C-Path Collaborators

CRITICAL PATH INSTITUTE

Industry

Abbott · Boehringer Ingelheim · Actelion · Bristol-Myers Squibb · Daiichi-Sankyo · Genentech · Merck · Orion · Sunovion · Takeda · Otsuka · Allergan · Celgene Global Health · Eisai · GlaxoSmithKline · Millennium · Teva · Amgen · Roche · Mitsubishi Tanabe Pharma · Pfizer · UCB · Astellas · Cepheid · GE Healthcare · Novartis · Sanofi · Lilly · Ironwood · Shire · Vertex · AstraZeneca · clinXus · Forest Laboratories, Inc. · Johnson & Johnson · novo nordisk

Partners

Bill & Melinda Gates Foundation · iCardiac Technologies · CDISC · International Genomics Consortium · Engelberg Center for Health Care Reform at Brookings · Oracle Health Sciences · ephibian · STC · TB Alliance

Patients

Alliance for Aging Research · PKD Foundation · alzheimer's association · TAG Treatment Action Group · AFA Alzheimer's Foundation of America · National Health Council

Research

ASU · The University of Arizona · Emory University · Center for Translational Social Neuroscience · University of Colorado Boulder · FOX · SRI International · Mayo Clinic · Tufts University

Government

CDC · NIDDK · FDA · National Institute of Neurological Disorders and Stroke · National Institute on Aging · PMDA Japan · European Medicines Agency · imi · National Institute of Allergy and Infectious Diseases · FNIH · National Institutes of Health · World Health Organization

Consortia

Consortia	Title	Regulatory Qualifica
PSTC CRITICAL PATH INSTITUTE	Predictive Safety Testing Consortium	Preclinical and clin biomarkers
PRO CONSORTIUM CRITICAL PATH INSTITUTE	Patient-Reported Outcome Consortium	PRO instruments
CAMD CRITICAL PATH INSTITUTE	Coalition Against Major Diseases	Pooled clinical trial and imaging bioma quantitative diseas progression model
PKD CONSORTIUM CRITICAL PATH INSTITUTE	Polycystic Kidney Disease Consortium	Quantitative diseas progression model kidney volume by M
CPTR	Critical Path to TB Drug Regimens	Drug development combination drug c

Asthma, cancer, depression, arthritis, irritable bowel, MCI, functional dyspepsia

Alzheimer's disease, Parkinson's disease

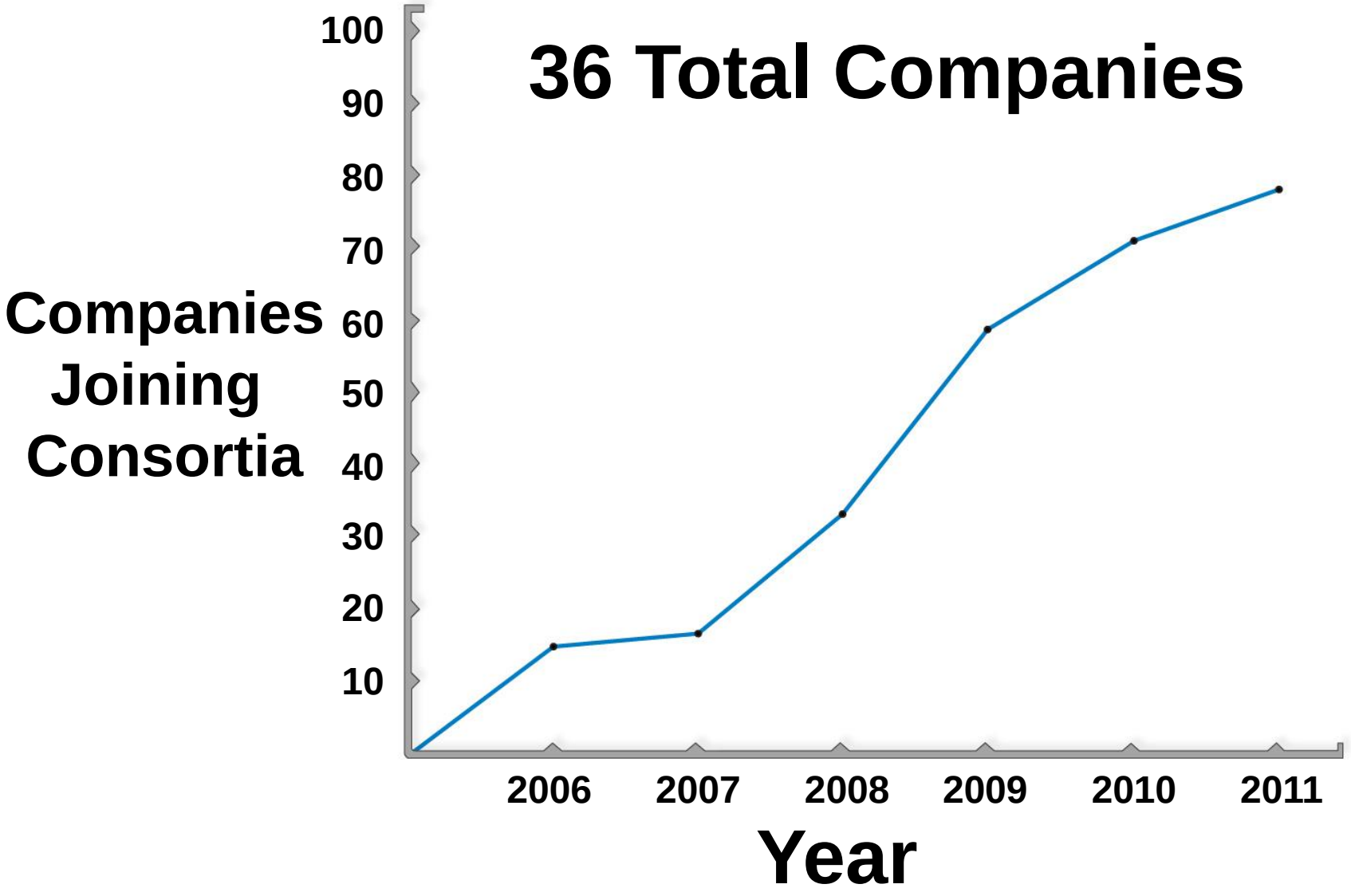
Autosomal dominant polycystic kidney disease

Tuberculosis

Creating Consensus

	Members	Industry	FDA
PSTC CRITICAL PATH INSTITUTE	18	239	36
PRO CONSORTIUM CRITICAL PATH INSTITUTE	25	167	19
CAMD CRITICAL PATH INSTITUTE	14	172	27
PKD CONSORTIUM CRITICAL PATH INSTITUTE	3*	10	11
CPTR	10	54	11

Growing Collaborations:



Neutral 3rd Party

Total Initial Funding $24 Million

Annual Budget $8 million

50 % Arizona

25% FDA

12% Gates Foundation

6% Other Foundations

7% Philanthropy

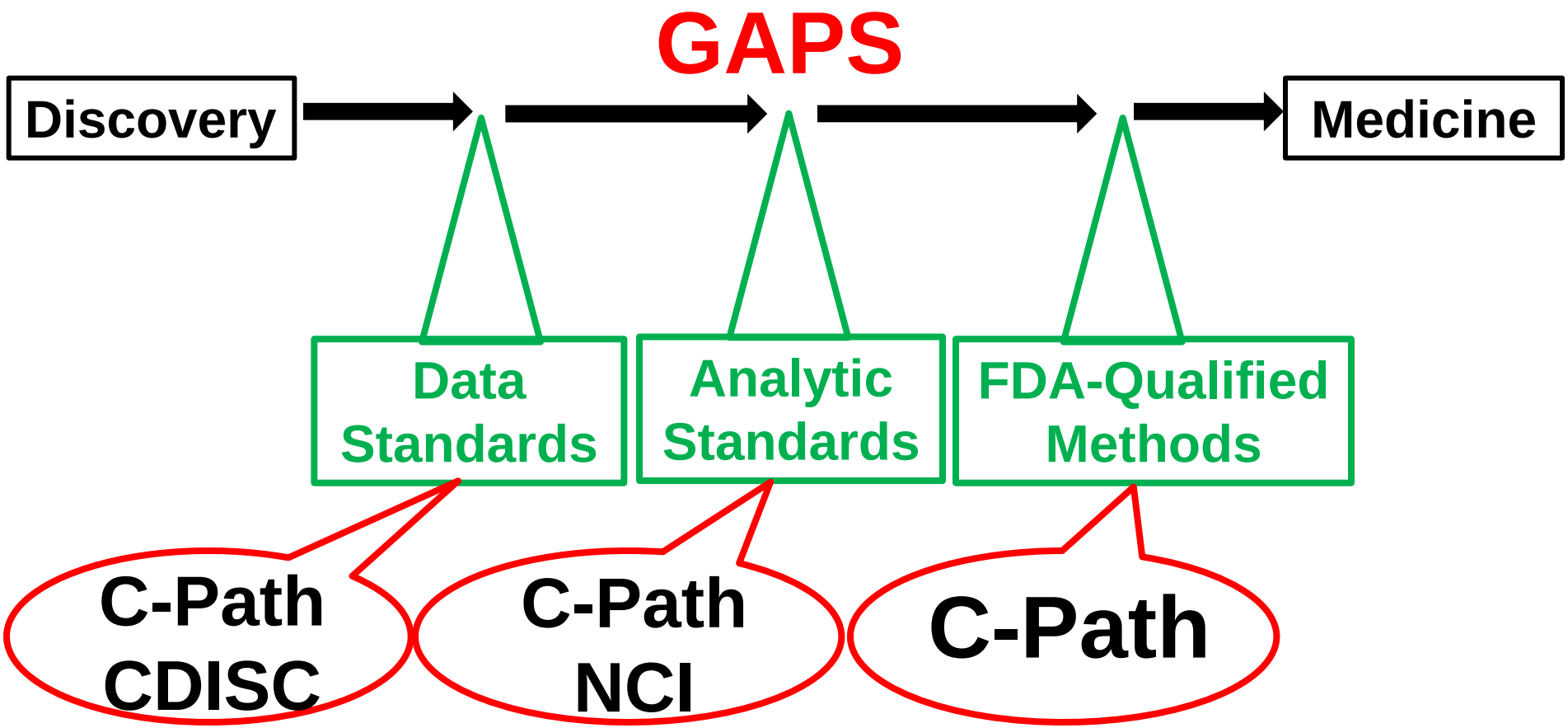
Industry Support:

600 Scientists

Data valued at over $350 Million

Consortium Research - $7 million

Structural Gaps



All Precompetitive

Qualification

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Guidance for Industry

Qualification Process for Drug Development Tools

October, 2010

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Shaniece Gathers, 301-796-2600.

New Drug Development Tools

- 7 Safety biomarkers "Qualified" by FDA, EMA, and PMDA and being used by industry
- ~ 60 Biomarkers/PROs in process
- CDISC Data Standards set for Alzheimer's disease

  (Parkinson's, TB, and PKD in process)
- Database of 11 pooled industry trials opened for researchers (~5000 Alzheimer's disease patients)
- Alzheimer's: MRI qualified by EMA and disease progression model & CSF biomarkers in FDA review

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

- **Seven companies remapped and pooled data from 11 trials for ~5000 patients: value = $350 Million**
- **Database open to >200 qualified research teams in 35 countries**

What was learned?
ADAS-Cog Variability

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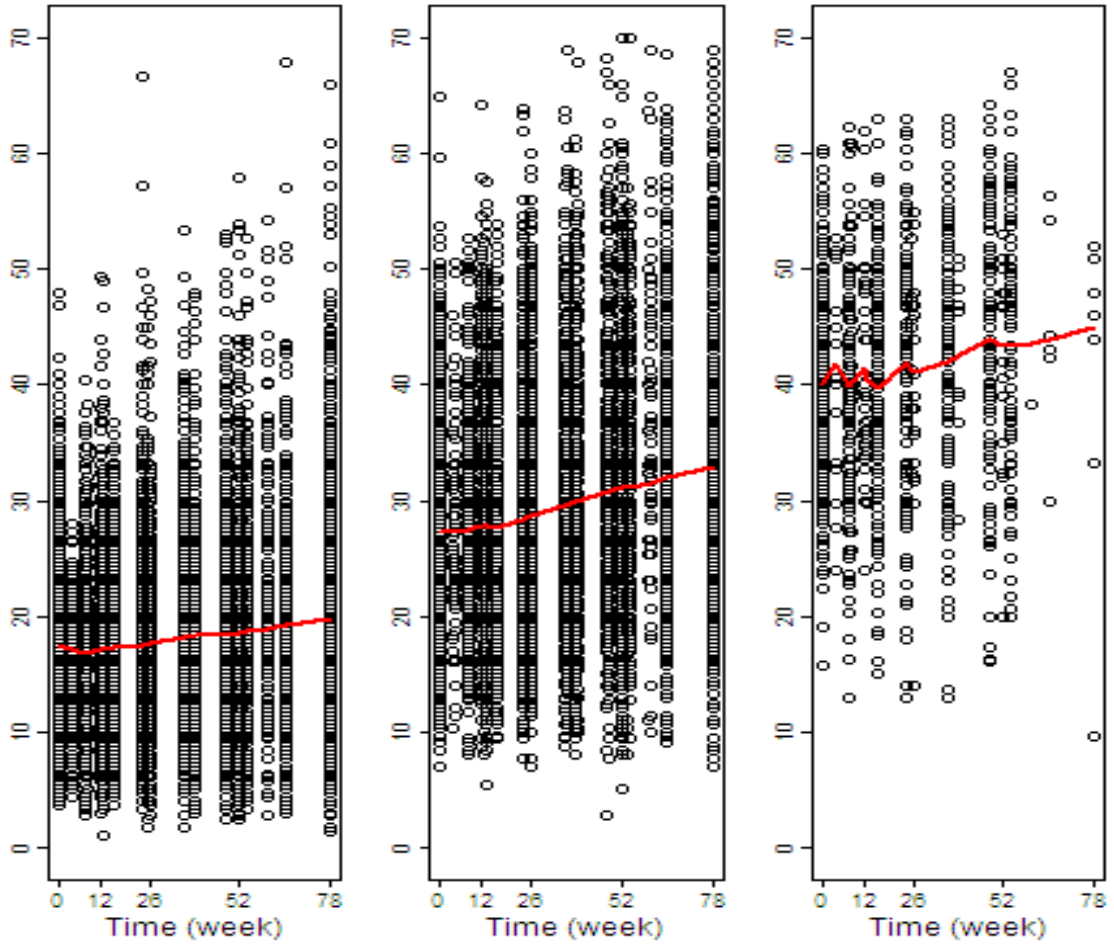
	ADNI	J&J	Wyeth	sanofi-aventis	Pfizer	AstraZeneca	Abbott
Item 1	Word Recall	Word Recall	Word Recall	Word Recall	Word Recall	Word Recall	Word Recall
Item 2	Commands	Name Obj/fing.	Name Obj/fing.	Commands	Name Obj/fing.	Name Obj/fing.	Name Obj/fing.
Item 3	Constr. Praxis	Delayed recall	Commands	Constr. Praxis	Commands	Commands	Commands
Item 4	Delayed recall	Commands	Constr. Praxis	Delayed recall	Delayed recall	Constr. Praxis	Constr. Praxis
Item 5	Naming Obj/fing.	Constr. Praxis	Idea Praxis	Name Obj/fing.	Constr. Praxis	Idea. Praxis	Idea. Praxis
Item 6	Idea. Praxis	Idea Praxis	Orientation	Idea. Praxis	Idea. Praxis	Orientation	Orientation
Item 7	Orientation	Orientation	Word Recog	Orientation	Orientation	Word Recog	Word Recog
Item 8	Word Recog.	Word Recog.	Remem. Instr.	Word Recog	Word Recog	Remem. Instr.	Spoken Lang Abil.
Item 9	Remem Instr.	Remem Instr.	Spoken Lang. Abil.	Remem. Instr.	Remem. Instr.	Spoken Lang. Abil.	Comprehension
Item 10	Comprehension	Spoken Lang. Abil.	Word Finding Dif.	Spoken Lang Abil.	Spoken Lang Abil.	Word Finding Dif.	Word Finding Dif.
Item 11	Word Finding Dif.	Word Finding Dif.	Comprehension	Diff. Spont. Speech	Word Finding Dif.	Comprehension	Remem. Instr.
Item 12	Spoken Lang. Abil.	Comprehension	Concentration	Comprehension	Comprehension	Concentration	
Item 13	Number cancel.	Concentration		Concentration	Concentration		

CAMD Database

Baseline: **Mild** **Moderate** **Moderately Severe**

Observed ADAS-cog



LOWESS in Red
(Locally Weighted Scatterpoint Smoothing)

10-Year Disease Progression by Severity at Entry

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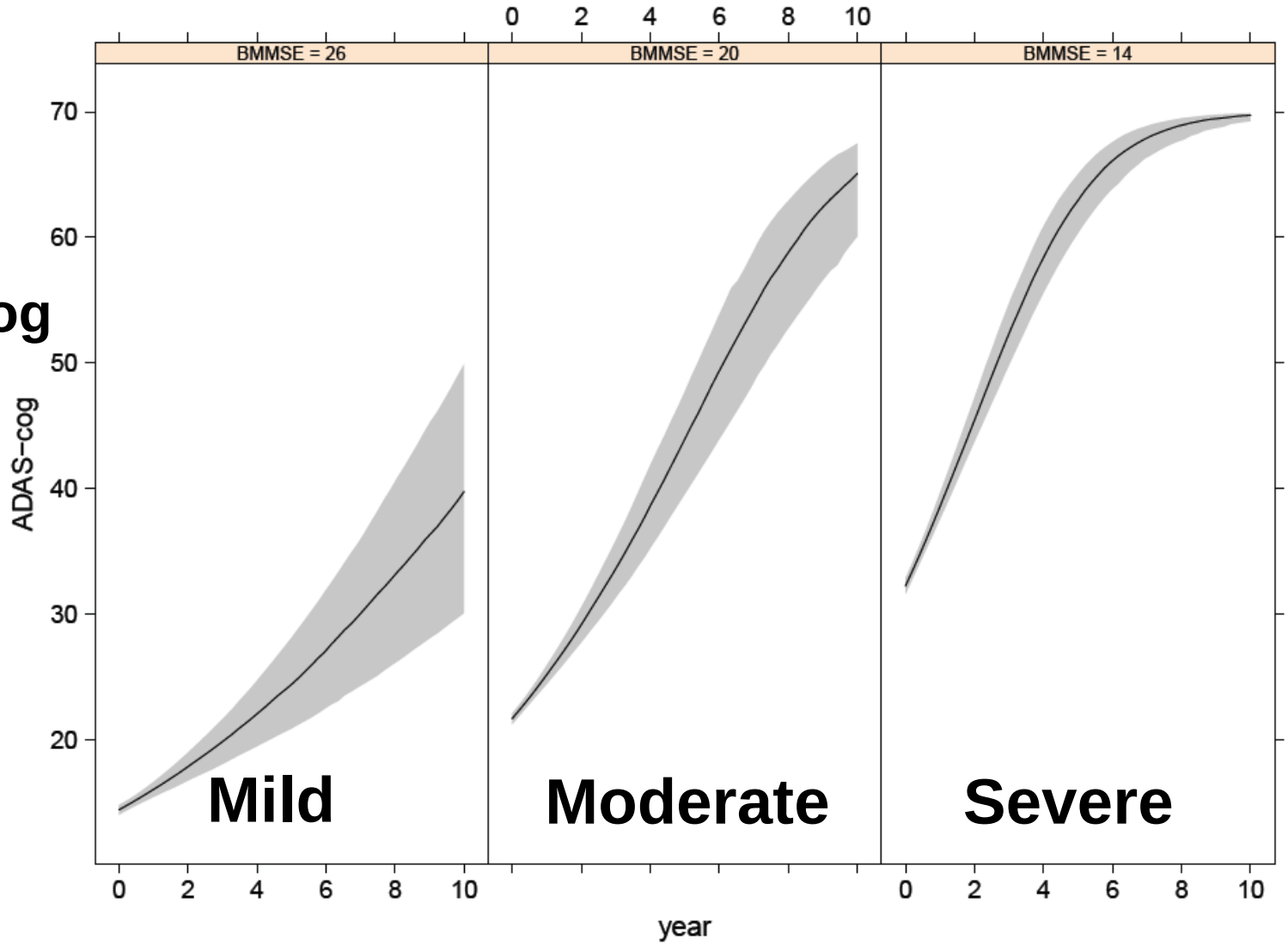
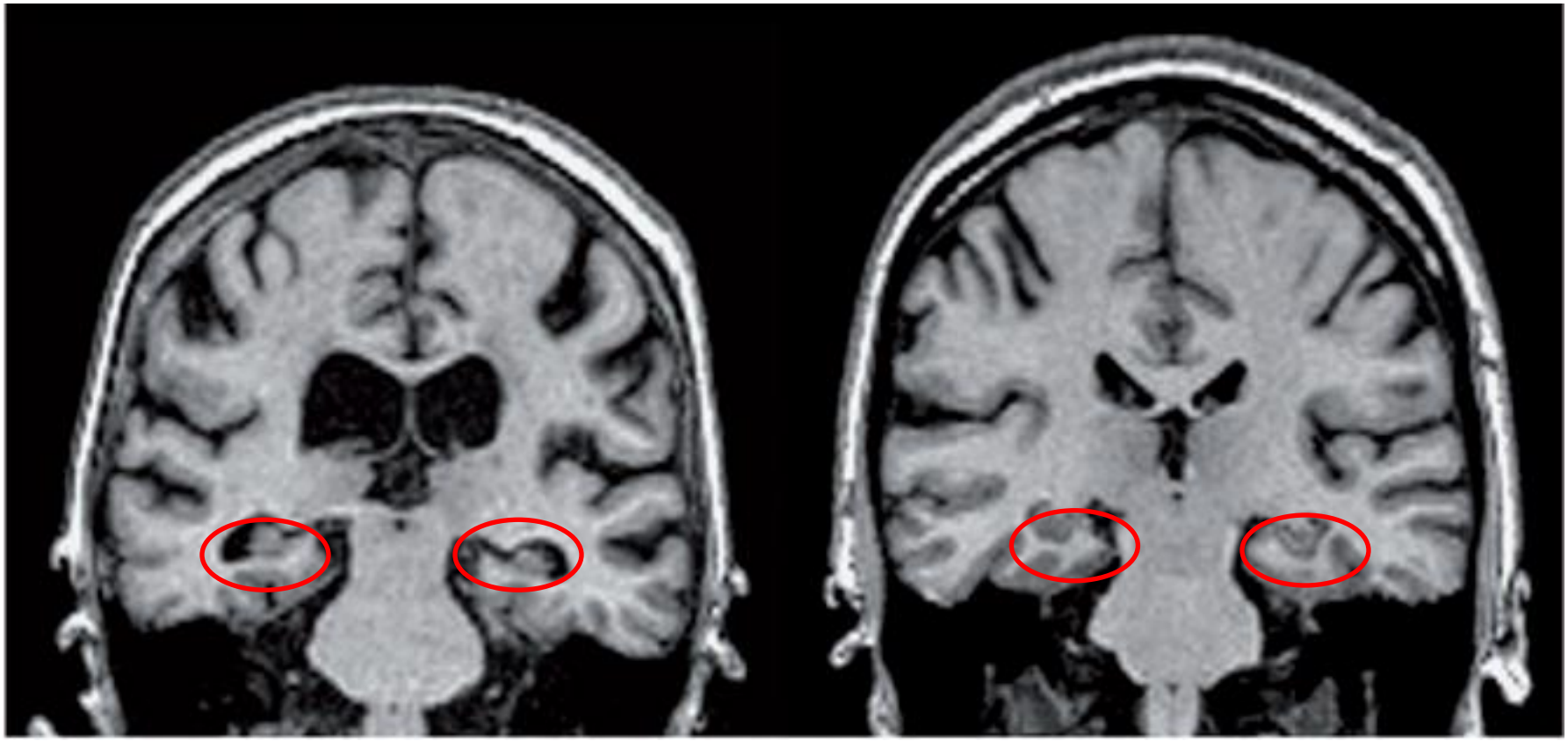
ADAS-cog



Hippocampal Volume: Now Qualified by IMI



Mild Cognitive Impairment, progressor

Mild Cognitive Impairment, nonprogressor

*From **J**ack et al, Brain 33:3336-48, 2010*

MRI as a drug development tool for patient enrichment

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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

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

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

The Future ?

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Setting Precompetitive Standards

Clinical Trials	Clinical Trials Date of Birth
What is the average age of patients enrolled in 11 industry trials for Alzheimer's Disease?	Jan. 15, 2011 January 15, 2011 1/15/11 1/15/2011 15/1/11 1-15-11 15-1-11 2011-1-11

C-Path and CDISC Collaborations

C-Path – FDA Qualification

Collaborations

CAMD – Alzheimer's
CAMD – Parkinson's
PKD – Polycystic Kidney Disease
PSTC – Safety Testing
CPTR – Tuberculosis

CDISC – Data Standards

FDA High Priority, Therapeutic Area Standards

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* existing projects

Tier 1		
Acne	Pain*	Schizophrenia
Alzheimer's Disease*	Parkinson's Disease*	Solid organ transplantation
Anti-diabetic agents*	Prevention of pregnancy	Treatment of Hepatitis C*
Crohn's Disease	Psoriasis	Treatment of postmenopausal osteoporosis
Infections of skin and/or subcutaneous tissue	QT Studies	Tuberculosis*
Oncology: time to efficacy event other than overall survival*	Rheumatoid arthritis	Urinary tract infections
Tier 2		
Addiction	Gastroesophageal reflux disease	Pneumonia
Anticonvulsants	Influenza	Prevention of HIV
Asthma	Irritable bowel syndrome	Treatment of HIV
Bipolar Disorder	Lipid-altering drug groups	Treatment of overactive bladder
Clostridium difficile colitis	Major depressive disorder	Treatment of vasomotor symptoms due to menopause
Diabetic nephropathy	Objective tumor response*	Ulcerative colitis
Tier 3		
Actinic keratoses	Decompensated CHF	Tinea pedis
Aerosolized antimicrobals for cystic fibrosis	Diagnostic radiopharmaceuticals	Tramatic brain injury
Atrial fibrillation	General Anxiety Disorder	Treatment of cough
Attention Deficit Hyperactivity Disorder	Helicobacter pylori ulcer disease	Treatment of erectile dysfunction
Bacterial vaginosis	Infectious diseases of the abdomen	Treatment of hepatitis B
Chemotherapy-induced nausea	MRI contrast agents	
COPD	Recombinant human growth hormone	

55n5 ---

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55 Therapeutic Areas in 5 Years

C-Path and CDISC Collaboration

- Establish Clinical Data Standards

CDISC

- Establish Clinical Trial Databases

- Certify Testing Methods
  for Specific Context of Use