



2009

Annual Highlights

LETTER FROM THE CHAIRMAN



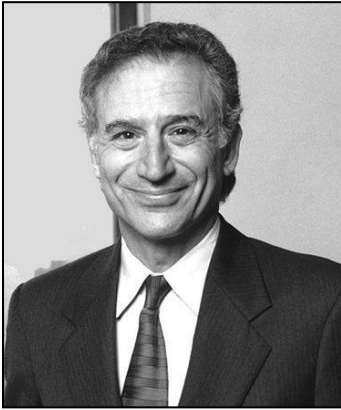
As chairman of the Alzheimer's Drug Discovery Foundation (ADDF), finding treatments, and a cure, for Alzheimer's disease is my goal in life. The ADDF exists solely to speed up the process of bringing effective new drugs to market. Under the direction of our extraordinary executive director, Dr. Howard Fillit, the Foundation is working hard toward this end, providing funding for promising drug research.

Our strategy is distinctive. We focus on underfunded research areas, financing programs to catapult a successful start-up project to the next stage of development. Then, other funders with deeper pockets can step forward to support our grantees in bringing their research to market.

We have accomplished a great deal in recent years and there is much to hope for today. Please join me in supporting the efforts of the ADDF.

Leonard A. Lauder
Chairman

LETTER FROM THE EXECUTIVE DIRECTOR



In 2009 the Alzheimer's Drug Discovery Foundation (ADDF) provided crucial funding to help researchers translate basic understanding of Alzheimer's disease into practical treatments that can benefit patients.

Following the rigorous screening of 160 grant proposals, we awarded \$3.8 million to 29 cutting-edge research programs, advancing research on 19 different Alzheimer's drug targets. We also organized and convened six scientific conferences and symposia — opportunities for experts to exchange knowledge and catalyze new research directions.

\$1.2 million of our total funding was awarded to six biotechnology companies through the ADDF's Biotechnology Development Program. By supporting early-stage companies, the ADDF helps propel them to the point where they can attract the follow-on commitments and partnerships that will advance them to the next level.

Of course, the true test for any new drug is in human clinical trials. In 2010, we will launch our first campaign to accelerate clinical trials of novel therapies for Alzheimer's-related dementias and cognitive aging. The ADDF's *Program to Accelerate Clinical Trials (PACT)* will enable testing of new Alzheimer's drugs in humans at the crucial Phase IIA (proof-of-concept) stage — helping to ensure that no promising potential treatment stalls in its development due to a lack of funding.

— *continued next page*

LETTER FROM THE EXECUTIVE DIRECTOR *(continued)*

The ADDF will focus its resources on Phase IIA because positive results at this stage can help create a “tipping point” in the development of new drugs. Showing that a therapeutic outcome translates from preclinical experiments to human testing is critical to attracting significant follow-on funding from the pharmaceutical industry and venture capital organizations. This funding in turn allows drugs to move forward into later— phase human testing, one step closer to regulatory approval and pharmacy shelves.

We look forward to continued success resulting from our efforts to support novel preclinical and clinical drug development. With your help, we will realize our goal of preventing, treating and curing Alzheimer’s disease.

Thank you for being part of our work.

Howard Fillit, MD
Executive Director

OUR MISSION: SPEED BETTER THERAPEUTIC OPTIONS TO PATIENTS

The Alzheimer’s Drug Discovery Foundation (ADDF) is the only public charity whose sole mission is to rapidly accelerate the discovery and development of drugs to prevent, treat and cure Alzheimer’s disease, related dementias and cognitive aging.

What We Do

The ADDF pursues multiple avenues to bridge the worldwide funding gap between basic research and later-stage drug development, using any return on investment to support new research. Our funds are available to academic and biotechnology scientists. We also provide seed funding to help establish new biotechnology company start-ups — all with the single goal of bringing effective drugs to market.

As a public foundation, our financial support is not limited to any single scientific method, institution, approach or solution. Rather, we are building a network of partnerships and supporting promising, diverse and innovative research projects worldwide to increase “shots on goal” in the development of disease-modifying Alzheimer’s drugs.

We take a hands-on, proactive approach to funding science. The ADDF’s scientific staff actively seeks out novel research ideas for new drugs, then advises the scientists on developing their drug discovery program. More than 150 academic and industry scientists from all around the world serve on our Scientific Review Board (SRB), lending their expertise to the evaluation of the hundreds of grant proposals we receive each year. They are assisted by our Business Advisory Board (BAB), comprising leaders in the venture capital, biotechnology and pharmaceutical industries.

Together, our staff and advisors carefully vet each grant application, lend guidance on the research proposed, establish concrete milestones, provide strategic management assistance, and monitor progress to maintain the highest level of accountability and maximize every program’s full potential.

The Institute for the Study of Aging (ISOA), a private foundation created by the Estee Lauder family in 1998, provides substantial financial support to the Alzheimer's Drug Discovery Foundation so that the ADDF's donor-raised funds can go directly to research. In 2009, 86 cents of every dollar spent by the ADDF went directly to scientific research and programs.

Knowledge Sharing Through Partnership and Collaboration

Our founder, Leonard Lauder, launched the Alzheimer's Drug Discovery Foundation to serve as both a catalyst and a resource for the Alzheimer's research field. To help realize his vision, we proactively forge partnerships that will facilitate knowledge exchange and accelerate the development of critically needed new Alzheimer's drugs. Today the ADDF has a track record of creating powerful and successful partnerships.

In 2009, the third year of our partnership with The Association of Frontotemporal Dementia (AFTD), we awarded three grants totaling \$300,000 to investigators in Belgium and New York City. We also co-funded and administered *The Morgan Family AFTD/ADDF Award for TDP-43 Research* (made possible by a family donation to AFTD). Under this joint program, we made a \$120,000 award to a Zurich researcher screening drugs for a newly discovered disease protein, TDP-43, relevant to frontotemporal dementia research.

We launched a new partnership with the Lewy Body Dementia Association to advance treatments for Lewy body dementia, which affects an estimated 1.5 million individuals and their families in the United States. The ADDF earmarked \$100,000 for investigator-initiated biomarker research projects to differentiate Lewy body dementia from other forms of dementia, critical to developing better treatments. The awardee, selected from 20 applicants, will be announced in 2010.

Conferences: Education, Critical Idea Exchange and Networking

2009 marked the 10th anniversary of the ADDF's *Annual International Conference for Alzheimer's Drug Discovery*. This two-day conference drew 150 scientists from government, industry and academia to the New York City area to engage in discussion and cross-fertilization of ideas for their drug discovery programs.

The ADDF also hosted its annual *Drug Discovery for Neurodegeneration* conference, this year in Washington, D.C. Now in its fourth year, this meeting is developed and sponsored in collaboration with the National Institutes of Health. The two-day comprehensive course introduces participants to the fundamentals of drug discovery, ushering new scientists into the search for drugs to treat and prevent neurodegenerative disease including Alzheimer's, Parkinson's, Huntington's, multiple sclerosis and amyotrophic lateral sclerosis. In 2009, 140 scientists attended and 30 young investigators were awarded scholarships.

In a first-time alliance with the New York Academy of Sciences, the ADDF hosted the *Therapeutics for Cognitive Aging Conference*. The meeting convened prominent scientists who study cognitive and neurobiological aspects of aging. The symposium attracted 200 participants.

In 2010 and 2011, we plan to expand our global outreach by organizing three European conferences in addition to our U.S. conferences.

OUR IMPACT

Since 1998, the ADDF and ISOA have awarded \$40 million for almost 300 research programs in 15 countries. Our strategy to transition promising research into drug discovery programs has led to significant advances toward treatments for patients and their families. Among our accomplishments:

- Scientists funded by the ADDF have entered human clinical trials with over 30 potential new treatments.
- The 42 biotechnology companies we have supported with a total investment of \$9.6 million have gone on to receive over \$1 billion in follow-on commitments.
- Three successful biotechnology company start-ups established by the ADDF have either entered clinical trials or received substantial follow-on commitments to accelerate their programs.

HELP US FUND SCIENCE

Today more than 5.5 million Americans suffer from Alzheimer's disease. The number will quadruple to 19 million by 2050 if no treatment or cure is discovered.

The ADDF is at the forefront of the battle against Alzheimer's disease. We will keep working until we conquer this devastating disease. But we cannot do it alone. We need your help to continue accelerating the discovery and development of effective new drugs to cure the disease. Please give generously today at www.alzdiscovery.org.

PROFILES OF PROGRESS

Drug Discovery Program

In 2009, 85 percent of our funding went toward “drug discovery” programs diversified across 19 different disease targets.

Carmela R. Abraham, PhD, Boston University School of Medicine

The recently discovered klotho protein is named for the Greek goddess of fate who spins the thread of life. Its absence shortens lifespan in laboratory mice, causing signs of aging that closely resemble aging in humans. Drugs that enhance klotho production could affect cellular pathways to counteract multiple effects of aging. With an ADDF grant of \$175,000, Dr. Abraham’s team will validate the effectiveness of 10 compounds to increase klotho. If successful, her work could identify compounds with significant potential to be developed into drugs that may slow or stop the pathogenesis of Alzheimer’s disease.

Biomarkers and Early Detection Program

In our ongoing efforts to enable early diagnosis and prevention of Alzheimer’s, 10 percent of our funds in 2009 went to the discovery of reliable biomarkers. Biomarkers would not only allow for treatment from the earliest onset of Alzheimer’s disease (when it is most effective) but also are critical to accurately track the effects of experimental drugs in patients.

Dawn Matthews, MS, MBA, Abiant, Inc.

The lack of standardized image interpretation in dementia disorders is a longstanding hurdle to the discovery of reliable and consistent imaging-based biomarkers. Abiant co-founder Dawn Matthews is helming the company’s mission to capitalize on recent significant advances in brain PET and MRI scans through the use of advanced pattern-recognition algorithms. With a \$200,000 grant from the ADDF, the company is developing new pattern-recognition software to allow measurement of brain regions that are early predictors of decline. It also will distinguish between different forms of dementia, quantify the complex changes associated with them, and make them interpretable for accurate, standardized clinical use — transforming the way clinicians diagnose dementia and track disease in patients.

Pilot Clinical Trials

In 2009, 5 percent of our funding supported pilot clinical trials in humans — a critical and costly phase in the development of any treatment. The ADDF plans to expand its clinical program in coming years.

José Luchsinger, MPH, MD, Columbia University

Diabetes and high insulin levels have emerged as important risk factors for Alzheimer's disease. Dr. Luchsinger is investigating whether Glucophage (metformin), a medication that lowers insulin in Type 2 diabetes, can prevent the progression from amnesic mild cognitive impairment to Alzheimer's disease by reducing insulin levels in the central nervous system. With a \$180,000 grant from the ADDF (raised through the fund-a-scientist auction at our 2009 Connoisseurs dinner), he is expanding his pilot Phase II clinical trial of metformin. The ADDF grant will allow Dr. Luchsinger to recruit additional patients and generate feasibility data for a larger Phase III clinical study. If positive results are confirmed, metformin, a safe and effective drug that is already on the market, can immediately be prescribed for early-stage Alzheimer's disease to slow disease progression.

Early-stage Biotechnology Research Program

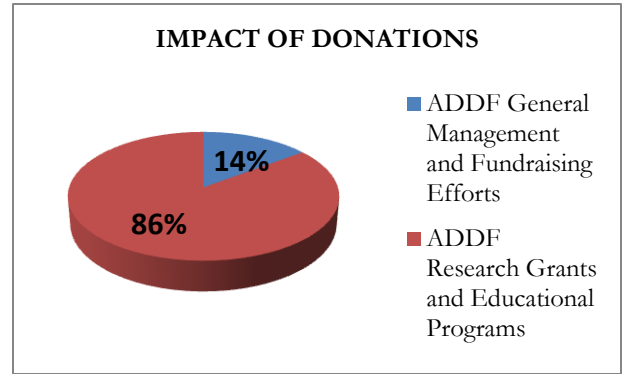
In 2009, 31 percent of our grants went to biotechnology companies (69 percent to academia) to help bring early-stage efforts to the point where they could attract significant follow-on funding.

Jeffrey Stock, PhD, Signum Biosciences

Preclinical research in Dr. Stock's Princeton University lab indicates that the enzyme *phosphoprotein phosphatase 2A* (PP2A) can return the protein tau, which forms "tangles" in the brain of those with Alzheimer's and other dementias, to a healthy state. Signum Biosciences has developed a compound, SIG1012, from a naturally occurring product found in botanicals; this compound enhances the activity of PP2A. The ADDF provided \$269,000 to Signum to accelerate research on SIG1012. If it proves successful at improving cognitive and metabolic health, it could be rapidly advanced to human trials and become the first commercially available supplement to target the tangles in Alzheimer's disease and related dementias.

2009 DONOR LISTING

Thanks to the generosity of the following contributing partners, the ADDF raised approximately \$2.4 million in 2009, bringing total funding in our first five years of operation to over \$11.2 million. Your support enabled us to advance our mission of accelerating drug discovery research for Alzheimer's disease, related dementias and cognitive aging.



Over \$1,000,000

Estée Lauder Trust

\$100,000 to \$999,999

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Dementias

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Stand Up NY Comedy Club & Bar
Style Therapy
Tapeo 29 - Tapas Wine Bar
Tarra Rosenbaum
Zagat Survey
Zeitgeis

2009 GRANTEES

Academic Programs

Carmela R. Abraham, PhD

Boston University School of Medicine
Development of Klotho Enhancers as Novel Therapeutics for Alzheimer's Disease
Award: \$175,000

Ottavio Arancio, MD, PhD

Columbia University
Novel PDE5 Inhibitors as a Therapeutic Tool Against Alzheimer's Disease
Award: \$116,600

Ilya Bezprozvanny, PhD

The University of Texas Southwestern Medical Center at Dallas
Ryanodine Receptor Type 2 as a Target for Alzheimer's Disease
Award: \$100,000

Bart De Strooper, MD, PhD

VIB
High-throughput-screening for Compounds Against A β 1B-gamma-secretase
Award: \$150,000

Rashid Deane, PhD

University of Rochester
Early Toxicology and ADME Studies with our Lead RAGE Inhibitors
Award: \$155,300

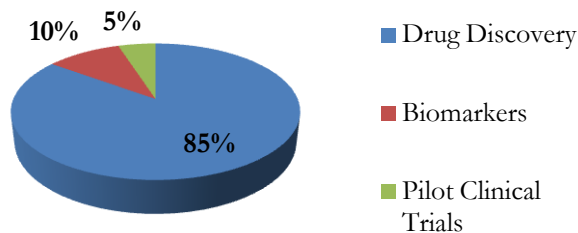
Karen Duff, PhD

Columbia University
Disaggregation of Tau as a Therapeutic Approach to Tauopathies
Award: \$75,000

Susan Greenfield, PhD

University of Oxford
Characterization In Vivo of a Newly Identified Peptide of Potential Pivotal Significance to Alzheimer's Disease
Award: \$84,625

ADDF/ISOA 2009 Grant Allocation (\$)



Stephen Albert Johnston, PhD

Arizona State University
Immunosignatures: A Simple Method to Potentially Diagnose Alzheimer's Disease
Award: \$75,000

Rima Kaddurah-Daouk, PhD

Duke University Medical Center
Metabolomic Signatures of Preclinical and Early Alzheimer's Disease: Discovery of Novel Biomarkers for Drug and Disease Monitoring
Award: \$120,000

Tae-Wan Kim, PhD

Columbia University Medical Center
Screening for Small Molecule Agonists of Phosphatidylinositol 4-kinase
Award: \$100,000

Paul Lombroso, MD

Yale University
Screening for Inhibitors of STEP
Award: \$138,600

José Luchsinger, MD, MPH

Columbia University
Pilot Trial of Metformin in the Prevention of Alzheimer's Disease
Award: \$180,000

Robert Marr, PhD

Rosalind Franklin University of Medicine and Science
Investigation of the Role of SEP in Controlling Cerebral Beta-amyloid Pathology
Award: \$64,174

Scott Noggle, PhD

The New York Stem Cell Foundation
Disease-Modeling Initiative for Alzheimer's Disease
Award: \$175,000

Academic Programs (continued)

Chris Schaffer, PhD

Cornell University
Microvascular Blood Flow Disruptions in the Vicinity of Amyloid-beta Plaques
Award: \$50,000

Eric Schon, PhD

Columbia University
Mitochondria-associated Membranes in Alzheimer Disease: A New Target for Drug Discovery
Award: \$121,800

Zhiqun Tan, MD, PhD

University of California, Irvine
Efficacy of Herbal Extract, Tetramethylpyrazine, in Alzheimer's Transgenic Mice
Award: \$100,000

Eugenia Trushina, PhD

Mayo Clinic Rochester
Tricyclic Pyrone Compounds and Axonal Trafficking Dysfunction in Alzheimer's Disease
Award: \$145,000

Cheryl Wellington, PhD

University of British Columbia Hospital
The Therapeutic Potential of ABCA1 and apoE for Alzheimer's Disease
Award: \$75,000

Biotechnology Programs

Jerry Colca, PhD

Metabolic Solutions Development Company
Evaluation of PPAR-sparing Thiazolidinediones as Potential Treatments of Alzheimer's Disease
Award: \$100,000

Frank M. Longo, MD, PhD

Pharmatrophix
Inhibition of Alzheimer-related Neurodegeneration by Small Molecule Neurotrophin Receptor Ligands
Award: \$180,000

Dawn Matthews, MS, MBA

Abiant, Inc.
A Highly Accurate and Predictive Imaging Tool for the Diagnosis of Dementias
Award: \$200,000

Jeffrey Stock, PhD

Signum Biosciences, Inc.
Phosphoprotein Phosphatase 2A (PP2A): A Novel Therapeutic Target for Alzheimer's Disease
Award: \$269,000

Brandon Wustman, PhD

Amicus Therapeutics
Modulation of Ganglioside Catabolism Using Pharmacological Chaperones: A Novel Therapeutic Approach for Treating Alzheimer's Disease
Award: \$210,300

Vincent Zurawski, PhD

Varinel Inc.
M30-Derived Neuroprotective-Neurorescue Drugs for Alzheimer's Disease
Award: \$239,700

ADDF/AFTD* Partnership Grants

** The Association for Frontotemporal Dementias*

Manuela Neumann, MD

Institute of Neuropathology, University of Zurich

Large-scale RNAi Screen to Identify Kinases Modulating TDP-43 Phosphorylation State

Award: \$120,000

Einar M. Sigurdsson, PhD

New York University School of Medicine

Passive Immunotherapy for Frontotemporal Dementia

Award: \$100,000

Philip Van Damme, MD, PhD

VIB

Drug Discovery for Progranulin-Mediated Frontotemporal Lobar Degeneration

Award: \$130,000

W. Haung Yu, PhD

Columbia University

Tau Clearance by Autophagy

Award: \$70,000

Conference

Andrew Robertson, PhD

Keystone Symposia on Molecular and Cellular Biology

Alzheimer's Disease Beyond Abeta

Award: \$2,500

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Alzheimer's Drug Discovery Foundation

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