working group of around 50 world-leading experts across industry and academia who first met at the 2022 Alzheimer's Association International Conference, organized by the Alzheimer's Association, to develop a harmonization approach.

"Industry, academia, and nonprofits collaborated in unprecedented ways to accelerate the path to new treatments across a range of key mechanisms including tau-targeting therapies," said Greg Klein, Ph.D., Head of Clinical Imaging, Neuroscience and Rare Diseases Biomarkers and Translational Technology at Roche and industry co-chair of CPAD's Tau PET Working Groups.

Dr. Diane Stephenson, interim Executive Director of CPAD, emphasized that this project would not have been possible without the AD community coming together, nor without the scientific leadership of Dr. Antoine Leuzy and Dr. Lars Lau Raket, first authors on the paper. The publication highlights the consensus on a unified methodology and reporting of tau PET results. The method is envisioned to accelerate tau PET use as a powerful biomarker that has the potential to allow for treatment earlier in the disease process, which is key in brain diseases as treatments may be more effective before irreversible symptoms appear.
"To intervene early in the disease, it is imperative to be able to visualize the hallmark biomarkers of disease as early as possible, ideally before the first symptoms become apparent," Dr. Hartmuth Kolb, scientific advisor for Critical Path for Alzheimer's Disease (CPAD) consortium said. "My team developed the first imaging tracer to detect Tau in humans, 18F-Flortaucipir (aka T-807 or AV-1451), which allows us to detect and measure the key protein Tau in the brains of living patients, so we can now track its progression in

context of cognitive decline. The use of TauPET imaging with 18F-Flortaucipir and second generation tracers, such as 18F-MK6240, 18F-PI2620, 18F-RO948, 18F-GTP1, in clinical trials holds true potential to aid in the evaluation of clinically meaningful treatment effects in Alzheimer's Disease."
"AD research is moving forward rapidly, with innovation in regulatory science that is paving the way to success. Such advances in the global regulatory ecosystem are linked to greater industry collaborations aimed to develop novel therapies," said Stephenson. "Key to C-Path's successes with drug development tools is based on the aggregation of clinical trials, and it is our hope to create tools that will inform innovative clinical trial designs, which can help expedite drug development programs"
"We need new treatments that address Alzheimer's and all other dementia from every possible angle," said Maria C. Carrillo, Ph.D., chief science officer and medical affairs lead at the Alzheimer's Association. "In this new era of treatment, the Alzheimer's research field is accelerating at a rapid pace to move the most effective and safest therapeutic candidates in the pipeline forward with efficiency. This collaboration to develop a harmonized tau PET methodology is another example of how the highly collaborative nature of the Alzheimer's research community can produce new tools to accelerate therapeutic development for the benefit of patients and their families."
Critical Path Institute has successfully led the regulatory endorsement and qualification of imaging biomarkers across a range of disease areas including Parkinson's disease, polycystic kidney disease and Alzheimer's disease.

About Critical Path Institute

Critical Path Institute (C-Path) is an independent, nonprofit organization established in 2005 as a public and private partnership. C-Path's mission is to catalyze the development of new approaches that advance medical innovation and regulatory science, accelerating the path to a healthier world. An international leader in forming collaborations, C-Path has established numerous global consortia that currently include more than 1,600 scientists from government and regulatory agencies, academia, patient organizations, disease foundations, and hundreds of pharmaceutical and biotech companies. C-Path U.S. is headquartered in Tucson, Arizona and C-Path in Europe is headquartered in Amsterdam, Netherlands with additional staff in multiple other locations. For more information, visit c-path.org.

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