

In Recognition of 10th Anniversary, Raymond Woosley and Janet Woodcock Address CPAD Consortium's 2018 Annual Meeting and Regulatory Science Workshop

At its 10th Annual Meeting and Regulatory Science Workshop, November 13, 2018, in Bethesda, MD, C-Path's Critical Path for Alzheimer's Disease (CPAD) consortium hosted key stakeholders who gathered to review the progress made over the past year and identify and prioritize regulatory science needs for Alzheimer disease (AD) and related dementias. At the meeting, CPAD took time out to announce that it has refined and refocused its mission in celebration of the consortium's 10-year anniversary.

Launched in 2008, and originally named the Coalition Against Major Diseases (CAMD) consortium, CPAD is a ground-breaking development for C-Path and the community dedicated to advancing treatment of Alzheimer disease. Since then, the consortium has made extraordinary progress in data sharing, disease modeling, biomarker development and a number of other areas of regulatory science. The 2018 name refresh reflects the consortium's primary focus on Alzheimer disease.

The annual meeting, which is open to the public, brings together representatives from the biotech and pharmaceutical industries, key academic thought leaders, government and regulatory agencies and patient advocacy groups.

This year, attendees saw video messages covering CPAD's origins, successes, challenges and opportunities, by Critical Path Institute's founder Raymond Woosley, M.D., Ph.D., and Janet Woodcock, M.D., Director of the Center for Drug Evaluation and Research, U.S. Food and Drug Administration (FDA).

Sharing and collaboration have yielded success

In his message, Woosley took the opportunity to celebrate CPAD's 10-year milestone and reflect on the consortium's origins.

Although CPAD officially was launched in 2008, Woosley noted, its roots began in the 80s and 90s when drug development was undergoing turbulent times. There was excitement around the potential role of biomarkers, but in 1988, a landmark clinical trial, the Cardiac Arrhythmia Suppression Trial, found that some biomarkers could be unreliable and even dangerous. Additional drug safety problems came to light in the 1990s, and rare adverse events led to drugs being removed from the market or taken out of development. Of note, many investigational drugs were failing in phase 3 trials after considerable time and money had been invested in their development.

This perception that “drug development is in crisis,” Woosley explained, led to Congressional hearings, resulting in legislation to create federally funded academic centers, or Centers for Education and Research on Therapeutics (CERTs), which were directed by law to work with FDA. Early on, leaders at these centers realized that, to make an impact, they required active participation by the drug industry, along with its scientific knowledge and specialized expertise. That’s when Janet Woodcock and then commissioner Mark McClellan described the Critical Path Initiative and helped launch C-Path Institute.

Woosley noted that there were numerous skeptics at the time, who didn’t think that FDA (the regulators) should work with industry (the regulated). But there are very few skeptics left today, as the fruit of such collaborations has brought about qualified biomarkers, qualitative disease progression models and other successes that only could have been realized through sharing and collaboration. Ten years of collaboration, a growing team, growing industry participation and commitment from patient advocacy groups working to end AD has led to a wealth of opportunity.

“For CPAD,” Woosley said, “the sky is the limit!”

‘Ahead of your time’

In her message to attendees, Woodcock discussed the historical need to create consortia like CPAD, noting that she was there at the beginning when CAMD formed to make collective strides against disease. It was unusual and groundbreaking, she said. “You were really ahead of your time.”

Now, translational work is needed to advance the field, Woodcock said, suggesting that better evaluative tools are needed, along with better ways to assess progress quickly (e.g., biomarkers), better trial design and better models for neurological disease.

Woodcock noted the rise of patient-focused drug development, which emphasizes the patient's voice in a "robust and authentic manner" in every phase of therapy development. An area under intense exploration is the utility of new tools that can help scientists understand the patient voice with regard to function and feeling — for example, wearable technology.

She addressed what consortia like CPAD can do to facilitate the AD community to transform real-world data to real-world evidence as a means of bolstering understanding of post-market, natural history of disease, etc., and she encouraged CPAD and other consortia to seek to understand the low-hanging fruit in each of their respective fields, to work in areas that are ripe for progress and that no one else is working on, so that duplication of efforts can be avoided.

Woodcock noted that the AD field faces serious challenges now, with families, political groups and others feeling frustration at the pace of research and therapy development. She noted that early diagnosis is critical so that interventions can be implemented earlier, but that there also is a growing population that needs interventions for the later stages of AD as well.

Poised to capitalize on early successes

CPAD can count many milestones to its credit, including:

- A qualification opinion granted by the European Medicines Agency (EMA) for the use of low-baseline hippocampal volume for patient enrichment in pre-dementia trials
- Development and publication of the first Clinical Data Interchange Standards Consortium therapeutic user guide for AD in partnership with [CDISC](#)
- The first drug-disease trial model and clinical trial stimulation tool endorsed by the FDA and qualified by the EMA for mild-to-moderate AD
- Recognition of the consortium, in FDA Letters of Support, encouraging the further study and use of cerebrospinal fluid analytes, and of hippocampal volumes measured by magnetic resonance imaging,

as exploratory prognostic biomarkers for enrichment in AD trials

- An EMA Letter of Support encouraging industry sponsors to share patient-level data from completed phase II and III clinical trials with CPAD

In addition, CPAD's [Critical Path Institute Online Data Repository \(CODR\): Critical Path for Alzheimer's Disease \(CPAD\) Consortium Database](#) is the first and largest open database of CDISC-standardized clinical trial data for AD. It stores patient-level, control-arm data collected from clinical trials conducted by consortium member companies.

As it rounds out its tenth year, CPAD is positioned for success. The broad spectrum of foundational research it has facilitated, in combination with ongoing analysis of CODR data, will support current and future efforts to design efficient clinical trials to test experimental treatments and more rapidly identify potential therapies able to prevent AD or halt its progression.