Coalition Against Major Diseases
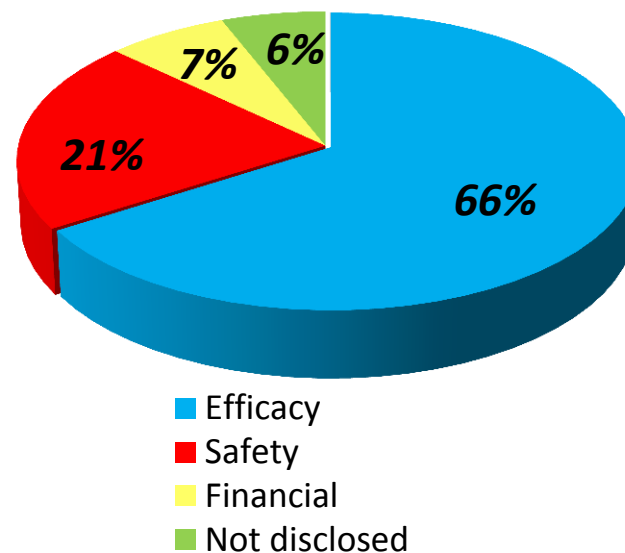## *Regulatory Science can Accelerate Drug Development for Neurodegeneration*

Diane Stephenson, PhD

Executive Director, CAMD

Critical Path Institute

Collaborating for Cures – March 7, 2013- Brussels

After recent AD Phase III failures... What's next?

Reasons for Phase III & Submission Failures: 2007-2010

- Efficacy — 66%
- Safety — 21%
- Financial — 7%
- Not disclosed — 6%

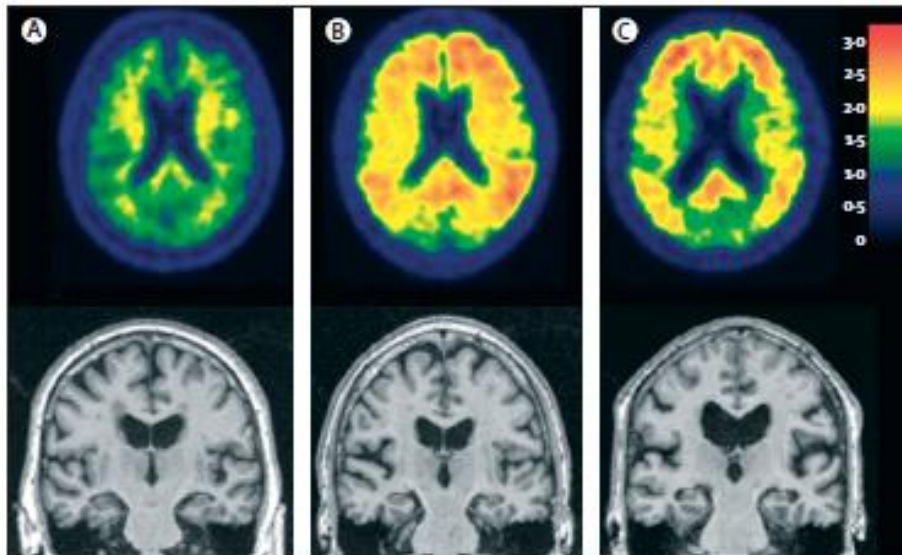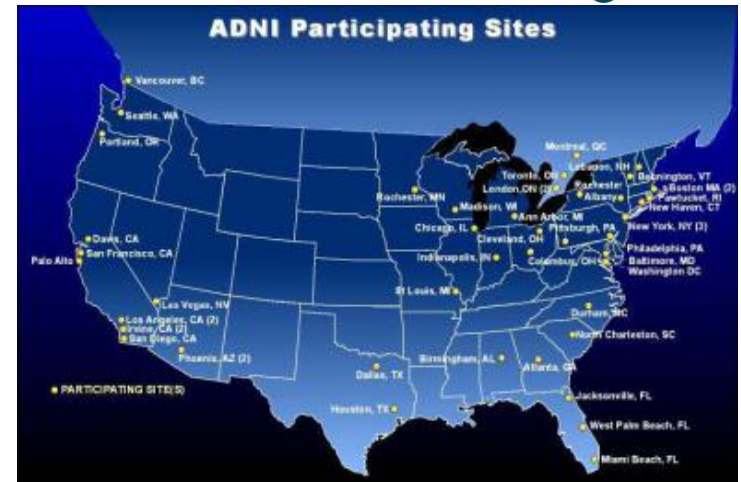*Arrowsmith J. Nature Reviews Drug Discovery Feb 2011*
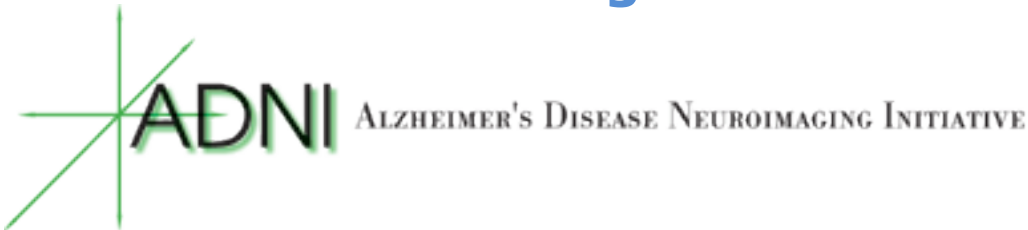
The Solution....Collaborations

that enable ......

- Sharing knowledge

- Learning from failures

- Public-Private Partnerships

Our Knowledge of Alzheimer's Disease has been Transformed through PPPs

ADNI ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

- **ADNI provided seminal new information concerning the pathophysiology of AD**
- **Defined early detection methods for Identification of risk**
- **Improved treatment trials for assessing predictors and outcomes**
- **Accelerated a path leading to the treatment and prevention of AD**
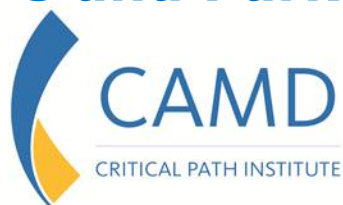
Biomarker staging of AD

CAMD

The mission of CAMD is to advance innovative tools and technologies through a regulatory path that accelerates development of medical products for brain diseases.

Firsts:

- **Therapeutic Area clinical data standards published by CDISC (AD and PD)**
- **Unified CDISC database of Alzheimer's disease clinical trial information provided by multiple pharmaceutical companies**
- **Clinical trial modeling and simulation tool advanced for a regulatory decision**
- **Neuroimaging biomarker for Alzheimer's Disease qualified by a regulatory agency (EMA)**

CAMD: Tools to Advance Effective Treatments for Alzheimer's and Parkinson's Disease

Nonmember participants: **Academic key opinion leaders, CROs**

First CDISC Therapeutic Area Data Standard

Alzheimer's Disease-specific Therapeutic Area Supplement to the Study Data Tabulation Model User Guide

Prepared by the

Coalition Against Major Diseases (CAMD)

http://www.cdisc.org/stuff/contentmgr/files/0/464c32d97e58d1e0640c77ab2809f0ef/misc/sdtmug_alzheimer__s_2011_09_23_final_revised.pdf

Published Sept 2011

C-Path's Data Repository for Alzheimer's Disease

- **Nine companies remapped and pooled data from 24 trials for ~6500 patients**

- **Database open to >200 qualified research teams in 35 countries**

C-Path's track record: Data and Modeling & Simulation tools

Biomarkers are being actively employed in AD therapeutic trials

Blennow, Nature Med 2010 16(11) 1218
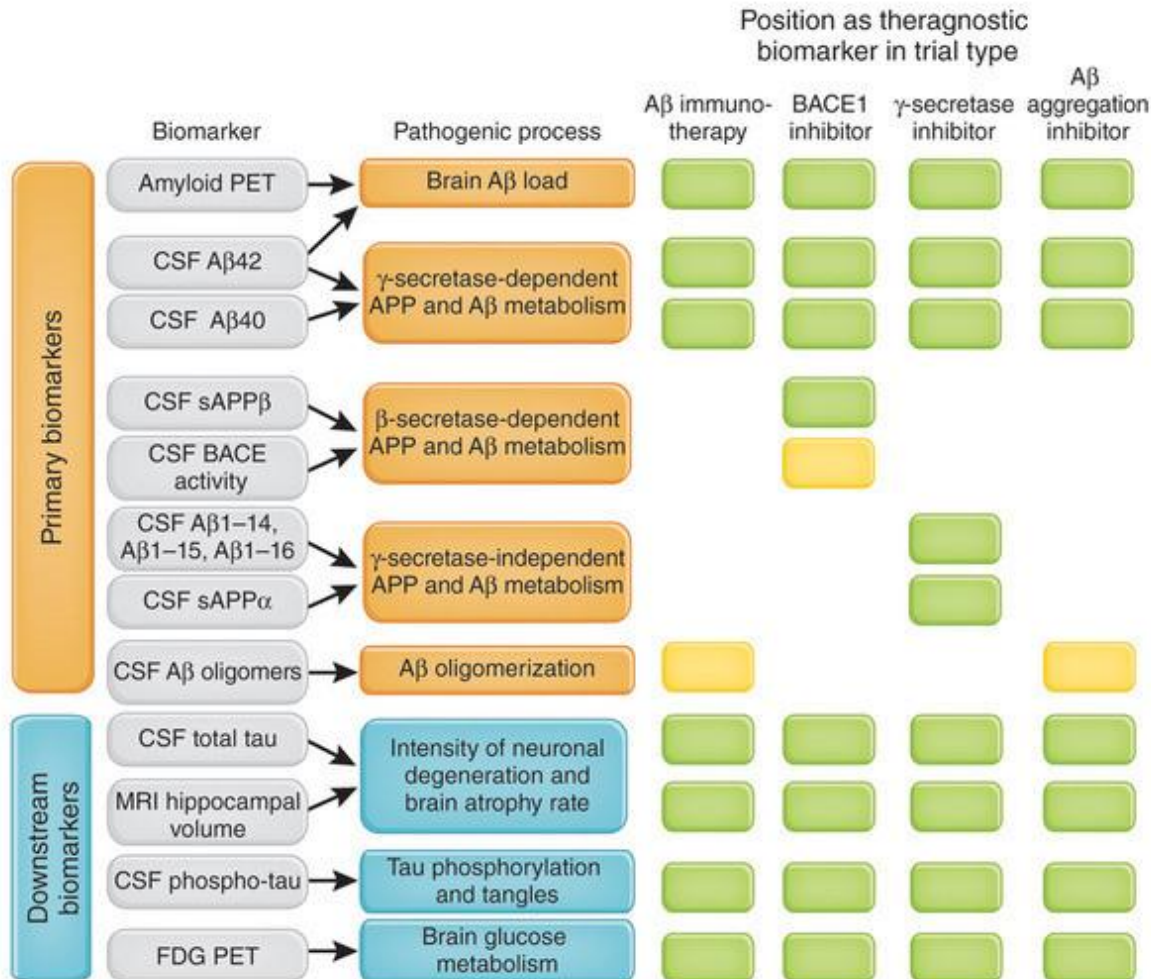
Biomarkers for Choosing the Right Patients

Baseline hippocampal volume
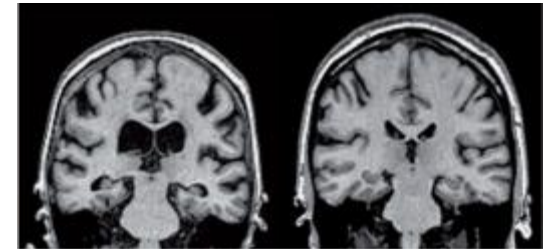
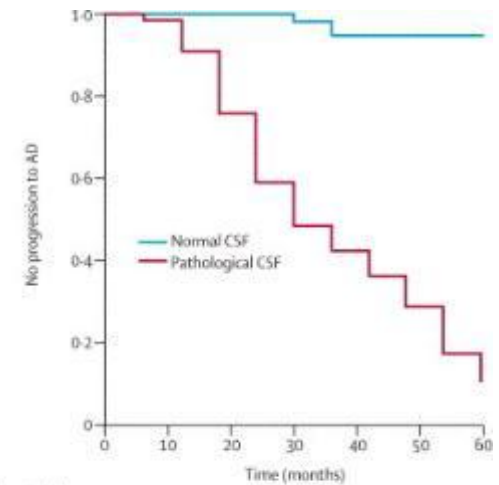*Jack et al, Brain 33:3336-48, 2010*

CSF biomarkers

SLIDE 3

Conceptual Model Depicting the Approach to Earlier Alzheimer's Disease Diagnosis
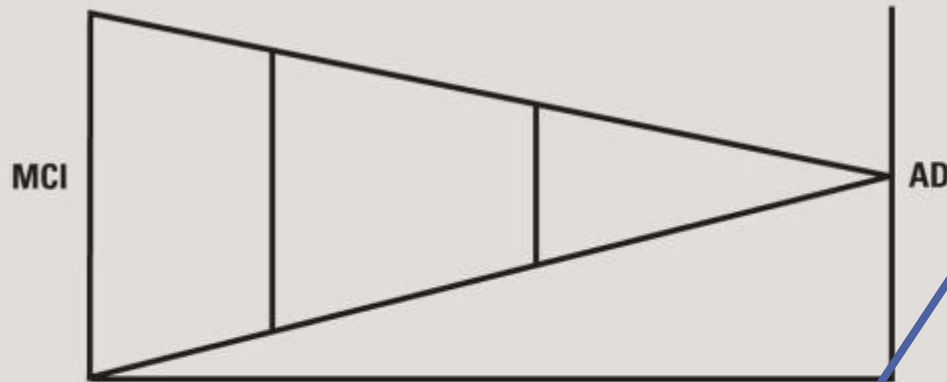
Clinical Factors	Biomarkers
Episodic memory	ApoE4 status
Vascular risk factors	Structural imaging
Depression	CSF Aβ/tau/phosphotau
	Functional imaging

MCI=mild cognitive impairment; AD=Alzheimer's disease; ApoE4= apolipoprotein E4; CSF=cerebrospinal fluid; Aβ=amyloid β.

Feldman, CNS Spectr. 2008;13(3 Suppl 3):4-7

Hansson et al., Lancet Neurol 5(3):228, 2006

Neuroimaging as a drug development tool for patient enrichment

1   10 October 2011
2   EMA/CHMP/SAWP/809208/2011
3   Committee for Medicinal Products for Human Use (CHMP)

4   Qualification opinion of low hippocampal volume
5   (atrophy) by MRI for use in regulatory clinical trials - in
6   pre-dementia stage of Alzheimer's disease

7

Agreed by Scientific Advice Working Party	1 September 2011
Adoption by CHMP for release for consultation	22 September 2011
End of consultation (deadline for comments)	1 November 2011

8

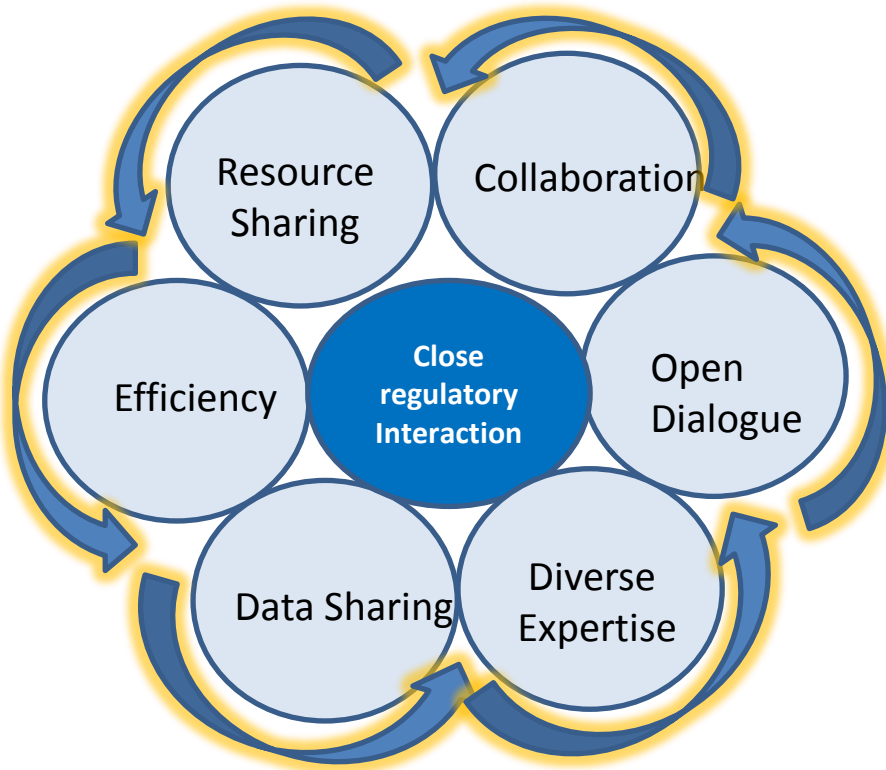# CAMD Aligns with Relevant PPPs

Public-Private Partnerships

Global Standardization Biomarkers Consortium

Alzheimer's Prevention Initiative

Global CEO initiative

Opportunity and Challenges

- Resource constraints at all levels
- Consortia fatigue
- Organizational Structure and Governance
- Data Sharing
- Communication among partners
- Culture
- Financing
- Incentives
- Risk Mitigation
- Respect for confidentiality

- Given the CAMD and IMI summarizes of work-scope just presented do you see the gaps that are not being addressed, but would be critical to advancing the Alzheimer's disease initiatives?

- What opportunities do you see for synergy/ leveraging both efforts? Given the global scale of this disease we all agree that information and data "sharing" is critical. (Whether it is sharing across companies or PPP's).

- Do you view sharing of information as a continued challenge and if so what can be done to improve the environment?

- What do you see as the regulatory impact of these efforts and/or areas of future focus; "harmonization of efforts" Have we done enough to empower/include/enthuse the public/patients/caregivers and if not how might we?

- Data sharing and joint-working seems to be working really well with clinical studies and human-data. How about preclinical and animal studies?