Private Public Partnerships: Perspectives from the Foundation for the NIH

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Research Partnerships
Foundation for the National Institutes of Health
PURPOSE
Support the mission of the NIH
Advance collaboration with biomedical researchers from universities, industry, not-for-profit organizations

STRUCTURE
501(c)(3) not-for profit foundation created by Congress
Independent Board of Directors with NIH Director and FDA Commissioner as ex-officio Board members

HIGHLIGHTS
Raised over $800 million since 1996
Supported nearly 500 projects
94 cents of every dollar spent directly funds programs
Our role...

*What we do, how we do it...*

**Identify:**
- Important scientific problems
- Key players
- Resources required and sources of support
- Neutral convener; trusted party to provide safe harbor for discussions

**Establish:**
- Highest level of ethical standards
- Clear goals and milestones
- Effective mechanism to generate scientific consensus
- Nimble infrastructure and project expert project management

**Facilitate:**
- Discussions with key opinion leaders and regulatory decision makers
- Integrated approach to cross-sector partnerships
- Communications; ensure all partners’ voices are heard;

**Enable:**
- Sharing of data and expertise to collaboratively address medical needs
- Resource mobilization
- Manage grants, contracts, and projects; oversee and conduct research
Our history of support for hundreds of projects since 1996 offers many models for partnerships between the public and the private sectors, ranging from simple fund transfers to highly complex and interactive programs.
How we Fund Our Programs

FNIH has no endowment
Funding & Partnership Models

Model 1
- Private Sector Funders
- FNIH
- NIH
- Intramural or Extramural Lab

Model 2
- Private Partners
- FNIH
- NIH
- Scientific Programs & Research

NIH Steering Committee/Project Team

$Flow$

Scientific Interaction
# Major FNIH Research Partnerships

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Funding</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accelerating Medicines Partnership</td>
<td>$230M</td>
<td>NIH (OD), NIA, NIAMS, NIDDK, 10 companies, 7 non-profits</td>
</tr>
<tr>
<td>Grand Challenges in Global Health (GCGH)</td>
<td>$201M</td>
<td>Bill &amp; Melinda Gates Foundation</td>
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<tr>
<td>LungMAP: Master Lung Protocol Trial</td>
<td>$163M</td>
<td>NCI (SWOG), FDA, Friends of Cancer Research, 5 companies to date</td>
</tr>
<tr>
<td>Alzheimer’s Disease Neuroimaging Initiative (ADNI)</td>
<td>$148M</td>
<td>NIA,NIBIB &amp; 20 companies/2 non-profits</td>
</tr>
<tr>
<td>Vector-Based Control of Emission (VCTR)</td>
<td>$78M</td>
<td>Bill &amp; Melinda Gates Foundation</td>
</tr>
<tr>
<td>The Biomarkers Consortium</td>
<td>$60M</td>
<td>FDA, NIH, CMS, PhRMA, BIO, 17 companies, 16 non-profits</td>
</tr>
<tr>
<td>Comprehensive T Cell Vaccine immune Monitoring Consortium (CT-VIMC)</td>
<td>$50M</td>
<td>VRC/NIAID, Bill &amp; Melinda Gates Foundation, NIAID</td>
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<tr>
<td>MAL-ED: The Interactions of Malnutrition and Enteric Infections, Effect on Childhood Development</td>
<td>$46M</td>
<td>Bill &amp; Melinda Gates Foundation, FIC</td>
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Alzheimer’s Disease Neuroimaging Initiative (ADNI)

GOALS

1. To detect AD at the earliest stage possible and identify ways to track the disease through biomarkers.

2. To support advances in AD intervention, prevention and treatment through the application of new diagnostic methods to apply at the earliest stages technically possible - when intervention may be most effective.

3. To continually develop ADNI’s data access policy and continuously improve and expand the unprecedented data sharing model.
Current PPSB Partners for ADNI2

Private Partner Scientific Board (PPSB): Independent, open, and pre-competitive forum
Accelerating Medicines Partnership: AMP

Transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets of disease.

Drug Companies Join NIH in Study of Alzheimer’s, Diabetes, Rheumatoid Arthritis, Lupus

Ten Drug Companies Form Pact With NIH to Find Path for Alzheimer’s

Ten rival drug companies partner with government

Rival drug companies plan to collaborate on research against key diseases.

NIH, 10 Drug Companies Partner to Study Four Diseases

NIH announces novel venture with drug companies to fight major diseases

NIH, drug companies team up to target diseases

The National Institutes of Health is partnering with researchers from 10 rival drug companies to develop new treatments for Alzheimer’s disease, diabetes, rheumatoid arthritis, and lupus.

The partners plan to change the way drugs are developed.

In an unprecedented move designed to jump-start medical science, 10 rival drug companies that normally compete fiercely against each other will now cooperate not just with government researchers and non-profits, but with each other.
AMP: the problem

Developing effective new medicines takes too long, costs too much and fails too often.
Lack of efficacy currently accounts for more than half of all drug failures in Phase II clinical studies.

AMP’s target validation efforts aimed at improving efficacy and increasing success rate.

Current targets
- Animal models
- Cell lines

AMP targets
- Emerging Technologies
  - DNA sequencing
  - Proteomics
  - Single-cell analysis
  - Bioengineered cells
  - Imaging
- Extensive Human Data
  - Tissue/blood samples
  - Clinical information
  - Demographics
- Big Data Tools

AMP: Improving R&D Efficacy
# AMP – Research Initiatives

<table>
<thead>
<tr>
<th>Disease area</th>
<th>Research plan topics</th>
<th>Deliverables and approach</th>
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</table>
| Alzheimer's disease           | Exploratory biomarker validation in clinical trials and network analysis on human tissue | • **Embed biomarkers in NIH-funded clinical trials** to develop biomarkers of disease progression and surrogate endpoints  
• **Conduct network analysis in human brain samples** to identify genetic nodes & networks linked to AD to support target identification & validation |
| Type 2 Diabetes               | Sequencing & phenotyping of targets of interest and a tool to enable easy interrogation of all available data | • **Create a knowledge portal** containing comprehensive genotype/phenotype data sets – apply informatics to identify predictors of risk and potential drug targets  
• **Conduct targeted sequencing/genotyping** of high priority targets of interest (as defined by industry) |
| RA, SLE & related autoimmune diseases | Immune module deconstruction with blood/tissue and cross-disease comparisons       | • **Conduct extensive profiling of key immune modules** in highly refined subsets of relevant cells in informative cohorts to establish pathway/network maps of RA & SLE; high priority targets identified from pathway analysis to be validated via RNAi.  
• **Make the data available in a knowledge portal**  
  - Informative cohorts include: Early RA, Established RA (responder/non-responder), Lupus Nephritis, Skin Lupus |
AMP-AD

Project A: Biomarkers Project

• Alzheimer’s Disease Cooperative Study (ADCS) Anti-Amyloid Treatment in Asymptomatic Alzheimer’s Disease Trial (A4 Trial) (U19AG010483) Reisa Sperling, Harvard Medical School; Paul Aisen, University of California, San Diego

• Dominantly Inherited Alzheimer Network (DIAN) Trial (U01AG042791) Randall Bateman, Washington University

• Alzheimer's Prevention Initiative APOE4 Trial (API APOE) (UF1AG046150-01) Eric Reiman, Banner Alzheimer’s Institute; Pierre Tariot, Banner Alzheimer’s Institute

Baseline data from the trials will be made broadly available through the Alzheimer Association’s GAAIN collaborative platform
AMP-AD

Project B: Target Discovery and Preclinical Validation Project — The cooperative agreement grants that constitute the consortium were developed in response to the NIA funding opportunity RFA AG13-013:

- **Pathway Discovery, Validation and Compound Identification for Alzheimer's Disease** (U01AG046152) Philip L. De Jager, Brigham and Women's Hospital and the Broad Institute, Inc. David A. Bennett, Rush University
- **Integrative Biology Approach to Complexity of Alzheimer's Disease** (U01AG046170) Eric Schadt (Contact PI), Icahn School of Medicine at Mount Sinai
- **A System Approach to Targeting Innate Immunity in Alzheimer’s Disease** (U01AG046139) Todd Golde (Contact PI), University of Florida
- **Discovery of Novel Proteomic Targets for Treatment of Alzheimer's Disease** (U01AG046161) Allan Levey, Emory University David A. Bennett, Rush University

*Sage Bionetworks* facilitates data sharing and data integration activities within the Target Discovery and Preclinical Validation AMP-AD project. – *AMP_AD Knowledge Portal*
The Biomarkers Consortium

*Fosters the exchange of knowledge and expertise among industry, academic, and government leaders*

- Develops biomarkers for specific applications in diagnosing disease, predicting therapeutic response, and improving clinical practice
- Generates information useful to inform **regulatory decision-making** in the qualification process
- Employs rigorous, inclusive governance and project management with clearly defined goals and milestones
- Addresses a broad range of disease / therapeutic areas
- Pre-competitive; makes consortium project results broadly available to the entire scientific community

Our Founding Partners: FDA, NIH, FNIH, PhRMA, BIO, CMS
Biomarkers Consortium governance selects and plans projects

Executive Committee
NIH / FDA / CMS / industry / FNIH

Cancer Steering Committee
Inflammation & Immunity Steering Committee
Metabolic Disorders Steering Committee
Neuroscience Steering Committee

Multiple Project Teams
Representatives from NIH, FDA, Industry, Subject Experts from Academia
Biomarkers Consortium: 
19 Launched Projects to Date

**Executive Committee**
- Kidney Safety Biomarkers
- Skin Infection Pneumonia (CABP/ABSSSI)
- Hospital-Acquired & Ventilator Acquired Bacterial Pneumonia

**Cancer**
- FDG-PET in Lung Cancer
- FDG-PET in Lymphoma
- I-SPY 2 Trial**
- Minimal Residual Disease in ALL
- Volumetric CT for Clinical Trials

**Inflammation and Immunity**
- Osteoarthritis Biomarkers

**Neuroscience**
- PET Radioligand in Neuroinflammation
- Alzheimer’s Plasma Proteomics
- Alzheimer’s CSF Proteomics*
- Alzheimer’s / MCI Placebo Data Analysis*

**Metabolic Disorders**
- Adiponectin
- Carotid MRI Reproducibility
- Sarcopenia Consensus Definition
- Atherosclerosis In-Silico Modeling
- Beta Cell Clinical Studies
- Bone Quality

- Completed Projects
- Ongoing Projects

* Final publication pending
** Transitioned to standing trial
Biomarkers Consortium Results

- Total projects launched: 19
- Projects completed: 7
- Drugs approved or advanced with support from Consortium data: 6
- FDA guidances completed using our contributions: 4
- Over $60 Million raised from the private sector to fund projects: 60
- Journal articles published (and BC efforts cited in over 50 others): 30
Applying Precision Medicine to Clinical Trials

**Umbrella**
Test impact of different drugs on different mutations in a **single type of cancer**
• BATTLE
• I-SPY2
• SWOG Squamous Lung Master

**Basket**
Test the effect of a **drug(s)** on a single mutation(s) in a variety of cancer types
• Imatinib Basket
• BRAF+
• NCI MATCH
Applying Precision Medicine to Clinical Trials
S1400

**MASTER PROTOCOL**

**Common Broad Platform/CLIA Biomarker Profiling**

- **PI3K**
  - M: PIK3CA mut

  - **GDC-0032**
    - CT*
    - Endpoint: PFS/OS

- **CDK4/6**
  - M: CCND1, CCND2, CCND3, cdk4 ampl

  - **Palbociclib**
    - CT*
    - Endpoint: PFS/OS

- **FGFR**
  - M: FGFR ampl, mut, fusion

  - **AZD4547**
    - CT*
    - Endpoint: PFS/OS

**Non-match**

- **Anti-PD-L1: MEDI4736**

**Endpoint**

- PFS/OS

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TT=Targeted therapy, CT=chemotherapy (docetaxel or gemcitabine), E=erlotinib

*Archival FFPE tumor, fresh CNB if needed

Target/M: Drug target and biomarker
Partnerships – Lessons Learned

• A matrix that is greater than the sum of its parts

• Well defined objectives, budgets, milestones and deliverables

• Common governance, rules and legal framework

• Realistic funding goals, expectations and timelines

• Projects aligned with donor interest

• Appreciation of the value of gifts

• Collaboration adds complexity: must “play nice with others!”

• Nimble, transparent and accountable

“When you’ve seen one partnership, you’ve seen one partnership.”
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Neuroscience
Rosa Canet-Aviles
Scientific Program Manager
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Alternate Slides
FNIH Research Projects in the R&D context

Discovery
• MAL-ED
• Research Partnership Cognitive Aging
• OAI2
• SHRP
• Beene Global Neurodiscovery Challenge

Pre-clinical
• AMP
• ADNI
• HIT-TB
• CECI
• SPIROMICS

• 2nd Gen HIV NAb

Clinical
• Biomarkers Consortium
• I-SPY 2
• LungMAP
• AREDS2
• SPIROMICS Exacerbation
• Cognitive Remediation

• Burkitt Lymphoma

Grand Challenges in Global Health
Vector-Based Control of Transmission

PROGNOSTIC/DIAGNOSTIC TOOL DEVELOPMENT/PLATFORMS
Coding for Cancer    ADAS-Cog    CAVD    DILIN    Visceral Leishmaniasis    River Blindness Markers
Alzheimer’s Disease Neuroimaging Initiative (ADNI)

- Launched in 2004 by the National Institute on Aging (NIA) as an innovative $60M collaborative effort supported with funding from both the federal government and the private sector; coordinated by the Foundation for the NIH.
- Designed to be a multi-site longitudinal study of normal cognitive aging, mild cognitive impairment (MCI) and early Alzheimer’s disease (AD).
- Plan to validate, standardize and optimize:
  - neuroimaging and other biomarkers for use in clinical trials in Alzheimer’s Disease
  - biomarker methods for early detection and disease progression via a collaborative network of clinical and imaging sites.
- Aims to help create a world-wide network to improve AD studies and clinical trials for disease-modifying treatments.
- In 2011 ADNI2 launched with an additional $70M. Builds up on the successes of earlier ADNI phases and seeks to identify the earliest changes in brain structure and function as people transition from normal cognitive aging to mild cognitive impairment (MCI) to AD.
- ADNI 3 planning is now underway.
## AMP Participants by Disease Area

<table>
<thead>
<tr>
<th>Industry members</th>
<th>Government members</th>
<th>Non-profit members</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>AbbVie</em> &lt;br&gt; <em>Biogen</em> &lt;br&gt; <em>GSK</em> &lt;br&gt; <em>Lilly</em></td>
<td><em>NIH</em> National Institute on Aging &lt;br&gt; <em>NIH</em> National Institute of Neurological Disorders and Stroke</td>
<td><em>Alzheimer’s Association</em> &lt;br&gt; <em>American Diabetes Association</em> &lt;br&gt; <em>JDRF</em> &lt;br&gt; <em>Lupus Research Institute</em> &lt;br&gt; <em>Alliance for Lupus Research</em> &lt;br&gt; <em>Rheumatology Research Foundation</em> &lt;br&gt; <em>Pfizer</em> &lt;br&gt; <em>Sanofi</em> &lt;br&gt; <em>Sanofi</em> &lt;br&gt; <em>Takeda</em></td>
</tr>
<tr>
<td><em>AbbVie</em></td>
<td><em>NIH</em> National Institute of Diabetes and Digestive and Kidney Diseases</td>
<td><em>Alzheimer’s Association</em> &lt;br&gt; <em>American Diabetes Association</em> &lt;br&gt; <em>JDRF</em> &lt;br&gt; <em>Lupus Research Institute</em> &lt;br&gt; <em>Alliance for Lupus Research</em> &lt;br&gt; <em>Rheumatology Research Foundation</em> &lt;br&gt; <em>Pfizer</em> &lt;br&gt; <em>Sanofi</em> &lt;br&gt; <em>Sanofi</em> &lt;br&gt; <em>Takeda</em></td>
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<td><em>AbbVie</em></td>
<td><em>NIH</em> National Institute of Arthritis and Musculoskeletal and Skin Diseases</td>
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### Disease Areas
- **Alzheimer’s Disease**
- **Type 2 Diabetes**
- **RA, SLE & related**
## Current AMP Funding Commitments (total: 5 years)

<table>
<thead>
<tr>
<th>Disease area</th>
<th>Total project funding ($M)</th>
<th>Total NIH funding ($M)</th>
<th>Total industry funding ($M)</th>
<th>Total non-profit funding ($M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>92.5</td>
<td>69.6</td>
<td>21.9*</td>
<td>1.0</td>
</tr>
<tr>
<td>T2D</td>
<td>52.8</td>
<td>31 + **</td>
<td>21.5*</td>
<td>.3</td>
</tr>
<tr>
<td>RA/SLE</td>
<td>41.9</td>
<td>20.9</td>
<td>20.7</td>
<td>.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>187.2</td>
<td>121.5</td>
<td>64.1</td>
<td>1.6</td>
</tr>
</tbody>
</table>

* Does not include in-kind contributions of $40M to AD and $6.5M to T2D
** Additional funding anticipated
Biomarkers Consortium
Contributing Partners

For-Profit Companies
Actelion
Amgen
AstraZeneca
Crescendo Bioscience
Daiichi Sankyo, Inc
Eisai, Inc
Johnson & Johnson
Eli Lilly & Company
Lundbeck
Merck Sharpe & Dohme Corp.
Metabolon
Mitsubishi Tanabe Pharma America, Inc
Myriad RBM
Pfizer, Inc
Regeneron Pharmaceuticals, Inc.
Sanofi
Takeda Pharmaceuticals USA, Inc

Non-Profit Organizations
Alzheimer’s Association
American Diabetes Association
American Orthopaedic Society for Sports Medicine
Arthritis Foundation
Autism Speaks
Biotechnology Industry Organization
California Dairy Research Foundation (CDRF)
Centre for Proteomic and Genomic Research
CHDI Foundation
Dairy Research Institute
Foundation for Health Improvement and Technology
Juvenile Diabetes Research Foundation
Pharmaceutical Research and Manufacturers of America
PROOF Centre of Excellence
Radiological Society of North America
US Pharmacopeia
Alzheimer’s Disease Neuroimaging Initiative (ADNI)

- Industry leaders work together in a proven, pre-competitive environment
  - Cost sharing and cost savings
  - High level interactions with top clinical/biomarker AD investigators
  - Idea and data sharing not possible in competitive environment
  - Interaction with FDA – ongoing guidance on endpoints and validation

- Study design and objectives address industry needs, i.e.:
  - Standardization of all methods for regulatory approval
  - Identification of patients at risk in the pre-dementia stage
  - Validation of biomarkers to measure change and treatment effects
  - Validation of biomarkers to identify early AD pathology
  - Longitudinal data with biomarkers for design and powering of trials

- ADNI plays a major role in:
  - Providing new information concerning the pathophysiology of AD
  - Developing early detection methods and improved treatment trials
  - Determining diagnostic requirements
  - Providing tools for evaluating milder patients
  - Understanding disease progression/rate of change during different stages of disease
AMP – IP & Data Sharing

• Research supported by AMP will be precompetitive

• All data will be shared broadly

• AMP supported research will not be patented
Lung-MAP Objectives and Rationale

• *Multi-arm Master Protocol*
  - Homogeneous patient populations & consistent eligibility from arm to arm;
  - Each arm independent of the others;
  - Infrastructure facilitates opening new arms faster;
  - *Phase II-III design* allows rapid drug/biomarker testing for detection of “large effects.”

• *Screening large numbers of patients* for multiple targets by a broad-based NGS platform reduces the screen failure rate.

• Provides a *sufficient “hit rate”* to engage patients & physicians.

• *Bring safe & effective drugs to patients faster.*

• Designed to facilitate *FDA approval* of new drugs.