Coalition Against Major Diseases

Regulatory Science can Accelerate Drug Development for Neurodegeneration

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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: 21%
Safety: 7%
Financial: 6%
Not disclosed: 66%

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 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
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)

Published Sept 2011

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

Mixed Legacy Data

Data Standards

Integrated Data
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

CSF biomarkers

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

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

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>Agreed by Scientific Advice Working Party</td>
<td>1 September 2011</td>
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<tr>
<td>Adoption by CHMP for release for consultation</td>
<td>22 September 2011</td>
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<tr>
<td>End of consultation (deadline for comments)</td>
<td>1 November 2011</td>
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CAMD Aligns with Relevant PPPs

Public-Private Partnerships

- ACT-AD
- Alzheimer's Association Research Roundtable
- Banner Alzheimer's Institute
- Global Standardization Biomarkers Consortium
- ADNI
- FNIH
- The Biomarkers Consortium
- IMI
- ADCS
- Regional Alliance for Neuroimaging
- 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?