

## **An Open Source Approach to Fighting Alzheimer's Disease**

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Chairman USA2

**Mission:** The past two decades have seen amazing growth in the ability to generate genomic, clinical and other health data fueled, in part, by the rapidly decreasing cost of information technology, including, importantly, high-throughput genomic technologies. Unfortunately, a key impediment to more rapid advances in the treatment of human diseases is the relatively closed nature of scientific research that stems from both the publication-grant-work cycle of academic research as well as the historic close-to-the-vest approach of industry and the historic inaccessibility of patient-level data in electronic health records or clinical trial settings. That may be changing. Innovative patient-centric organizations like Stand Up to Cancer (SU2C), CF Foundation and the Michael J. Fox Foundation are creating funding mechanisms to incent multi-disciplinary, milestone-driven 'team' approaches to discovery; declining pharmaceutical R&D productivity is opening up an increased willingness on the part of industry to share pre-competitive data; and safety, efficiency and unmet therapeutic leads are causing regulatory agencies to encourage (or mandate) data standardization, disclosure and sharing. Is this leading to a new 'open source' approach to biomedical research and do we have the tools and protocols to take advantage of this emerging new path to biomedical discovery.

Sage Bionetworks has recently incorporated the [IBM DREAM](#) project to run open computational competitions as an innovative method to create a collaborative research environment with the goal of accelerating the pace of addressing challenging therapeutic areas, such as Alzheimer's. In spite of the fact that over 5 million Americans and almost 40 million people globally are experiencing Alzheimer's today (a number that is growing rapidly as demography drives population aging around the world), there are no disease-modifying therapies available for Alzheimer's. Current research funding levels are inadequate and, at least in the US, not likely to increase in the foreseeable future, making new innovative approaches to discovery, development and evaluation of therapies for Alzheimer's imperative.

Our mission is to examine new approaches to overcome barriers to and incentives for sharing -- including the use of Challenges using on Alzheimer's imaging clinical, genetics and epidemiological data from the Alzheimer's Disease Neuro-imaging Initiative (ADNI) – so that multi-disciplinary teams of researchers will combine their expertise to create a roadmap of Alzheimer's pathology and new targets for Alzheimer's drug development.

### ***Realities to be highlighted:***

- ***Overcoming barriers to collaboration:*** Much of the potential for interrogating disparate but intersecting datasets of Alzheimer's-related epidemiological, biological, imaging, clinical and genetics data remains untapped. Datasets are small, non-standardized and decentralized and experts on genetics, imaging, neurobiology, physics, systems biology or disease pathology rarely work together, even when they are studying the same organ, the same disease or the same pathological process. Companies are concerned about giving up their intellectual property generated in clinical trials, or breaching the data privacy of individuals, or losing some perceived competitive edge in treating as proprietary why their therapies failed (with the consequence that other companies duplicate investments in what are previously-failed mechanisms of action).
- ***Getting scientists to share – finding the right carrot:*** Being first to publish with its associated secrecy about data and results is the traditional way of conducting research. Hiding a company's failure is the standard 'business-as-usual'. Encouraging collaboration cannot be done by only

## Project N)

appealing to the altruistic side of academic or industry researchers, but requires the development of new paradigms in building incentives that reward collaboration. What are the benefits of understanding failure? Why will open source systems of discovery produce a faster learning, faster failing and more productive discovery process?

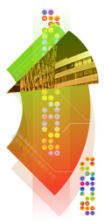
### **Proposition:**

- **Creating an open source community:** Pooling standardized data and making it available for research is of high value, but it does not create a community by itself. An open computational platform, such as Sage Bionetwork's [Synapse](#), serves not just as a data repository but also a set of tools for conducting collaborative analysis. We will discuss how such toolsets, such as Synapse, might be used to access available imaging, biological, clinical and genome sequencing data from a large cohort from ADNI and thus to serve as the collaborative infrastructure where multi-disciplinary teams can work to document, refine and share ideas. Potentially, participants will be able to share their approaches and outcomes openly, so everyone can learn from each other's scientific and technical insights. Other approaches in the Alzheimer's therapeutic area, such as Global Alzheimer's Association Interactive Network (GAAIN) and Coalition Against Major Diseases (CAMD) or in other therapeutic areas (DataSphere), will be discussed.
- **The scientific question:** ADNI has a unique collection of MRI and PET images, genetics, clinical data and cognitive tests on a large cohort with Alzheimer's, Mild Cognitive Impairment, and controls. We will discuss how a Scientific Advisory Board might formulate the best questions to be posed for one or more prize-based Challenges to incent teams to form and address critical issues in Alzheimer's research. Some possible Challenge approaches might include asking Challenge participants to develop a computational model based on how well it describes certain aspects of Alzheimer's and asked to confirm this model in a second hidden dataset. Potential questions could range from predicting genes associated with Alzheimer's, prediction of the rate of disease progression based on the combination of genetics and imaging data, identification of biomarkers which best categorize subjects into groups such as controls, MCI and AD, or which best predict conversion from controls to MCI to AD.
- **Incentives:** Rewards need to be developed to provide incentives to researchers who make the greatest leap forward in predictive performance as well as those who provide the most biological insight. Incremental progress might be rewarded so that researchers have an incentive to share early, including a means of modeling sustainable and persistent open source platforms with a continuous and progressive series of competitions building on earlier insights or discoveries. Also, potential prizes such as publication in top journals or financial prizes will be discussed. In addition, participation in competitions may provide an opportunity to initiate collaborations that may be advantageous for future work outside of a competition itself.
- **Restrictions:** Of utmost importance is the adherence to data privacy of ADNI participants. Open sharing and collaborative research must take into account the individual participant in contributing data, and assessing any limitations in relying on HIPAA-compliant de-identified data. Defining and assessing flexible yet appropriate and practical approaches to new means of obtaining informed consent will be key.

Over to You

# N- An Open Source Approach to Fighting Alzheimer's Disease

<u>G</u>	<u>Organization</u>	<u>Last name</u>	<u>First</u>
N	One Mind	Chiarelli	Peter
N	DREAM	Costello	Jim
N-Anchor	Sage Bionetworks	Gaiteri	Chris
N	UCSF	Hesse	Joe
N	Carnegie Mellon University	Komek	Kubra
N	HIV activist	Lange	Joep
N	NIH/NIMH	Lehner	Thomas
N	DREAM	Menden	Michael
N	University of Miami	Myers	Amanda
N	NIH/National Institute on Aging	Petanceska	Suzana
N-Anchor	Sage Bionetworks	Peters	Mette
N	Pfizer	Rejto	Paul
N	Takeda	Shinobu	Leslie
N	Aegis	Smith	Craig
N	One Mind/IMHRO	Staglin	Garen
N	Allen Brain Institute	Stewart	Lance
N-Lead	USAgainst Alzheimer's	Vradenburg	George
N	Jackson Laboratory	Wagner	Joel



# Project N: An Open Source Approach to Fighting Alzheimer's Disease

## Project Lead: George Vradenburg, USA2

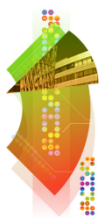
### Major Themes

- Alzheimer's disease affects >5 million Americans and almost 40 million people worldwide
- No disease modifying therapies
- Enormous monetary and social cost
- Disease starts 15-20 years before clinical signs
  - How to identify population at risk before disease onset



# Potential alignment with existing Commons' approaches

- Structured question for a Sage/Dream challenge
  - What is the best combination of predictors of the persons at risk for the cognitive and functional impairments due to AD
    - Including, but not limited to biological, genetic, imaging, clinical predictors
    - What combinations gives the most predictive power and why
    - What combinations best predict rate of decline in cognitive and functional impairments
    - What datasets were used
    - Most affordable and least invasive screening test
- Objective criteria for evaluation
  - Use of multiple validation datasets (to be defined)
- Possible incentives
  - Cash prize
  - Publication
  - Funding for validation
  - Ability to propose drug targets
  - Public benefit



# Unmet needs and issues

- Validation datasets
- Choice of incentives
- Inventory of publicly available test datasets



# 1-year vision for the future of this project

- Have a fully formed challenge ready for launch
  
- By this time next year we will have gained consensus from the AD and the broader scientific community on the challenge:
  - Language
  - Incentives
  - Validation