A Vaccine for Alzheimer’s Disease?
A brief summary of important potential treatments and CAF’s related research

There has been a lot of attention over the last several years about vaccines and Alzheimer’s disease (AD). The buildup of a protein in the brain, our body normally produces, called “amyloid-beta” plays an important role in AD. The accumulation of amyloid-beta in the brain leads to ongoing nerve cell injury and this ultimately contributes to the cognitive decline we see in patients. It has been theorized if one could prevent the buildup of amyloid-beta or could clear away what does build up, this could serve a treatment.

In 1999, it was shown if mice that develop amyloid buildup in the brain were actively immunized with the amyloid-beta protein itself (amyloid-beta was injected under the skin of mice), they developed antibodies against amyloid-beta and had much less buildup in their brain. It was later shown, if one directly infused antibodies against amyloid-beta (called passive immunization) into mice, this would also decrease the buildup of amyloid-beta and in some cases, improve the cognitive deficits seen in the animals. Because of these exciting findings, many research groups began studies to better understand how active and passive immunization work and some companies moved ahead with clinical trials to see if these approaches might be useful to people.

- **Vaccine Trials in Humans**

Soon after the realization of the potential therapeutic potential of active or passive immunization, Elan and Wyeth pharmaceuticals together began a trial in which amyloid-beta was directly administered to humans subcutaneously (active immunization). Over 300 patients were entered into these trials in the US and Europe. It was noted that ~ 6% of the patients developed a potentially serious complication called acute encephalitis (confusion with variable neurological deficits associated with inflammation in the brain). This trial was then halted. Interestingly, the complication did not seem to be due to antibodies generated against amyloid-beta, but another type of inflammation induced by the treatment. Several of the patients from this trial have died for other reasons and, interestingly, most have evidence that a large amount of amyloid was cleared from the brain. Further, while the trial was aborted, there is also evidence that memory has not worsened as much as in those people who developed antibodies to amyloid-beta.

The field continues to move forward in this area. Because passive immunization (direct administration of anti-amyloid antibodies) should not, in theory, have the same complications as active immunization, companies such as Elan/Wyeth, Lilly, and others have started human trials to see if infusion of these type of antibodies can have beneficial effects. Results from these trials should emerge in the next 2 years. In addition, some companies are also starting active immunization trials again with modified versions of amyloid-beta that they believe will not have the same side effects.

- **How is Cure Alzheimer’s Fund Involved?**

There are three researchers funded by Cure Alzheimer’s Fund that are collaborating on work related to immunization and AD. Drs. Virginia Lee, Charles Glabe, and David Holtzman are all exploring the detailed role of specific forms of the amyloid-beta protein called oligomers. They are looking at whether particular antibodies targeting amyloid-beta can tell us more about the cause of AD and new ways for treatment. Coupling findings from this new research, with new discoveries from the laboratory of Dr. Rudy Tanzi on genetic risk factors for AD, should allow us to begin treatment for AD much earlier than is currently possible. The bottom line is that there is good reason to believe these approaches have significant potential as treatments in the future. However, it is critical for future studies to figure out how to best clear amyloid from the brain without inducing serious side effects.
Q&A with Cure Alzheimer’s Fund
President Tim Armour

With the venture approach to philanthropy, does Cure Alzheimer’s Fund have a license to the commercialization of developed therapies? Will you get involved with pharmaceutical companies and profit from discoveries found through your funded research?

No, we do not require the rights to license or commercialize any product or process emanating from our funding and do not intend to go that route. We fund basic “foundational” and “applied” research, almost all of which is done in academic institutions. Each academic researcher and his/her institution has their own arrangements for intellectual property, but most commonly, work done by the researcher is the property of the institution. Breaking into that chain is difficult, costly, and could delay partnering with biotech/pharma for drug discovery and development based on new research findings.

Since we don’t own the IP, we do everything in our modest power to accelerate publication and sharing with other researchers as broadly as possible. Another condition for funding, in addition to no overhead support, is that results of CAF funded research must be promulgated as quickly and broadly as possible so that other researchers working research areas “downstream” from the foundational research can incorporate the results in their work, which will accelerate progress toward a cure.

Regarding “biotech/pharma,” we believe we can begin to facilitate movement of foundational research to the stage at which big pharma is interested in investing in the kinds of trials and market development for which only they have the funds. We will do this primarily by providing more funding for the promising research to push it further along, therefore lowering the risk and making the proposed therapy more attractive. At that point, the biotech/pharma companies can get involved and license the most promising “downstream” therapeutics and hopefully bring them to market.

Financial Report
President Tim Armour reports our progress as follows. Dollars are in cash received and rounded to the nearest $1,000; no pledges or commitments are included. Please note that the Cure Alzheimer’s Fund 2005 tax return, form 990, is now online at www.curealzfund.org.

**How much have we raised?**
Total funds raised from inception to October 1, 2006: $2,783,000 100%

**How are we putting that money to work?**
Total distributed for Research from inception to October 1, 2006: $1,750,000 64%
Total operating expenses from inception to October 1, 2006: $487,000 17%*
Reserve before additional research in 2006: $536,000 19%

**Projected Research Budget for 2007**
$6,000,000

*Provided by the Founders; not paid for by other donors

If you have questions about Alzheimer’s research or what we’re doing at CAF, please let us know. We’re always happy to provide information and you might end up in the Quarterly Report!
Update from Board Member Phyllis Rappaport

Curing Alzheimer’s Gene by Gene - It’s my Future!™

My husband and I work hard and creatively on designing our philanthropy because we want our results to have big impact and make significant change. We are thoughtful and pragmatic about selecting philanthropic partnerships and always seek measurable results. So far, our partners have included Harvard and Suffolk Universities, several New England colleges and private schools, hospitals in the Harvard system, and a local museum.

Co-starting Cure Alzheimer’s Fund is the first time we have ever created a new public charitable entity and we do this with great pride and excitement. We believe there is an enormous opportunity right now to make significant progress towards a prevention or cure for this disease and we are grateful to each one of you who is helping us make this a national effort to focus top talent in eliminating this hugely burgeoning disease.

So why am I—already challenged by my large and ever-growing family, business, and foundation—involved?

For many years now, Jerry and I have funded young researchers in neurologic disease and mental illness at several Harvard hospitals. In May 2003, I met Dr. Rudy Tanzi, Alzheimer’s geneticist and now Chairman of the Cure Alzheimer’s Fund Research Consortium, and very simply, he changed and charged my world.

I was amazed that a co-founder of three of the four known genes for Alzheimer’s, the first co-founder of a gene for any neurologic disease, and an acclaimed scientist with strong NIH support, was still struggling to figure out how to get enough research funding to keep pace with his rapidly expanding capabilities for discovery. I was struck by the fact that fundraising for breast and other cancers has become rightfully and highly popular, and yet a disease that is just as prevalent, and growing exponentially, was out of sight and out of mind of the general public.

I quickly realized that I am a baby boomer and mine is the biggest generation ever to hit this world. My generation has changed the world in many positive ways but as we age, our Alzheimer’s and the care we demand is going to bankrupt Medicare and Medicaid and drain state and national treasuries. I don’t want that to be our legacy.

I lost sleep realizing that Alzheimer’s is a disease with no pretty faces, no survivors, and few persons fighting for money nationally to stop its spread. I observe that Alzheimer’s is not a disease people like to talk about, perhaps because those of us without affected family members think we can ignore it and those with an afflicted family member often are too emotionally or physically drained to raise their voice. I coined and trademarked these words: Curing Alzheimer’s Gene by Gene - It’s My Future!™ with hopes that a double entendre (jean by jean) might lead to some retail marketing play with blue jeans but, most of all, I imagine this as a headline for my picture and for your picture and or everyone else who joins us in envisioning our future without this disease.

So my story is a very simple one. I was inspired by Rudy and networked to find others who shared my passion. Jeff Morby and Henry McCance were moving in the same direction. To-gether we have enlisted scientific and management talent to aid in our entrepreneurial venture. Fortunately, many of you have joined forces with us to help solve this disease. We want all of you to join us again and again when you make decisions for your giving and philanthropy.

This is good company. We are motivated and intelligent investors, backing Cure Alzheimer’s Fund to follow a focused, well managed path of research to improve our future and our children’s future. Thank you.
Mission Statement
Fund research with the highest probability of slowing, stopping or reversing Alzheimer's disease by 2016.

Research Consortium
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Charity Designation
Cure Alzheimer's Fund™ is a “doing business as” name for the Alzheimer's Disease Research Foundation, a 501c3 public charity with federal tax ID # 52-2396428, and, as defined by the IRS, a 509a3 supporting organization to The Pittsburgh Foundation.

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.

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