

# **NIA ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE (ADNI)**

**Michael W Weiner**

**Leon Thal**

**Ronald Petersen**

**Clifford Jack**

**William Jagust**

**Arthur Toga**

**John Trojanowski**

**Laurel Beckett**

# OVERVIEW

- **Introductions**
- **Overview and Administrative Core: Weiner**
- **Statistics Core: Beckett**
- **Clinical Core: Thal**
- **MRI Core: Jack**
- **PET Core: Jagust**
- **Biomarkers Core: Trojanowski**
- **Informatics Core: Toga**

# **WHAT WE WANT TO ACCOMPLISH TODAY**

- **We will briefly review our proposed work**
- **We want your candid feedback**
  - **What are the anticipated problems**
  - **Suggested approaches to the problems**
- **In addition to our annual meetings**
  - **We may come to you with questions**
  - **We invite your feedback at all times**

# GOALS

- **We want this project to be a huge success!**
- **We want to achieve the stated aims in the proposal**
- **To set a new standard for:**
  - **Public release of data**
  - **Public-Private partnerships**
- **Increase the impact of the ADNI beyond the proposal**
- **Plan renewal**

# **INCREASING ROLE OF IMAGING & BIOMARKERS IN AD TREATMENT TRIALS AND DETECTION**

- **Many studies have shown changes in the brain of normal aging and in AD**
- **Structural MRI shows shrinkage, esp of median temporal lobe and cortex**
- **FDG PET shows reduced metabolism**
- **AD Biomarkers can improve diagnosis and reflect disease progression**
- **Great potential for use in clinical trials and for early detection**

# **ROLE OF IMAGING IN TREATMENT TRIALS**

- **Current trials using ADAS-cog etc have large sample size**
  - **Cognitive measures do not easily determine disease modifying effects of treatment**
- **PHARMA has high interest in use of imaging for treatment trials**
- **Current data from many labs, different methods, different subjects**

# **BRIEF HISTORY OF THIS PROJECT**

- **Buckholz/Potter: original concept**
- **2001 MRI multisite study proposed:**
  - **Initially to industry**
  - **Then to NIA**
- **NIA initiated a series of workshops**
- **RFP released in Oct 2003, due Jan 17 2004**
- **Reviewed in May 2004, funded last week**
- **Funded 2/3 by NIA, 1/3 by Industry**

# **GOALS OF THE ADNI LONGITUDINAL MULTISITE OBSERVATIONAL STUDY**

- **Develop “standards” for imaging**
- **Improve methods for clinical trials**
- **Determine the optimum methods for acquiring and processing images**
- **“Validate” imaging and biomarker data by correlating with neuropsych and behavioral data**
- **Provide a data base and biological samples for PHARMA**

# OVERALL GOALS

Major goal is *collection of data and to establish a brain imaging and biomarker database*

- **Also development of improved methods for trials**
- **Clinical Core, Neuroimaging Core: public access**
- **Emphasis on MCI, with some AD and controls**
- **Processing of MRI, PET, and biomarkers**

# ANTICIPATED FUNDING

- **\$12 million/yr, 5 years:**
  - **Total funding \$ 60 million**
    - **\$40 Million provided by NIH (NIA, NIBIB)**
    - **\$20 Million to be provided by industry**
- Cooperative agreement (U01)**

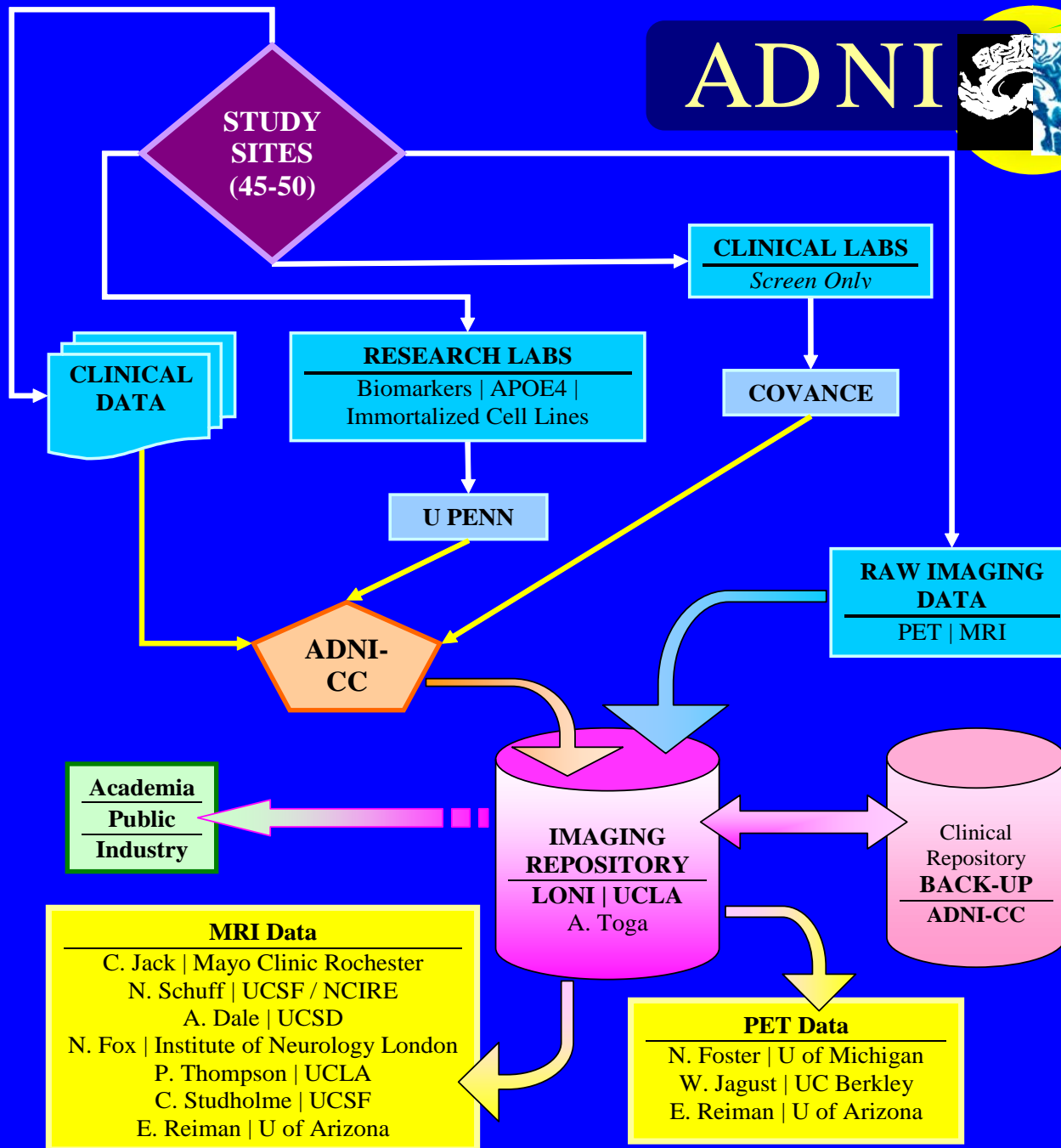
# STRUCTURE

- **Administrative Core: Weiner**
- **Clinical Core: Leon Thal, Ron Petersen, Marilyn Albert, Pierre Tariot, David Salmon**
  - **Based at ADCS at UCSD**
- **Neuroimaging Core**
  - **MRI: Cliff Jack, Norbert Schuff, Anders Dale, Nick Fox, Charles DeCarli, Matt Bernstein, Joel Felmlee**
  - **PET: Bill Jagust, Norm Foster, Eric Reiman, Bob Koeppe**
- **Informatics: Art Toga UCLA/LONI**
- **Biomarker Core: J.Q. Trojanowski, Les Shaw**
- **Statistics: Laurel Beckett**
- **45+ performance sites**

# STUDY DESIGN

- **MCI (n= 400): 0, 6, 12, 18, 24, 36 months**
- **AD (n= 200): 0, 6, 12, 24 months**
- **Controls (n= 200): 0, 6, 12, 24, 36 months**
- **Clinical, MRI (1.5 T) at all time points**
- **FDG PET at all time points in 50%**
- **3 T MRI at all time points in 25%**
- **Blood and urine at all time points from all subjects, CSF from 20% of subjects less often**

# ADNI



# IMAGING INFOMATICS

- Goal is rapid public access of *all raw and processed data*
- Art Toga at LONI will receive all QA'd MRI and PET data
- Images for processing downloaded from LONI, and results uploaded to LONI
- All image data will be available from LONI
- Clinical data base at ADCS/UCSD will be linked

# **INVOLVEMENT BY INDUSTRY IN THE APPLICATION**

- **PHARMA and Imaging Companies will directly provide funds through the NIH Foundation. They will serve on the Steering Committee.**
- **Scientific participation by industry is desirable!**
  - **Expect involvement with all Cores**

# **SITE REQUIREMENTS**

- **45-50 sites have been selected**
- **Major requirement: demonstrated ability to recruit MCI subjects for trials**
- **Also need acceptable 1.5 T MRI**
- **Some sites will provide 3 T and PET**

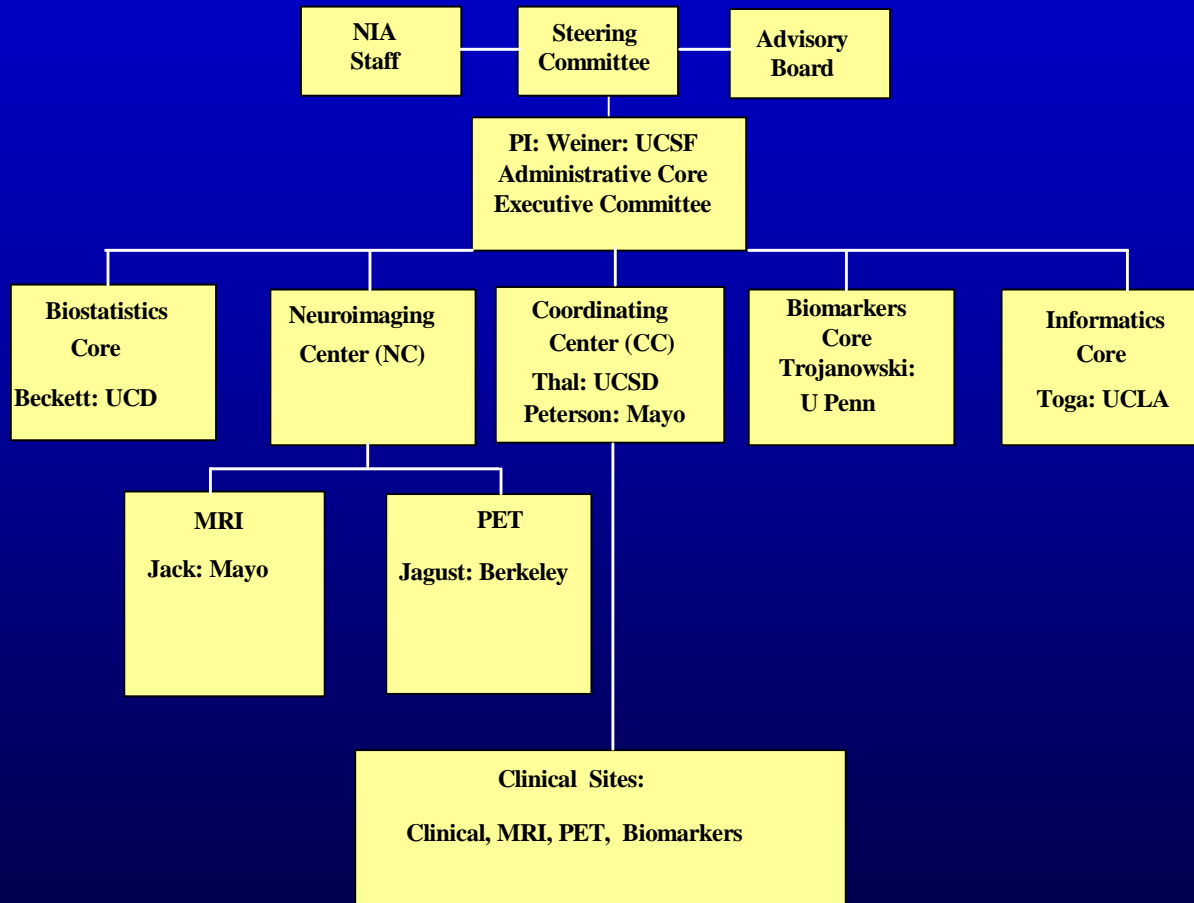
# **TIME LINE**

- **Some (not all) funds awarded last week**
- **Preparatory Phase Oct –April**
- **Patient enrollment begins April-July 2005**
- **Enrollment ends July 2006. Completion 2009**

# **GOVERNANCE AND OPERATIONS**

- **The RFP states that governance will be performed by the Steering Committee: Funded investigators, all sites, NIH, Industry, FDA: Over 120 people**
- **Exec Com will oversee operations**
  - **Each Core will oversee its own work**
  - **Clinical Core oversees site performance**

# ADNI GOVERNANCE



# ADNI Participating Sites



# ANTICIPATED PROBLEMS

- **The study is very arduous with many procedures and many time points**
  - **Recruitment**
  - **Retention**
  - **Getting started on time. Completion of study goals within the 5yr funding period**
- **Requests for “Add on” Studies**
- **Distribution of Biomarker samples**
- **Organizing and making sense of so much data**

# LINKS TO EUROPE

- **A world-wide study would have the greatest impact**
- **Problems included: language, data monitoring, complexity, IDC restrictions**
- **Links to GSK study and a European initiative are being discussed**

# CONCLUSION

- **This is an exciting and challenging project**
- **We solicit your candid criticism and suggestions**
- **We greatly appreciate your working with us to accomplish our mutual goals**