CRITICAL PATH INSTITUTE

Improving the Path for Innovative Therapies

DATE: March 22, 2012
SUBJECT: Making the case for Public Private Partnerships for NAPA

The Problem
A crisis in medicine today is that there are increasing investments in biomedical research but decreasing numbers of new medical products, especially drugs, that obtain FDA approval and are available to patients.[1, 2] In order to respond to this crisis, the field of drug development is undergoing transformational changes.

Taking a basic scientific discovery through development and regulatory approval of a medical product that finally reaches patients faces overwhelming challenges including the long length of research, high rate of failures of potential candidates and enormous costs. This research and development process is so difficult it is called the "Valley of Death." As many as 80-95% of promising drug candidates fail.[3, 4] Drug companies will spend tens of thousands to perform research on millions of compounds and spend in excess of a billion dollars over a 10- to 20-year period just to have one drug reach patients.[5] A pressing example is Alzheimer's Disease (AD) for which diagnosis is difficult and there are only a few FDA approved treatments to temporarily slow the disease but no cure, at a time when this debilitating disease is exploding in the aging population. In fact, the pace for development and FDA approval of Central Nervous System (CNS) drugs is even longer than other drug classes.[6]

These challenges mean that companies have to be smarter and more efficient in managing drug discovery and development. Innovation is needed to create greater efficiencies to help move therapies through development, review and approval for patient use. John Castellani, President PhRMA, stated that "The regulatory process is a strategic priority that if done right can reduce time, cost and uncertainty in drug development."[4]

The Solution: Increasingly, public private partnerships (PPP) are presenting an opportunity to meet these challenges. Partnerships between the private sector, regulatory and other government agencies, academic institutions, nonprofit organizations, and patient groups represent a new model offering innovation and efficiencies in drug development. Innovation comes from focusing on science that can improve the process of drug development and be applied to regulatory decisions. Efficiencies come from building collaborations and sharing.

The flagship success of PPPs in AD is the Alzheimer's Disease Neuroimaging Initiative 1 (**ADNI1**), a $60 million, 5-year study to test whether imaging and biological markers, and clinical and neuropsychological assessments could measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD). Begun by the National Institute on Aging (NIA) and supported by other federal agencies, private-sector companies and organizations, the ADNI1 investment would have been prohibitive for a single stakeholder. However, ADNI1 has transformed the understanding of the pathophysiology of AD. Additionally, many other PPPs are having an impact in AD, some of which are described below:

> **ADNI2**: Approximately 1,000 people aged 55 to 90 will be followed with imaging and biomarker measures to identify who is at risk for AD, track progression, and devise tests to measure the effectiveness of potential interventions. This ~ $60 million study is funded by NIH and companies.

1730 E. River Road, Suite 200
Tucson, Arizona 85718
T 520-547-3440 F 520-547-3456
www.c-path.org

FNIH Biomarkers Consortium: One project is the first part of a multi-phased effort to utilize ADNI samples to construct multiplex panels in plasma and CSF to diagnose patients with AD and monitor disease progression.

Alliance for Aging Research: The Alliance initiated Accelerate Cure/Treatment for Alzheimer's Disease, a coalition of national organizations representing patients, providers, caregivers, consumers, older Americans, researchers, employers, and health care industries seeking to accelerate development of potential cures and treatments for AD.

Alzheimer's Association Global Standardization: This organization is leading global efforts to standardize Alzheimer's biomarkers with the World Wide AD Neuroimaging Initiative (WW-ADNI) and the Alzheimer's Association Cerebrospinal Fluid (CSF) Quality Control Program.

Alzheimer's Association Research Roundtable: Members facilitate the development and implementation of new treatments for Alzheimer's disease by collectively addressing obstacles to research and development, clinical care and public health education.

Critical Path Institute's Coalition Against Major Diseases (CAMD): CAMD accelerates the development of therapies for AD by advancing drug development tools for regulatory approval. CAMD developed AD data standards with CDISC, a pooled clinical trial database with 6,000 patients, and a clinical disease progression model. CAMD obtained regulatory approval for imaging biomarkers from the EMA and is collaborating with the FDA on CSF and imaging biomarkers.

Critical Path Institute's Patient Reported Outcome (PRO) Consortium: A workgroup is developing and evaluating a PRO instrument on MCI for use in clinical trials designed to evaluate the safety and efficacy of new AD drugs.

IMI PharmaCog: The five-year €20M PharmaCog project, funded under the European Innovative Medicine Initiative (IMI), will provide tools to define the potential of a drug candidate, reduce the development time of new drugs and thus accelerate the approvals of promising new medicines.

While the impact of these PPPs is extensive, there are still significant challenges and opportunities for preventing and treating AD. One challenge is in the regulatory arena. For approval of a new drug, a pharmaceutical company engages exclusively with the regulatory agency and all information within the drug approval process is proprietary. Lessons learned from one AD drug trial are not shared, so any insights on why drugs fail or how particular biomarkers track with disease progression are lost. However, in recognizing the need for change, the FDA established an innovative approach in the Critical Path Initiative. The FDA formalized a process for submitting tools as biomarkers and clinical outcome assessments to be "qualified" for specific uses in supporting drug development.[7] Tools that receive a designation of "fit for use" from the FDA's qualification process[8] can then be widely shared.

Recommendations

Providing the extensive evidence needed for qualification of tools by regulatory authorities can optimally be carried out through public-private partnerships. PPPs can support publicly accessible clinical trial databases that can be mined for information on biomarkers and disease progression. Drug companies can contribute data and conduct prospective trials that may be required to provide the regulatory levels of evidence to assure qualification of new drug tools. Academics can also provide clinical data and analysis to identify optimal biomarkers for qualification.

The challenge then becomes funding PPPs that move products toward regulatory approval. The cost of qualification for a single biomarker is several million dollars over a time frame of up to 5

years. Such costs require significant investment by both public and private sectors and in-kind contributions in order to be successful. However, the end product is a tool that FDA can have confidence in to produce better data and be used by all drug companies in clinical trials. The result benefits all stakeholders, including patients.

Since not all PPPs conduct research as ADNI does, there needs to be new models of PPP funding, within or possibly outside of NIH, especially for non-profit organizations and those working toward improving the process of drug development and regulatory review. Infrastructure support for such an AD PPP could be provided through HHS or other governmental agency appropriations. Because PPPs rely upon multi-stakeholder collaborations, it is critical that oversight be provided by a multi-stakeholder board to represent the broad spectrum of the various entities (industry, regulatory agencies, government funding, non-profits, academic experts, and patients).

Reference List

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Carolyn Compton MD

Carolyn C. Compton, MD, PhD
President & CEO
Critical Path Institute