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RETHINKING HOW TO CONDUCT CLINICAL TRIALS FOR ALZHEIMER'S DISEASE

SAN DIEGO, CALIFORNIA, November 14, 2013. An international group of Alzheimer's disease researchers today called for changes in the way clinical drug trials are conducted, claiming that existing approaches have little chance of success. Speaking at a symposium held at the Clinical Trials in Alzheimer's Disease (CTAD) meeting, investigators from clinical centers in Toulouse, France; Las Vegas, Nevada; and San Francisco, California; "Alzheimer's disease drug development is broken and in the decade from 2002 to 2012 produced only one drug," said Dr. Jeffrey Cummings, Director of the Cleveland Clinic Lou Ruvo Center for Brain Health. "New solutions are urgently needed."

Alzheimer's disease currently affects more than 35 million people worldwide, and the prevalence is expected to triple by 2050. Yet although hundreds of clinical trials of drugs intended to treat AD have been conducted over the past three decades, no new therapies have been approved since 2003. Of the four drugs commonly used to treat AD, all alleviate symptoms but are not thought to slow the disease's relentless progression. Newer drugs in development, however, increasingly focus on modifying the underlying disease by interfering in the processes that lead to degeneration of the brain. Delaying the development of dementia by only a few years could dramatically decrease the worldwide prevalence.

The challenge is to design trials that can demonstrate disease modification over a relatively short period of time and in the earliest stages of the disease before the disease has destroyed large parts of the brain. Julien Delrieu, from the Toulouse Gérontopôle Alzheimer's Disease Research Clinical Center analyzed over 150 clinical trials conducted over the last five years. He concluded that in order effectively evaluate disease modifying therapies, there needs to be 1) an increased use of biomarkers both to identify appropriate subjects for the trial and assess outcomes; 2) inclusion of subjects at earlier stages of disease; and 3) longer duration of interventions. One of the consequences is less patients recruited by centers, longer duration of recruitment period and an dramatic increase center sites, resulting to high variability

According to Professor Bruno Vellas, also of Toulouse Gérontopôle and Alzheimer's Disease Research Clinical Center, more than 200 centers from many countries are currently needed to conduct a phase 2 clinical trial, with each center enrolling only a few patients. "This gives a lot of variability, and reduces the chance for a successful drug trial," he said. "We need to change the way we conduct trials, with fewer centers and more patients per center. We must build registries of patients willing to participate in drug trials as well as cohorts of specific patients such as those with evidence of Alzheimer's pathology."

The solution may be to establish specialized centers capable of recruiting large numbers of subjects and minimizing the variability that is introduced when studies are done at multiple locations, according to Pierre-Jean Ousset of the CeNGEPS Alzheimer Drug Trial Network in Toulouse CeNGEPS was established in France in 2007 to improve the performance of clinical trials. In a survey from the EADC (European Alzheimer's Disease Consortium) the investigator spend much more time in administrative work and less and less in contact with the patients.

Dr. Cummings discussed the Cleveland Clinic as a model of a health care system embracing clinical trials. As a result of health care reform, he said that trend will be for patients to receive care from a smaller number of larger systems such as this. "If those systems embrace both trials and quality, it could change the flow of patients into trials," he said.

Professor Vellas also pointed to the need to build a cohort of potential subjects for trials. A possible solution for this was described by Michael Weiner, M.D., director of the Center for Imaging of Neurodegenerative Diseases (CIND) at the San Francisco Veterans Affairs Medical Center and University of California, San Francisco. Weiner described The Brain Initiative: An internet-based registry for AD prevention trials and neuroscience research that was recently established in partnership with Lumos Labs, Inc., creators of Lumosity™, and CogState. Lumosity is a web-based cognitive training platform that has already registered more than 40 million participants and has collected at least one year of cognitive performance data from 600,000 older adults. CogState has created computerized systems for assessing, monitoring, and improving cognition. The Brain Initiative hopes to use the tools provide by Lumos Labs and CogState, along with other measures to identify individuals who may be at risk of developing brain diseases including AD.