Efforts to discover and develop effective treatments for Alzheimer’s disease (AD) are moving forward at lightning speed, according to researchers and clinicians meeting in Barcelona for the 8th international conference on Clinical Trials in Alzheimer’s Disease (CTAD) on Thursday. Noting the steadily increasing attendance at CTAD from less than 200 people in 2008 to over 900 in 2015, Professor Bruno Vellas, M.D., geriatrician and chair, Gérontopôle and the University of Toulouse, said, “If CTAD is a biomarker of progress [in AD drug development], we’ll have very big success and very soon.”

Eric Siemers, M.D., Distinguished Medical Fellow of the Alzheimer’s Disease Global Development Team at Eli Lilly questioned whether the perception that recent clinical trials have failed is warranted. “We haven’t gotten across the finish line, but I want to emphasize how far we’ve come along,” he said. For example, lessons learned from the past twenty years of clinical trials have supported hypotheses indicating a fifteen-year lag between the first signs of pathology and the onset of symptoms, shifting the focus of intervention efforts to the early stages of disease. And while none of the clinical trials of putative disease modifying therapies have thus far demonstrated efficacy, they have provided good evidence of target engagement and a downstream clinical effect, thus indicating that we are moving in the right direction. “There’s a good reason to be hopeful,” he said. “We have to make it clear to our patients that we haven’t failed” and develop in them the mindset that if they experience symptoms such as memory impairment, the first thing they should think about is enrolling in a clinical trial.

The path forward, according to Siemers and others who spoke at CTAD, includes increased collaboration and the development of new tools, such as biomarkers, to expedite and improve the productivity of clinical studies. Biomarkers are needed to select and stratify patients for clinical studies as well as to measure outcomes and disease progression, said Simon Lovestone, Ph.D., Professor of Old Age Psychiatry and Neuroscience at the Institute of Psychiatry, King’s College, London. Lovestone focused his comments on the development of blood-based biomarkers, which have the potential to provide highly sensitive but low cost and minimally invasive measures that would enable selection of individuals likely to progress to dementia. Lovestone described a decade-long effort to identify blood-based biomarkers that correlate with clinical characteristics of the disease. Technological advances now allow the measurement of hundreds of discrete proteins in the blood and have enabled scientists to correlate specific proteins or patterns of proteins with other measurable characteristics of disease such as cortical atrophy, cognition, and the speed of decline.

Lovestone added that the promise of blood-based biomarkers can only be realized through the analyses of massive numbers of samples from patients at all levels of disease progression. He described three programs recently established in Europe to make this possible -- the Dementias Platform UK, the Innovations in Medicine Initiative’s European Medical Information Framework (IMI-EMIF), and the IMI’s European Prevention of Alzheimer’s Disease (IMI-EPAD) program. Dementias Platform UK will aggregate phenotypic and biomarker data as well as biospecimens from existing cohorts, including some 500,000 volunteers enrolled in the UK Biobank. IMI-EMIF is establishing a registry of people who are interested in clinical trials to expedite the process of getting trials up and running. “This is an exemplar set of programs of huge numbers of people working together,” said Lovestone. Another major biomarker initiative was described by Marilyn Albert, Ph.D., Director of the Division of Cognitive Neuroscience in the Department of Neurology at the Johns Hopkins University School of Medicine. The BIOCARD study (Biomarkers of Cognitive Decline Among Normal Individuals) was started in 1995 by the National Institutes of Health (NIH) in the U.S. to capture biomarker data on a group of middle-aged, non-demented individuals with a family history of AD, with the aim of identifying predictors of disease progression. The study ended in 2005, but was re-established in 2009 through a cooperative agreement between NIH and Johns Hopkins, which enabled reenrollment of the initial cohort and collection of additional data from annual clinical and cognitive assessments. Analysis of those data in relation to previously collected data will allow investigators to develop algorithms capable of predicting the onset of clinical symptoms based on demographic, clinical, and biomarker characteristics; as well as an AD severity score to track the response to treatment in clinical trials.

Even as these platforms and collaborations are being developed, pharmaceutical companies and academic investigators have continued to press forward with efforts to bring experimental treatments to the clinic. Among the most highly anticipated of these development programs described at CTAD is that for aducanumab, a monoclonal antibody that targets the aggregated forms of beta-amyloid, which are deposited as plaques in the Alzheimer's brain. Biogen Idec's Vissia Viglietta, M.D., Ph.D., and Jeff Sevigny, M.D., presented data from the phase 1b PRIME study in patients with prodromal and mild AD, which while not demonstrating a treatment effect, did provide evidence of safety, tolerability and target engagement, leading Biogen to move forward with two large, 18 month duration, multi-site phase 3 studies.