

Cure Alzheimer's FUND
targeting breakthrough research

A N N U A L R E P O R T 2 0 0 6

Cure Alzheimer's^{FUND} **MISSION:**

To fund research with the highest probability of slowing, stopping or reversing Alzheimer's disease.

Message from the Chairman, Jeffrey Morby



We are pleased to present our first Annual Report, which covers the time from inception of the Foundation in the Fall of 2004 through December 2006. In a remarkably short time, we've grown from an idea

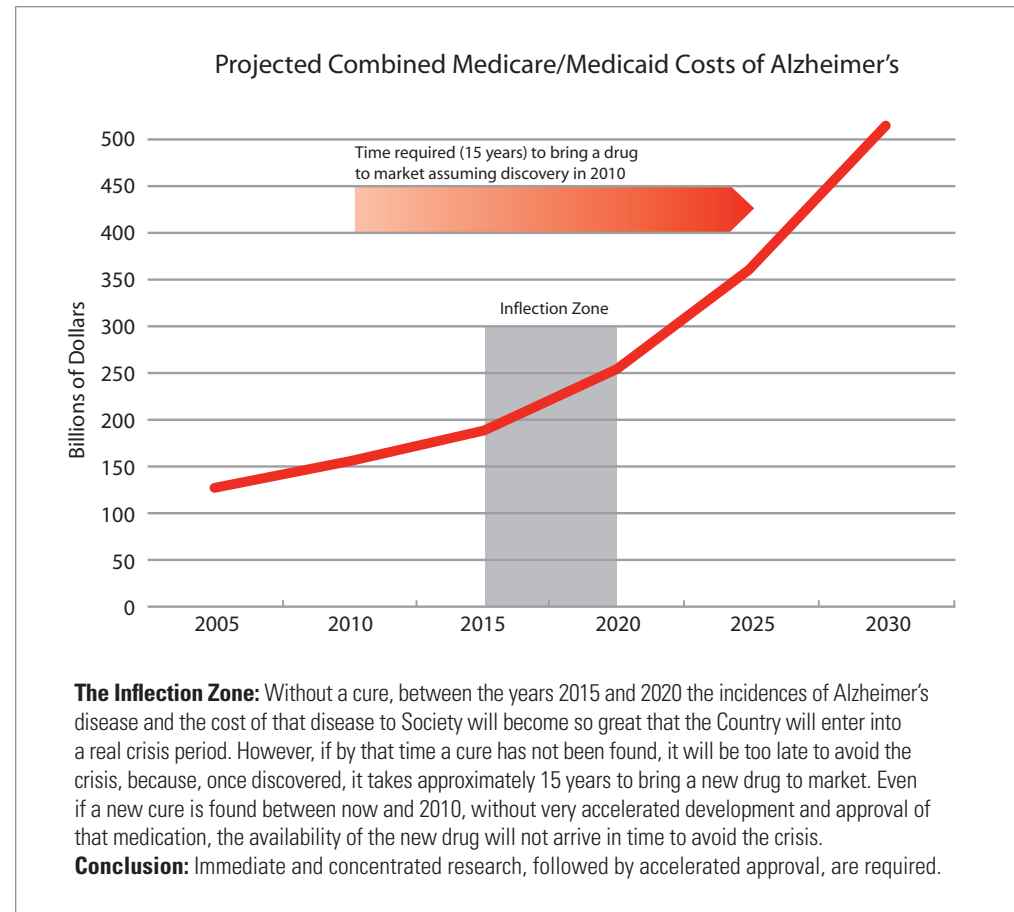
about how we might "make a difference" in the struggle against Alzheimer's disease to the reality of a national organization that has raised over \$4.6 million from more than 500 people and funded research projects that are already providing breakthrough information toward the development of effective therapies. We are pleased to share with you some of the highlights of this start-up period.

Why are we doing this? Each of the Founders has committed considerable financial resources and significant amounts of time to this challenge. Some of us have the misfortune of knowing this disease all too personally. Others of us see the struggle that over 5.1 million Americans share, and the tremendous, budget-breaking economic disaster that faces affected families as well as the entire U.S. health care system if this disease is not brought under control quickly.

The chart at right exhibits an inflection point for the suffering and financial disaster this disease poses and which motivates us to act now.

How can we help? While the government and other organizations are funding research, we have been concerned about the lack of any particular focus or overall strategy for developing effective therapies. We are persuaded that in order to control the disease, the research community must understand the basic contributors to the disease—the genes that affect risk for Alzheimer's, only a handful of which have been identified.

Therefore, our first goal is to complete the entire Alzheimer's genome, an effort we are pursuing uniquely through the Alzheimer's Genome Project which will identify all genes contributing to risk for Alzheimer's by the summer of 2008. Along the way, we will fund other promising projects derived from this genetic study as described in the Funded Research section of this Annual Report and on our website.



We believe that a “venture capital” approach to this challenge will be most effective. We describe this in greater detail elsewhere in this report, but the sum of it is to find the people doing the best work and give them the resources they need to move the effort ahead—not incrementally, but in significantly large steps. The “venture approach” also incorporates best practices from the business world. We run our nonprofit like we run our businesses—with transparency to all parties, an entrepreneurial culture and world class staff members, board of directors and scientific researchers. However, unlike the business world, Cure Alzheimer’s Fund does not seek a profit, and makes no attempt to claim intellectual property rights to the work it funds.

We are gratified that our work and the work of the researchers we are funding have been recognized already by prominent publications (see “Alzheimer’s in the News” at right). Our greatest thrill has been to see how others have rallied to this cause and how dedicated, committed researchers have been able to extend their leadership in the field with the resources we together have been able to contribute. It is a great start, but our greatest challenges lie ahead. We welcome you and thank you for your help!

—JEFFREY MORBY

Alzheimer’s in the News...

From *The Economist*, November 2, 2006 – “From bench to bedside”

“Tanzi and the CAF [Cure Alzheimer’s Fund] team are well on their way to decoding the “Alzheimer’s genome” within the next two years. This could lead to a cure. It might even produce a new business model to help cure the [pharmaceutical] industry’s own ills.”

From *Newsweek*, December 11, 2006 – “Peering into the Future”

“At Harvard, Dr. Rudolph Tanzi is using the Hap Map to track down gene mutations that cause the common, late-onset form of Alzheimer’s, which could strike as many as 16 million Americans by the year 2050. Tanzi’s work is funded by the Cure Alzheimer’s Fund, a nonprofit that is investing \$3 million to unravel the Alzheimer’s genome, which it hopes to complete by the summer of 2008. Tanzi says a prototype genetic chip to test for the disease could be available within five years.”

From *Business Week*, January 8, 2007 – “Decoding Alzheimer’s”

“This year, Tanzi started work on his biggest project yet: identifying all the genes involved in Alzheimer’s. He predicts he will have a genetic blueprint in hand within two years and a genetic test within five. Tanzi doesn’t have to scrape around for cash this time, either. The Cure Alzheimer’s Fund, founded by three Boston area families, pledged \$3 million to his lab for this genetic detective work, stepping in where the NIA and venture capitalists refuse to tread.”

From the *Pittsburgh Tribune-Review*, November 20, 2006 – “Fund Targets Alzheimer’s”

“Help could be on the way for the 4.5 million Americans with Alzheimer’s. Venture capitalists Jeffrey and Jacqueline Morby, of Shadyside, and Henry F. McCance and Phyllis Rappaport, of Boston, have set up the Cure Alzheimer’s Fund with offices Downtown and in Boston. Its goal is singular: supporting research that slows, stops or reverses the disease in 10 years.”

Message from the President and CEO, Tim Armour

Cure Alzheimer's Fund has had a great beginning, thanks mainly to four wonderful groups of people:



1. An inspired and active group of Founders whose breadth of vision is matched only by the level of energy they have committed to this project. Not only have they given generously themselves, including paying for all administrative expenses and overhead, but each has given immensely of their time and experience. "Passion" is an overworked term these days, but Cure Alzheimer's Fund founders personify that concept as applied to this venture.
2. A world-class team of Alzheimer's disease researchers who have agreed to work together to find the best and most expeditious ways to stop the disease. Members of the Research Consortium are sharing their insights on the next steps to take along our Roadmap and who is best to lead that research. Their dedication to finding a cure reaches beyond traditional institutional boundaries to embrace a new model of collaborative research.
3. The more than 500 individuals from across the nation who have contributed to the over \$4.6 million raised since inception. Gifts have ranged from \$10 to \$100,000, and all are tangible evidence of the belief in the Founders' vision and the Research Consortium's ability to fulfill it.

4. Bill Trueheart, President and CEO of The Pittsburgh Foundation; Richard Reed, Executive Vice President; Dr. Edith Shapiro and Mr. George Davidson, directors of The Pittsburgh Foundation who volunteered to be on our first Board of Directors. They, and the highly professional and dedicated staff at The Pittsburgh Foundation had faith enough in this venture to help us get started, provided invaluable administrative help and guidance, and have been a most welcome and reliable source of support.

Thanks to all these people plus a small but dedicated staff and a growing group of very capable volunteers, Cure Alzheimer's Fund has distributed about \$2.5 million of that as of March 1, 2007, and funded over twelve projects in nine labs in six states across the country.

But looking ahead is even more exciting. Together we have come through the initial start-up phases of this adventure better than we had imagined. With the advances in technology, a rapidly growing understanding of the role that genes play in the neurodegenerative diseases, a dedicated group of researchers hot on the trail of the causes of Alzheimer's disease, and a loyal and growing corps of supporters, Cure Alzheimer's Fund looks forward to even greater success in the fight against this disease.

We are proud of our past and excited about the future. Thank you to all of you who are such an important part of this success, and welcome aboard to those of you who would like to grow it to its full potential. 2007 will be a great year!

—TIM ARMOUR

Prevalence of Alzheimer's disease NOW

One in eight persons over 65 has Alzheimer's and nearly half of all people over age 85 have the disease.

In total an estimated 5.1 million Americans have Alzheimer's disease, and this number is growing rapidly.

Every 72 seconds a person in America develops Alzheimer's.

Future Concerns

There are no known cures, despite the fact that the disease was clinically described over 100 years ago. It currently takes 15 to 17 years to bring a new drug to the market—a huge concern for those in their 50's and 60's.

Alzheimer's is a genetic disease. If a close member of your family has Alzheimer's, you and your relatives are at increased risk of also contracting it.

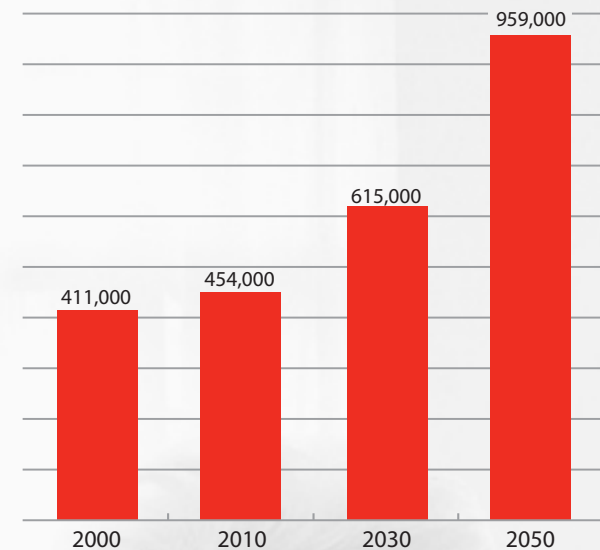
Some 25% of us will have the disease by the time we are in our 80's.

About 75 million Baby Boomers are coming into the Alzheimer's age range (age 60+) and by 2050, it is estimated that every 11 seconds someone will develop the disease.

Economic costs are staggering. World-wide the costs for caring for persons with Alzheimer's disease exceed \$248 billion annually.

Alzheimer's costs Medicare and Medicaid in excess of \$100 billion per year. By 2030, the number is projected to be over \$500 billion, potentially bankrupting the Medicare/Medicaid system.

Estimated New Cases of Alzheimer's Disease by Year



Why Cure Alzheimer's Fund?

Cure Alzheimer's Fund Mission

To fund research with the highest probability of slowing, stopping or reversing Alzheimer's disease.

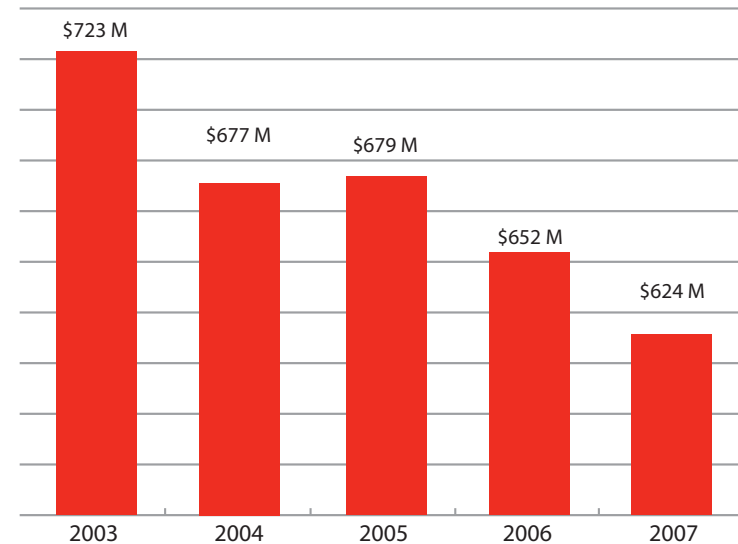
Why did we create Cure Alzheimer's Fund?

We believe that with a focused approach, excellent scientists, and good management, we can greatly accelerate the process of developing cures.

In the early spring of 2005, three families (the McCances, the Morbys and the Rappaports), all with experience in venture capital and corporate start-ups, came together around the realization that current efforts to find a cure for Alzheimer's disease were proceeding very slowly. In fact, such efforts were seemingly coming to a standstill with reductions in NIH funding, despite the fact that Alzheimer's is a major and growing concern.

After considerable research, the Founders came to the conclusion that even as little as several million dollars can make a difference. With a focused effort toward one and only one objective, to find a cure as soon as possible, the founders believed they could accelerate the process of developing a solution to this horrible disease.

Federal Research Funding for Alzheimer's Disease
Adjusted for Inflation
(in millions of year 2006 dollars)



National Institutes of Health (NIH) funding for research is declining substantially just at the point in time when newfound genetic and molecular studies are providing us with the information and tools needed to develop effective cures for the disease. In addition, a bulk of the existing NIH funding is going to older projects for which commitments were made before the slowdown in Government funding, leaving much new science without support. This is where Cure Alzheimer's Fund is stepping in.

Why Cure Alzheimer's Fund NOW?

- Potential breakthroughs based on new genetic and molecular discoveries offer the prospect of finding effective cures, but funding for these potential breakthroughs in many cases is insufficient or unavailable.
- The Founders' early investigations showed that current Alzheimer's research lacks a collective focus and has no overriding map to guide research and align them to

- work together efficiently. The Founders believed that a comprehensive strategy, implemented by world experts, could yield such a "map" (see our Research Roadmap) to guide Cure Alzheimer's to optimally fund the most promising research.
- Because it takes 15-17 years to bring a drug to market, prompt and decisive action is needed to avoid a significant health

care and Medicare/Medicaid disaster as the baby boomers move into their retirement years.

- The NIH budget for Alzheimer's is declining, just as the need for such funding has never been greater. Alzheimer's is now a national and international pandemic and will become more and more serious as the nation and the world age.

What makes Cure Alzheimer's Fund Unique?

- A totally focused strategy with one objective; to find a cure as soon as possible.
- A fully committed group of the world's leading researchers who are working together as a team.
- A fully committed and involved founder group that is dedicating substantial personal resources to the quest.
- A foundation structure created to ensure that 100% of third party contributions go directly into Alzheimer's research. To do this, the founders have agreed to pay all overhead costs.

Cure Alzheimer's Fund's Venture Capital Approach

Cure Alzheimer's Fund brings a venture capital approach to philanthropy, using basic principles and best practices from the venture capital world as its management and operating style.

- Identify "world-class" leaders: Cure Alzheimer's Fund supports a carefully selected group of world-class scientists, and has selected an outstanding CEO and staff with both business and philanthropic experience.
- Transparency to all parties: Executed through Quarterly Reports, Research Consortium meetings, AlzGene (sharing of AD research through www.alzgene.org).
- Create an efficient decision-making process: Cure Alzheimer's Fund is lean and mean with low overhead and minimal processes.
- Establish an entrepreneurial culture to encourage prudent risk-taking to maximize investment.
- Fund breakthrough research that will hasten the development of a cure.
- Cure Alzheimer's Fund has no profit objective.

Cure Alzheimer's Fund Milestones

- ➔ **September 2004** - Jeff and Jacqui Morby establish the Alzheimer's Disease Research Foundation.
- ➔ **October 2004** - First funding to Dora Kovacs, MassGeneral Hospital for the ACAT Inhibitor study.
- ➔ **February 2005** - The Rappaport family of Boston commits funding to Alzheimer's research at MassGeneral, and agrees to join the Morbys of Pittsburgh and Henry and Allison McCance of Boston in a combined and larger national effort to defeat the disease.
- ➔ **April 2005** - The Founding Families (McCances, Morbys and Rappaports) meet and develop strategy for Cure Alzheimer's Fund.
- ➔ **July 2005** - Full-time President and CEO hired and administrative office established.
- ➔ **September 2005** - Alzheimer's Disease Research Foundation officially becomes Cure Alzheimer's Fund and Dr. Rudy Tanzi, MassGeneral Hospital, accepts position as Chair of the Research Consortium.
- ➔ **October 2005** - First in-person meeting of the seven member Research Consortium in Washington, DC, at the Annual Meeting of the Society of Neurology.
- ➔ **November 2005** - First Cure Alzheimer's funding of \$100,000 to the Alzheimer's Genome Project.
- ➔ **December 2005** - First fundraising appeal letter sent.
- ➔ **June 2006** - First Collaborative Project Funded: Cure Alzheimer's Fund Research Consortium Collaborative to readdress the amyloid hypothesis by looking at Abeta oligomers.
- ➔ **November 2006** - Joshua and Anita Bekenstein join the founding families in support for Cure Alzheimer's Fund.
- ➔ **December 2006** - Raised over \$4.6 million since inception and distributed to 12 different projects in 9 different labs nationwide.

Research Background

Alzheimer's disease is a progressive neurodegenerative disorder affecting all aspects of cognition, and is the most common form of dementia in the elderly. If effective therapeutic strategies for prevention and treatment are not developed soon, AD carries the potential to bankrupt federal and state healthcare systems.

Epidemiological and genetic studies over the past three decades have documented a strong genetic component in the etiology of Alzheimer's disease. To date, four different genes have been firmly established to play a role in AD. These include three genes that can contain mutations that cause with certainty the rare "early-onset" familial forms of AD (approximately 5 % of AD patients). A common genetic variant of a fourth gene was identified as a frequent risk factor for late-onset AD which affects the large majority of AD patients.

Over the past two decades, it has become increasingly clear that our best chance for beating this disease requires identification of all genes associated with AD. Identification and characterization of AD genes have already provided an unprecedented window into the biological underpinnings of AD. Every new AD gene has furnished novel targets for drug discovery and unique opportunities to design innovative therapies to treat and prevent AD. Ultimate elucidation of all AD genes will also enable more accurate prediction and diagnosis of the

disease. One of the major findings to come out of previous AD genetics studies regards the AD-related brain lesions known as senile plaques, composed of a sticky and toxic substance called β -amyloid to be the principle cause of AD. The chief component of β -amyloid is a small part of a protein (peptide) called $A\beta$, most particularly a form called $A\beta_{42}$. Numerous lines of evidence point to accumulation of $A\beta_{42}$, a peptide found in great abundance in plaques, as a causative agent of the disease.

Recently, studies indicate that $A\beta_{42}$ mainly wreaks havoc on synapses, the connections made by nerve cells, which allow them to communicate to establish associative learning and memory. In an analogy to heart disease, accumulation of $A\beta$ in the brain is akin to the accumulation of cholesterol in blood vessels. The most effective heart disease therapies lower cholesterol production or enhance clearance and diminish toxicity. Likewise, our genetic studies of AD have taught us that the most effective AD therapies must be aimed at either lowering production of $A\beta_{42}$ or enhancing its clearance and breakdown, especially from nerve synapses required for normal cognitive function. Our best chance at achieving this pharmacological outcome comes from knowledge gained in studying the known AD genes. And our best chance to learn more about the disease comes from learning about the remaining AD genes.

The Roadmap

The Cure Alzheimer's Fund Roadmap, developed by members of the Research Consortium, is a logical framework for identifying the most promising and interrelated research projects to be undertaken by Cure Alzheimer's Fund researchers. It creates a structure to be followed to maximize the probability of discovering effective cures for Alzheimer's within the shortest possible time.

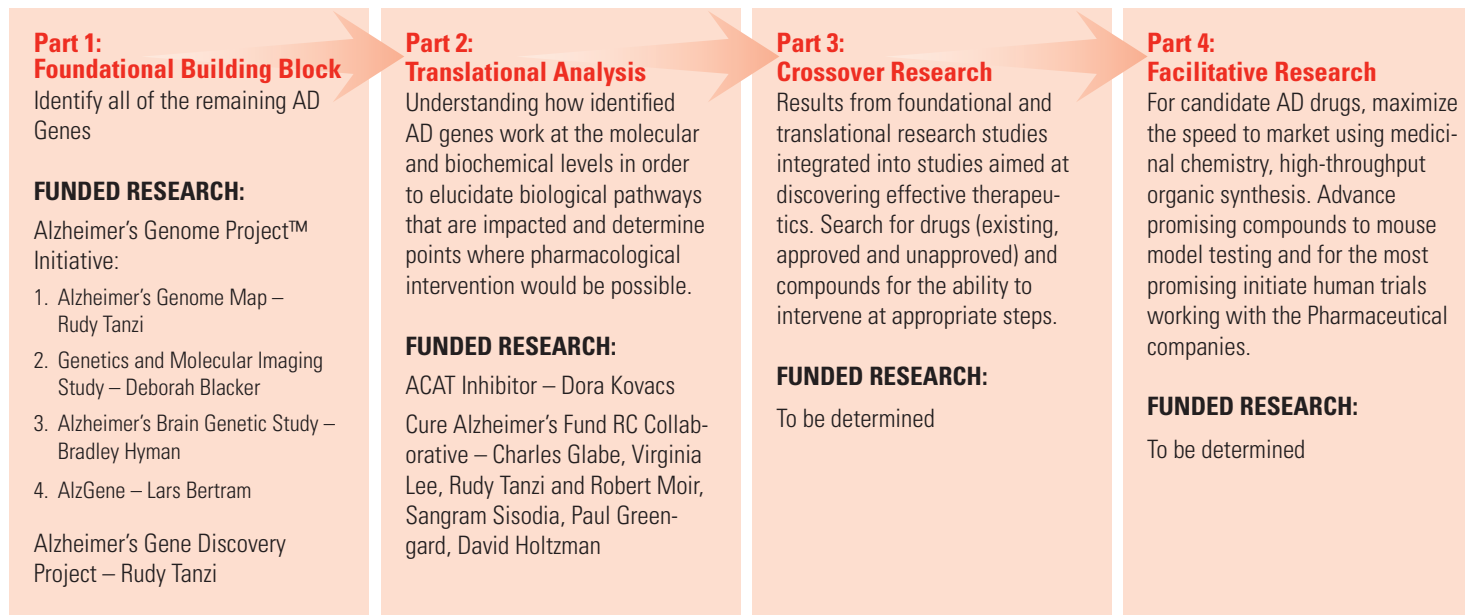
The initial goal of the roadmap to beating AD begins with experiments aimed at identifying all gene mutations and common genetic variants in the human genome that either cause AD or predispose an increased risk of developing AD with advancing age. Just as four known AD genes have begun to serve as the principle guide for drug design and development, identification of the several dozen suspected AD genes that remain unidentified will serve as the starting point, that will enable not only the accurate diagnosis and early prediction of AD, but also provide critical clues for the design and development of novel therapies aimed at effectively treating and preventing AD.

From *The Boston Globe* by Alice Dembner, November 2, 2006

The plan, completed in August 2005, calls for identifying all genes connected with Alzheimer's by the summer of 2008. Next, the foundation will focus on how these gene defects play out in the body and where and how scientists might intervene. A third phase will fund programs that explore potential drug candidates, and the fourth phase will help pay for tests of the drugs in animals and people.

Already, the foundation is funding some of the second and third phases of work, based on the four genes previously identified, which account for a small proportion of Alzheimer's cases. Besides Tanzi and two colleagues, the foundation is supporting work by five researchers at universities across the country who helped develop the research plan. The foundation expects the circle of scientists getting grants to expand worldwide as the work progresses.

Parts 2,3, and 4 of the Roadmap deal with the challenge of understanding the functioning of AD genes, finding cures, and bringing those cures to the public.



SCIENTIFIC ADVISORY BOARD • CURE ALZHEIMER'S FUND

Members of the Scientific Advisory Board provide advice and counsel to the Board of the Cure Alzheimer's Fund regarding the overall scientific soundness of the Research Consortium's approach to scientific discovery and the consistency of grant disbursement policy with criteria approved by the Board for project selection.

Paul Greengard, Ph.D.
Nobel Prize in Physiology or Medicine, 2000 • Head of the Laboratory of Molecular and Cellular Neuroscience • Vincent Astor Professor, The Rockefeller University.



Dr. Greengard is the Vincent Astor Professor of Molecular and Cellular Neuroscience at The Rockefeller University. He began his exploration of nerve cells in 1948 when he joined the Johns Hopkins biophysics laboratory then headed by Detlev Bronk. After receiving his Ph.D. from Johns Hopkins in 1953, Dr. Greengard spent five years in England receiving advanced training in brain biochemistry at the University of London, at Cambridge University, and at the National Institute of Medical Research.

Over the years, Dr. Greengard's achievements have earned him many distinguished awards including the Metropolitan Life Foundation Award for Medical Research, The Charles A. Dana Award for Pioneering Achievements in Health, the Ralph W. Gerard Prize in Neuroscience from the Society for Neuroscience, The National Academy of Sciences Award in the Neurosciences, the Bristol-Myers Award for Distinguished Achievement in Neuroscience Research, and the 3M Life Sciences Award of the Federation of American Societies for Experimental Biology. In the year

2000, Dr. Greengard was awarded the Nobel Prize in Physiology or Medicine. He has served on the editorial boards of over 25 journals, and advises a wide range of organizations, including the National Institutes of Health National Advisory Council on Aging.

John S. Lazo, Ph.D.
Chair, Cure Alzheimer's Fund Scientific Advisory Board • Allegheny Foundation Professor and Director of the Fiske Drug Discovery Laboratory • Department of Pharmacology, University of Pittsburgh School of Medicine • Co-Director of Molecular Therapeutics/Drug Discovery Program, Pittsburgh Cancer Institute.



Acclaimed for his work in cancer drug research, Dr. Lazo is the recipient of many awards and honors. Dr. Lazo graduated from The Johns Hopkins University with a Bachelor of Arts degree in chemistry, and received a Ph.D. in Pharmacology from the University of Michigan. He received postdoctoral training at Yale University and was a member of the pharmacology faculty. Dr. Lazo served as a Corporate Associate of Johnson & Johnson, has authored eleven books, published more than 200 scientific articles and reviews, and has been the principal investigator on numerous research projects.

Caleb Finch Ph.D.

ARCO/ Keischnick Professor of Gerontology and Biological Science • University Professor, University of Southern California • Director, Gerontology Research Institute • Chair, National Research Council Committee on Biodemography of Aging • Chair, Symposium on Slow Aging (SOSA).

Dr. Finch is a Professor of Gerontology and Biological Sciences with adjunct appointments in the Department of Psychology, and Department of Physiology and Neurology. He is also one of University of Southern California's twelve University Professors. Dr. Finch's major research interest is the study of genomic controls of mammalian development and aging.

Michael D. Walker, M.D.

Retired Director, Division of Stroke, Trauma, and Neurodegenerative Disorders, National Institute of Neurological Disorders and Stroke (NINDS) at the National Institutes of Health (NIH).

Dr. Walker's work directly influenced the practice of neurosurgery both nationally and internationally. In 1966 he founded the Brain Tumor Study Group which established the protocols for the clinical study of therapy for human brain tumors.

Dr. Walker is the recipient of numerous awards, and is the author of more than 100 publications, the founder and former editor-in-chief of the Journal of Neuro-Oncology and was deputy editor of The Annals of Neurology.

■ Alzheimer's Genome Project™ Initiative

The core research effort currently funded by Cure Alzheimer's Fund is the Alzheimer's Genome Project™ (AGP) initiative, an estimated three-year, \$3+ million project led by Dr. Rudy Tanzi, with four main components:

① Alzheimer's Genome Map

Funding to date: \$1.2 million

Total funding for project still needed for 2007: \$1.8 million

This project will include genotyping, analysis, follow-up, and confirmatory studies to identify more than 90% of all remaining AD genes thereby providing many more targets for the development of effective therapeutic intervention.

Researcher: Dr. Rudolph Tanzi, Ph.D.

Director, Genetics and Aging Research Unit, MassGeneral Institute for Neurodegenerative Diseases • Department of Neurology, Massachusetts General Hospital • Professor of Neurology (Neuroscience), Harvard Medical School

② Genetics and Molecular Imaging Study

December 2006: \$100,000

This study draws on a unique community-based longitudinal cohort of 378 subjects who span the range of impairment between normal aging and mild Alzheimer's disease (AD). This research focuses on two key steps to find AD genes and to understand their impact:

1. Investigate the relationship of amyloid deposition to memory impairment using Pittsburgh Compound B (PIB), a new imaging technique.
2. Collect DNA samples for a complete genome screen of the full cohort, and analyze using a set of optimal quantitative phenotypes. The hypothesis is that longitudinal quantitative phenotypes will provide greater power to detect AD genes than conventional affection status (AD vs. no AD) approaches.

Researcher: Deborah Blacker, M.D., Sc.D.

Associate Professor of Psychiatry, Harvard Medical School • MassGeneral Institute for Neurodegenerative Disease



③ Alzheimer's Brain Genetic Study

December 2006: \$100,000

The Massachusetts Alzheimer's Disease Center has collected approximately 800 brain samples, providing an extraordinary resource for clinical-pathological correlations for Alzheimer's disease and other dementias.

This research project involves comparing quantitative phenotypes to genetic markers. In earlier studies, these brain samples were used to study the consequences of inheritance of apolipoprotein E-ε4, and of the ubiquitin 1 risk alleles (described by Dr. Rudolph Tanzi). This research will use 500K chips to do a total genome scan, and also utilize the quantitative phenotypes noted above.

Such an analysis will give a window on discovering new genes that impact the rates of progression of patients, the amount of amyloid buildup and deposition, the formation of neurofibrillary tangles, and the amount of neuronal loss.

The research will give an outstanding pilot data set to test the hypothesis that genetic variations can impact the amount of "reserve" that individuals have against the disease process, and also evaluate genetic influences on rate of progression, amyloid generation, and amyloid deposition.

Researcher: Dr. Bradley T. Hyman, M.D., Ph.D.

MassGeneral Institute for Neurodegenerative Disease



④ AlzGene (www.alzgene.org) – An Alzheimer's Gene database and meta-analyses

November 2006: \$142,000

Cure Alzheimer's is funding the management and continued development of a revolutionary web-based database.

The AlzGene database is a revolutionary resource for Alzheimer's researchers providing data and meta-analyses from hundreds of genetic association studies in an easy-to-use, searchable, web-based database. This site allows researchers to post their findings and comment on other findings. It aggregates huge amounts of information that will help in the search for the genetic makeup of Alzheimer's. Currently, the database has more than 1,000 studies. The site also contains a continuously updated list displaying the genes most strongly associated with AD (on the website see "Top AlzGene Results"). Scientists interested in a particular gene can search for it in AlzGene to see what previous studies have reported, receiving a wealth of information in a very short amount of time.

A team of researchers at Massachusetts General Hospital, led by Dr. Lars Bertram, developed the AlzGene database in collaboration with the Alzheimer's Research Forum, and has recently published a paper on this contribution to finding a cure to Alzheimer's in the prestigious journal *Nature Genetics*.



Researcher: Lars Bertram, M.D.
 Assistant Professor of Neurology,
 Assistant in Genetics, Harvard Medical School/
 Massachusetts General Hospital

■ **ACAT Inhibitor Study**

First Study – September 2004: \$100,000

Second Study – June 2005: \$100,000

A two-part study focusing on enzyme inhibitors that prevent or decrease the production of Abeta in the brain, focusing on the effectiveness of a drug approved for other uses.



Researcher: Dora M. Kovacs, Ph.D.
 Associate Professor of Neurology, Harvard
 Medical School • Neurobiology of Disease
 Laboratory, Genetics and Aging Research Unit,
 Massachusetts General Hospital

■ **Alzheimer's Gene Discovery Project**

March 2005: \$138,000

This study is characterizing the ability of a novel AD candidate gene for the ability to regulate the enzyme, beta-secretase involved in Abeta production.

Researcher: Dr. Rudolph Tanzi, Ph.D.
 Director, Genetics and Aging Research Unit, MassGeneral Institute
 for Neurodegenerative Diseases • Department of Neurology,
 Massachusetts General Hospital • Professor of Neurology
 (Neuroscience), Harvard Medical School

■ **Cure Alzheimer's Fund Research Consortium Collaborative**

A collaboration of five of the members of the Research Consortium and a member of the Cure Alzheimer's Fund Scientific Advisory Board hypothesize that an abnormal increase in levels of synaptic Abeta and particularly, Abeta oligomers may lead to synaptic dysfunction, cognitive decline, and eventually dementia. This highly innovative collaborative project will readdresses the amyloid hypothesis by asking which types of Abeta oligomers detrimentally impact synaptic dysfunction and neuronal survival in the brain.

June 2006: \$100,000

Dr. Charles Glabe, University of California at Irvine
The Role of Oligomeric Abeta in Alzheimer's Disease

June 2006: \$100,000

Dr. Virginia M.-Y. Lee, University of Pennsylvania
Abeta Oligomers in Mouse Models of Alzheimer's Disease

June 2006: \$100,000

Drs. Rudolph Tanzi and Robert Moir,
 Massachusetts General Hospital
Identification of Agents that Inhibit the Generation and Neurotoxicity of Cross-linked Beta Amyloid Protein Species

June 2006: \$100,000

Dr. Sangram Sisodia, University of Chicago
*Molecular Analysis of Abeta*56 Structure and Function*

June 2006: \$100,000

Dr. Paul Greengard, The Rockefeller University
The Role of Oligomeric Abeta in Synaptic Transmission and Plasticity

June 2006: \$100,000

Dr. David Holtzman, Washington University in St. Louis
Role of Synaptic Activity and Neurotransmitter Modulation in the Dynamic Regulation of Interstitial Fluid Abeta and Oligomer Formation

RESEARCH CONSORTIUM • CURE ALZHEIMER'S FUND

Researchers and physicians are invited to serve voluntarily to provide and update the "roadmap for research" for the most effective and efficient route to slowing, stopping and/or reversing Alzheimer's disease.

**Rudolph
Tanzi, Ph.D.**
**Massachusetts General
Hospital**

Director, Genetics and Aging Research Unit, MassGeneral Institute for Neurodegenerative Diseases • Professor of Neurology (Neuroscience), Department of Neurology, Harvard Medical School.

Dr. Tanzi has been investigating human neurodegenerative disease at the genetic and biochemical levels since 1980 when he participated in the pioneering study that led to location of the Huntington disease gene, the first disease to be found solely by genetic linkage analysis. Dr. Tanzi is a world-renowned leader in studies of Alzheimer's disease genetics. He has identified and characterized several different AD genes, including the first Alzheimer's disease gene, the beta-amyloid protein precursor (APP).

Dr. Tanzi has won numerous awards and has spoken all over the world on Alzheimer's disease. He has started two companies to develop drugs based on his findings, published dozens of scientific papers, and written a history of Alzheimer's research called *Decoding Darkness* (2000). When he isn't solving genetic puzzles, he enjoys playing basketball, drinking fine wine and taking frequent trips to Fenway Park.



**Charles
Glabe, Ph.D.**
**University of California
at Irvine**

Professor, Molecular Biology and Biochemistry, School of Biological Sciences.

Dr. Glabe is a Professor of Molecular Biology and Biochemistry in the School of Biological Sciences at the University of California at Irvine. He is a leading world expert on the effects of amyloid on the brain. His research program is focused on amyloid structure and aggregation; beta-amyloid in particular, which is the key pathogenic hallmark of Alzheimer's disease. Dr. Glabe made the seminal discovery that protein components of amyloid share a common structure that is recognized by a conformation-specific antibody. This discovery indicates that amyloids likely share a common primary mechanism of pathogenesis in disease.



**David
Holtzman, M.D.**
**Washington University,
St. Louis**

The Andrew B. and Gretchen P. Jones Professor of Neurology and head of the Department of Neurology; Charlotte and Paul Hagemann Professor of Neurology and Molecular Biology and Pharmacology; the Associate Director of the Alzheimer's Disease Research Center; a member of the Hope Center for Neurological Disorders.

In addition to his laboratory, administrative, and teaching duties, Dr. Holtzman is involved in clinical and research activities at the Wash-



RESEARCH CONSORTIUM • CURE ALZHEIMER'S FUND

ington University Memory and Aging Project and the Alzheimer's Disease Research Center.

Dr. Holtzman has carried out groundbreaking studies of molecules involved in beta-amyloid (A β) metabolism and the initiation of Alzheimer's pathology and the role of vascular factors such as amyloid angiopathy in the disease. He has also contributed greatly to our understanding of how anti-amyloid antibodies affect Alzheimer's pathology and how A β is cleared from the brain of Alzheimer's disease patients.

Ilyas Kamboh Ph.D.

University of Pittsburgh
Professor and Acting Chair,
Department of Human
Genetics, Graduate School of
Public Health.

Dr. Kamboh's major research interest is the genetic epidemiology of Alzheimer's disease and cardiovascular disease. Over the past several years, Dr. Kamboh has been instrumental in identifying and characterizing Alzheimer's disease candidate genes. He has also assembled one of the largest and most powerful Alzheimer's disease samples for use in population-based studies of genetics.



Virginia Lee, Ph.D., MBA

University of Pennsylvania

The John H. Ware III Professor in Alzheimer's Research, Dept of Pathology and Laboratory Medicine; Director, Center for Neurodegenerative Disease.

Dr. Lee is a world-renowned leader in research on tau, alpha-synuclein and the beta-amyloid precursor protein, and their pathobiological roles in neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and frontotemporal dementias. In particular, Dr. Lee is attempting to determine the pathogenic roles of the abnormal proteins comprising senile plaques, Lewy bodies, and neurofibrillary tangles, major pathological lesions found in the brains of patients with Alzheimer's disease and other neurodegenerative diseases.



John Mazziotta, M.D., Ph.D.

UCLA School of Medicine

Chair, Department of Neurology; Director of the UCLA Brain Mapping Center; Associate Director of the Neuropsychiatric Institute; Frances Stark Chair of Neurology; Pierson-Lovelace Investigator; Professor of Neurology, Radiological Sciences and Pharmacology, Ahmanson-Lovelace Brain Mapping Center.

Dr. Mazziotta is a pioneer and leader in applying imaging technology to our understanding of the functions of the brain. His research, teaching, writing and presentations have furthered developments in brain mapping



through the use of such technologies as Position Emission Tomography. He is currently leading the International Consortium of Brain Mapping.

Sangram Sisodia, Ph.D.

University of Chicago

Thomas A. Reynolds Sr. Family
Professor of Neurosciences.

Dr. Sisodia is a leading expert on the molecular and cell biology of Alzheimer's disease pathology. He has been at the forefront of learning how the familial Alzheimer's disease (FAD) genes, including the amyloid precursor protein and the presenilins, function normally, and contribute to Alzheimer's disease pathogenesis.

Most recently, Dr. Sisodia's studies have shown that in mice, exercise has a remarkable ability to protect against Alzheimer's disease pathology by favorably changing gene activity in the brain.



STATEMENT OF FINANCIAL POSITION

	Year Ended Dec. 31, 2004	Year Ended Dec. 31, 2005	Year Ended Dec. 31, 2006
ASSETS			
Cash and cash equivalents	100,000	426,723	1,636,380
Pledges receivable	0	0	289,332
Funds in transit	0	661,563	132,164
Prepaid expense	0	0	2,114
Interest receivable	0	7,606	0
Deposits with foundations	10,000	22,694	23,020
Depreciable equipment	0	2,007	3,993
Less accumulated depreciation	0	-167	-932
Website, trademark	0	5,691	8,931
Less accumulated amortization	0	-206	-2,604
	<u>110,000</u>	<u>1,125,911</u>	<u>2,092,398</u>
LIABILITIES AND NET ASSETS			
Liabilities			
Accounts payable and accrued expenses	0	35,479	21,937
Net Assets			
Unrestricted	110,000	1,090,432	1,781,129
Temporarily restricted	0	0	289,332
	<u>110,000</u>	<u>1,090,432</u>	<u>2,070,461</u>
	<u>110,000</u>	<u>1,125,911</u>	<u>2,092,398</u>

STATEMENT OF ACTIVITIES

	Year Ended Dec. 31, 2004	Year Ended Dec. 31, 2005	Year Ended Dec. 31, 2006
REVENUE AND OTHER SUPPORT			
Contributions	110,000	1,294,753	3,257,941
Gifts in kind - Goods & Service	0	0	25,391
Investment Interest & Other Income	0	8,176	57,542
	<u>110,000</u>	<u>1,302,929</u>	<u>3,340,874</u>
EXPENDITURES			
Program grants and other program expenses	0	110,000	2,202,973
Management and general	68	68,768	218,682
Fundraising	0	66,355	228,523
	<u>68</u>	<u>245,123</u>	<u>2,650,178</u>
INCREASE IN UNRESTRICTED NET ASSETS	9,932	1,057,806	690,697
TEMPORARILY RESTRICTED NET ASSETS			
Pledges	0	0	289,332
INCREASE IN NET ASSETS	9,932	1,057,806	980,029
NET ASSETS, beginning of period	0	9,932	1,067,738
PRIOR PERIOD ADJUSTMENT	0	0	22,694
NET ASSETS, end of year	<u>109,932</u>	<u>1,067,738</u>	<u>2,070,461</u>

Fundraising

In an era of declining government support for Alzheimer's research, private support is essential to continue and maintain the excellent research opportunities and progress toward a cure.

Cure Alzheimer's Fund raises private funds from individuals and foundations. Support has grown steadily since our inception.

★ FUNDED RESEARCH SITES

Massachusetts General Hospital, Genetics and Aging Research Unit, Charlestown, MA

Massachusetts General Hospital, MassGeneral Institute for Neurodegenerative Disease, Charlestown, MA

Rockefeller University, New York, NY

University of California at Irvine, Irvine, CA

University of Pennsylvania, Philadelphia, PA

University of Chicago, Chicago, IL

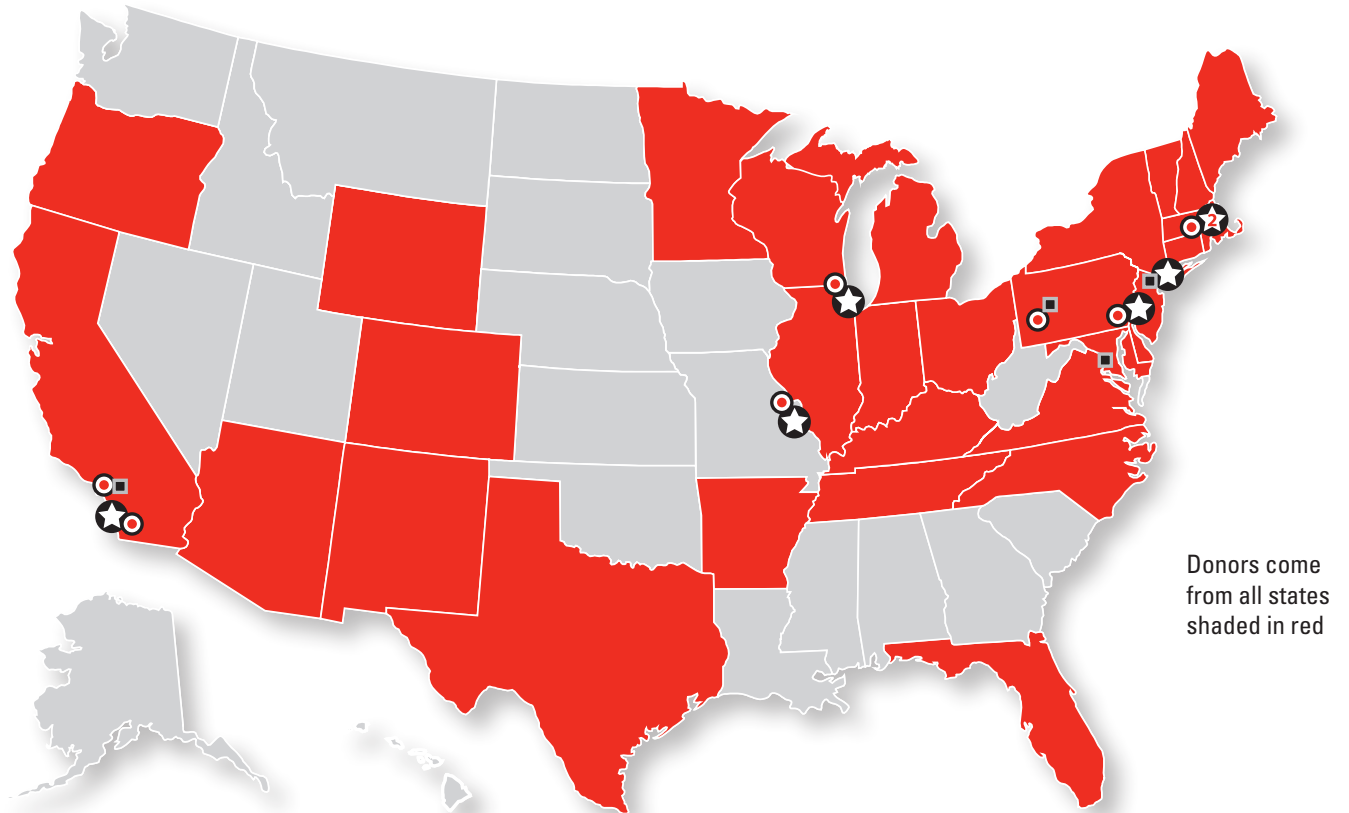
Washington University in St. Louis, St. Louis, MO

⊙ RESEARCH CONSORTIUM MEMBERS

■ SCIENTIFIC ADVISORY BOARD MEMBERS

Ours is a National Effort

Distribution of Donations, Funded Research, and Researchers

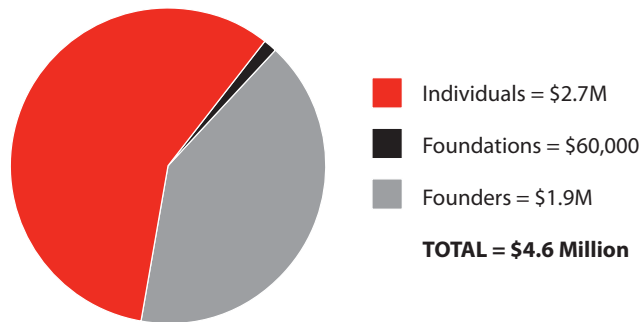


Fundraising Totals

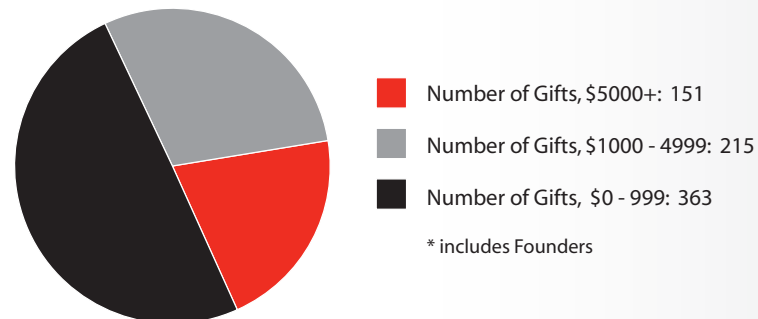
Year ending December 31	Funds raised from Individuals	Number of Gifts, not including Founders	Funds raised from Founders	Total Funds raised
2006	\$2,222,500	519	\$1,060,800	\$3,283,300
2005	\$573,800	210	\$721,000	\$1,294,800
2004	\$0	0	\$110,000	\$110,000
Total raised since inception thru 12/31/2006	\$2,796,300	729	\$1,891,800	\$4,688,100

\$ Rounded to the nearest 100

Distribution of Gifts from Individual Donors, Foundations and Founders



Distribution of Gifts* by Gift Size



Future Funding

Identifying all of the remaining genes for Alzheimer's disease, estimated for completion in the summer of 2008, will generate more and more research opportunities related to the newly discovered genes. The chart below shows our anticipated funding needs over the next five years.

	2007	2008	2009	2010	2011	Notes:
Part 1: Genetic Foundation	\$3.0	\$4.0	\$2.0	\$2.0	\$1.5	AGP completed by 2008, but other projects to be funded for further genetic information
Part 2: Translational Research	\$2.0	\$4.0	\$8.0	\$8.0	\$8.0	Several promising projects are now under way. Intense analysis begins in 2007.
Part 3: Crossover Research	\$5	\$1.0	\$4.0	\$4.0	\$4.0	One promising project now under way, could require additional funds in 2007
Part 4: Facilitative Research	\$5	\$1.0	\$1.0	\$1.0	\$1.0	Projects to arise in 2008 onward
Total Funding Need	\$6.0	\$10.0	\$15.0	\$15.0	\$15.0	
Minimum Funding Requirement	\$4.0	\$6.0	\$10.0	\$10.0	\$10.0	

2006 EVENTS

March 2006

Presentations in Cleveland and Pittsburgh “Progress in the Search to Find a Cure for Alzheimer’s Disease” by Rudy Tanzi

Stuart, FL House party hosted by Phyllis and Jerry Rappaport, presentation “Finding a Cure to Alzheimer’s Disease” by Rudy Tanzi

June 2006

World Health Summit, presentation by Jeff Morby titled “The Alzheimer’s Tsunami”

August 2006

Hyannis Port House Party, hosted by Judy and Rick Brand with presentation by Rudy Tanzi

Fishers Island House Party hosted by Henry and Allison McCance with presentation by Rudy Tanzi

Nantucket Island House Party hosted by Phyllis and Jerry Rappaport with presentation by Rudy Tanzi

Martha’s Vineyard House party hosted by Jacqui and Jeff Morby with presentation by Rudy Tanzi

September 2006

Harvard Business School Panel presentation: “Cure Alzheimer’s Fund: A Venture Capital Approach to Philanthropy” presented by Henry McCance moderated by Professor Bill Sahlman of Harvard Business School

October 2006

Palo Alto presentation “A Venture Approach to Philanthropy” by Henry McCance, Jeff Morby and Rudy Tanzi

December 2006

Annual Cure Alzheimer’s Fund Board Meeting, Pittsburgh

Thank you to our board members and Judy and Rick Brand for hosting Cure Alzheimer’s Fund parties in 2006.

If you would like to host a presentation on current Alzheimer’s research, please let us know.

We would be thrilled to organize an event in your community.

Cure Alzheimer's Fund Donors

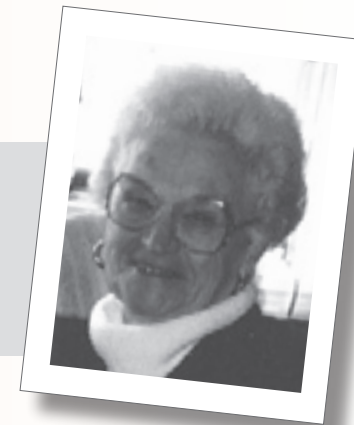
In addition to the founders, over 500 individuals have contributed over \$4.6 million through the end of 2006. Each of these donors is a hero, regardless of the size of the gift. Among the larger gifts are several well over \$100,000, some of which are in current gifts and some in the form of significant pledges over the next few years. We are grateful for the incredible support we have received since our inception.

One family in particular stands out as pace setters for Cure Alzheimer's Fund. Anita and Josh Bekenstein have been model philanthropists for numerous causes, including children's cancer and others. They have made a large and ongoing commitment to Cure Alzheimer's Fund reflecting their own unfortunate experience with the difficulties that all-too-often afflict the elderly, and which the statistics say may very well affect them and all of us as well. Their commitment has provided an incentive to our founders and others who have already been generous to stretch a little more in an effort to make a bigger difference sooner through Cure Alzheimer's Fund. We are deeply grateful to them for their help and faith in this effort, and appreciate their role in moving us all to a higher level.

Memorial Gifts

Many families decide to remember an Alzheimer's victim with donations to research and Cure Alzheimer's Fund is honored to accept gifts in memory of loved ones. For more information on our Memorial Gifts program, please visit our website www.curealzfund.org/donate.

Barbara S. DelCollo was honored by her son Ralph P. DelCollo in one of Cure Alzheimer's first memorial gifts. Mr. DelCollo had donations sent to Cure Alzheimer's Fund in lieu of flowers at her memorial service.



**We are so grateful for the generosity of our donors.
Thank you to all who are helping support our search for a cure.**

BOARD OF DIRECTORS • CURE ALZHEIMER'S FUND



John S. Lazo, Ph.D.

John S. Lazo, Ph.D. is a professor and chair in the department of pharmacology at the University of Pittsburgh School of Medicine and co-director of the molecular therapeutics/drug discovery program at the University of Pittsburgh Cancer Institute.

Dr. Lazo received his doctorate in pharmacology from the University of Michigan and completed postdoctoral training at Yale University. In 2003, Dr. Lazo was appointed chair of the Extramural Grants Council at the American Cancer Society. As chair, he leads a multidisciplinary panel of midlevel and senior scientists to determine ACS funding for investigator-led projects taking place at leading cancer centers across the country.

Dr. Lazo received his doctorate in pharmacology from the University of Michigan and completed postdoctoral training at Yale University. In 2003, Dr. Lazo was appointed chair of the Extramural Grants Council at the American Cancer Society. As chair, he leads a multidisciplinary panel of midlevel and senior scientists to determine ACS funding for investigator-led projects taking place at leading cancer centers across the country.



Henry F. McCance Founding Board Member

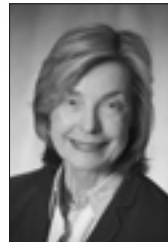
Henry F. McCance is Chairman of the Board and President of Greylock Management Corporation and General Partner in a variety of Greylock private, limited

partnerships for venture capital investments.

Mr. McCance serves on the board of Cabot Corporation, is a member of the Yale Investment Committee, and is on the Board of Advisors of the Yale School of Management. Mr. McCance served as the inaugural Entrepreneur in Residence, Harvard Business School, and served on numerous public and private corporate boards of directors. In 2004, he received the National Venture Capital As-

sociation's Lifetime Achievement Award.

Mr. McCance graduated from Harvard Graduate School of Business Administration with High Distinction, Baker Scholar, and from Yale University with a B.A. in economics, Magna Cum Laude and Phi Beta Kappa.



Jacqueline C. Morby Founding Board Member

Jacqueline Morby joined TA Associates in 1978. She was a Managing Director of TA Associates from 1982 to 2002, serving on the firm's four member Executive

Committee from 1988 to 2001. In 2003 she retired but continues to serve as Senior Director of the firm representing the TA private equity funds on Boards of Directors.

Mrs. Morby graduated from Stanford University with a Bachelor of Arts degree in Psychology and from the Simmons Graduate Management School with a Masters in Management degree. She is on the Boards of Directors of ANSYS, Inc., Axioma, Inc., J&B Software, Inc., and Pacific Life Corp. She has also served as a Director of the following public companies. Axent Technologies, Inc., BMC Software, Inc., Boron, LePore & Associates, Inc., Ontrack Computer Systems Inc., Econometry Corporation, System Software Associates, Sierra On-Line Inc., and AI Corp.

Mrs. Morby serves on the Boards of Trustees of Simmons College, the Andy Warhol Museum, the Carnegie Museums of Pittsburgh, and on the Boards of Directors of Lead Pittsburgh, and The Pittsburgh Life Sciences Greenhouse. Mrs. Morby serves as

the Chair of the Board of Population Action International in Washington D.C. She also serves on the Carnegie Mellon School of Computer Science Dean's Advisory Board and is a member of both the Committee of 200 and the International Women's Forum.



Jeffrey L. Morby Chairman of the Cure Alzheimer's Fund Board of Directors, Founding Board Member

Jeffrey L. Morby is is Managing Director of Amarna Corporation, LLC,

a privately-held merchant banking company specializing in financing and creating financial institutions. He is Chairman of the Morby Family Charitable Foundation, and director of the Andrew and Velda Morby Educational Foundation. He is also a Director of Horace Mann Educators Corporation, a publicly-traded insurance company providing insurance and investment products to educators.

Mr. Morby retired from Mellon Bank Corporation in 1996, where he was Vice-Chairman in charge of Wholesale activities, which encompassed all large commercial lending and international operations, investment banking, trading, and money market activities. In that capacity he was also Chairman of Mellon Bank Europe; Chairman of Mellon Capital Markets; and Chairman of Mellon's Proprietary Investment Committee.

Mr. Morby has an MBA from Harvard Graduate School of Business and an engineering degree from Stanford University.

BOARD OF DIRECTORS • CURE ALZHEIMER'S FUND



Phyllis C. Rappaport

Founding Board Member

Phyllis C. Rappaport chairs her family's philanthropy, the Jerome Lyle Rappaport Charitable Foundation and is a director of New Boston Fund, Inc., where she

oversees strategy planning, human resource planning and development, and organizational performance.

Ms. Rappaport was President of Millileaf, a software start-up company, from 1992 until its dissolution in 1996. Before holding several management positions at Digital Equipment Corporation from 1979 - 1991, Phyllis was a Coopers & Lybrand auditor specializing in banking and healthcare.

In 1986, Ms. Rappaport was elected to the Lincoln-Sudbury Regional School Committee and served as chair of that School Committee in 1992. Since 1993, she has been a trustee of the DeCordova Museum in Lincoln, MA. She is currently on the Taubman Center for State and Local Government at Harvard's Kennedy School of Government Advisory Board, a member of the Massachusetts General Hospital's Presidents Council and McLean Hospital National Council.

Ms. Rappaport is a graduate of Smith College and Simmons Graduate School of Management.



William E. Trueheart, Ed.D.

William E. Trueheart is President and Chief Executive Officer of The Pittsburgh Foundation.

Before joining The Pittsburgh Foundation, Dr.

Trueheart served as President and Chief Executive Officer of Reading Is Fundamental, Inc., Prior to that, he was President of Bryant College in Rhode Island, the first African American to head a four-year private college in New England. He also served Bryant College as Executive Vice President and member of its Board of Trustees. He was Associate Secretary of Harvard University in its Office of Governing Boards and served as Assistant Dean and Director of the Master in Public Administration Program at the John F. Kennedy School of Government.

Dr. Trueheart currently serves on the Boards of Independent Sector (Board Chair), the University of Pittsburgh, the Allegheny Conference on Community Development, Pittsburgh Regional Healthcare Initiative, the Nellie Mae Education Foundation, and Highmark Blue Cross/Blue Shield. He also serves on the Visiting Committee of the JFK School of Government at Harvard University.

Dr. Trueheart earned his BA degree in political science and economics at the University of Connecticut, his MPA at the Harvard University John F. Kennedy School of Government, and EdD at the Graduate School of Education at Harvard University.



Timothy W. Armour

Timothy W. Armour is President and Chief Executive Officer of the Cure Alzheimer's Fund.

Mr. Armour served for fifteen years as executive director and later execu-

tive vice president of the JASON Foundation for Education, a nonprofit organization committed to improving science and math motivation and performance among middle school students. Mr. Armour's earlier career includes start-up and executive roles in business as well as the senior external relations and fundraising official at Harvard Business School, and fundraising and alumni relations at Amherst College.

Mr. Armour earned his BA in Political Science from Amherst College, an MA in Political Science from the University of Massachusetts, and an MBA from Harvard Business School.



Cure Alzheimer's FUND

targeting breakthrough research

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General Hospital

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David Michael Holtzman, M.D.,
Washington University, St. Louis

M. Ilyas Kamboh, Ph.D., University of Pittsburgh

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President, Cure Alzheimer's Fund

*Founder

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Catherine Cotton, Manager, Fundraising Programs

John Epeneter, Controller

Karen Robertson, Accountant

Please help us fund research with the highest probability of slowing, stopping or reversing Alzheimer's disease. Donations can be made through our website www.curealzfund.org or sent directly to our office.

For gifts of securities or direct wire transfers, please contact Tim Armour at **877-CURE-ALZ (287-3259)** for further information.



Cure Alzheimer's FUND

targeting breakthrough research

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Wellesley Hills, MA 02481

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Pennsylvania Office

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