

Older Antihistamine 'Dimebon' Shows Potential as an Alzheimer's Treatment

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Cure Alzheimer's Fund aims to learn more and apply it to potential new targets

Dimebon® is a 25-year-old antihistamine recently touted as a potential breakthrough for the treatment of Alzheimer's disease. The drug originally was developed in Russia for hay fever and allergies but eventually was taken off the market as newer products became available.

Dimebon gained attention as a potential Alzheimer's treatment after positive animal studies in 2000; it more recently showed promising results in clinical studies in Russia and now is in trials in the United States and Europe.

In Russia, Dimebon was evaluated in a randomized, double-blind, placebo-controlled clinical trial of 183 patients with mild-to-moderate Alzheimer's disease. Patients treated with Dimebon experienced statistically significant improvements compared with the placebo in all key aspects of the disease: memory and thinking, activities of daily living, behavior and overall function. After both six months and a full year of treatment, Dimebon-treated patients were significantly better than placebo-treated patients in all key aspects of the disease. Dimebon was well-tolerated throughout the trial.

Although the Russian study included well-respected Alzheimer's researchers from the United States, Dimebon currently is being evaluated in a confirmatory pivotal Phase III trial of 525 mild-to-moderate Alzheimer's patients in the United States and Europe in an attempt to replicate the initial findings of the Russian study. The trial sponsors are Medivation and Pfizer, and if the results are successful, the drug could be on the market within two to three years. The Russian Dimebon pivotal trial is the first Alzheimer's disease study in which a drug has achieved statistically significant benefits of this breadth, size and duration in a one-year, well-controlled trial.

As exciting as these findings are, there still are many unknowns about Dimebon. It is not yet clear whether Dimebon alters the course of Alzheimer's disease for the long term or just alleviates symptoms temporarily. It also is not clear exactly how the drug works or what the explanation is for its clinical benefit. For those reasons, further study is required to elucidate the molecular mechanism underlying the regulation of amyloid beta metabolism by Dimebon. Dimebon also may be a useful chemical probe



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for advancing understanding of the role of amyloid beta in Alzheimer's disease and for identifying unexplored druggable mechanisms. Chronic Dimebon exposure also merits study.

With many of those unanswered questions in mind, Cure Alzheimer's Fund is sponsoring a study led by Sam Gandy, MD, Ph.D., an international expert in amyloid metabolism at the Mount Sinai School of Medicine in New York. His work will investigate the relationship between Dimebon and amyloid beta. Since deposition of amyloid beta in the brain is one of the main causes of Alzheimer's disease, interfering with amyloid beta metabolism is one of the primary approaches to prevent amyloid beta deposition and delay the onset of the disease.

Converging clues from genetics, clinical trials and molecular cell biology suggest that further investigation of Dimebon is expected to provide novel insight into the pathogenesis and therapy of Alzheimer's disease. At this point, it is not known whether Dimebon impinges on the activity of one of the amyloid beta metabolizing enzymes known as secretases. Dr. Gandy's research study will evaluate the effects of Dimebon on amyloid beta metabolism to help researchers better understand whether Dimebon represents the starting point for the development of future Alzheimer's therapies.

The first results of Dr. Gandy's work will be presented in mid-July at the International Conference on Alzheimer's Disease (ICAD) 2009 in Vienna, Austria.

Abeta Protein may be a Defense Against Microbes!



Dr. Robert Moir

Dr. Rob Moir, a researcher at Boston's Massachusetts General Hospital and member of the Cure Alzheimer's Fund Oligomer Collaborative, presented research supported by Cure Alzheimer's Fund in March to the International Conference on Alzheimer's Disease/Parkinson's Disease. The research points to evidence that the Abeta peptide, acknowledged to be implicated as a cause of Alzheimer's, may in fact be a "part of our evolutionary ancient innate immune system."

The work is a collaboration between Dr. Moir, Dr. Rudy Tanzi, the chairman of the Cure Alzheimer's Fund Research Consortium, Dr. Charlie Glabe of the University of California at Irvine and infectious disease expert Dr. James Kirby of Harvard Medical School and Beth Israel Deaconess Medical Center.

The Alzheimer Research Forum, the Web's most dynamic scientific community dedicated to understanding Alzheimer's disease and related disorders, has published an easy-to-read article by Gabrielle Stobel on this recent discovery. Check it out: <http://www.alzforum.org/new/detail.asp?id=2090>.

Can the Venture Capital Model Help Cure Alzheimer's?

Co-Founder Henry McCance Discusses Cure Alzheimer's Fund's VC Approach in Harvard Business Review

Cure Alzheimer's Fund co-founder Henry McCance discusses how the use of a venture capital approach to funding research has resulted in groundbreaking success in this recent *Harvard Business Review* interview.

The profile of Henry and Cure Alzheimer's Fund is by venture capitalist and *Harvard Business Review* contributor Anthony (Tony) Tjan. He is CEO, managing partner and founder of Cue Ball, a venture and early growth equity firm investing in the information media and consumer sectors. Read the interview and view the video: <http://blogs.harvardbusiness.org/tjan/2009/06/can-the-vc-model-help-cure-alz.html>.



Henry McCance



Tony Tjan

Financial Update

	This Quarter	This Year	Inception to date
Fundraising	\$545,000	\$735,000	\$12,402,000
Expenses Paid for by the Founders	\$161,000	\$279,000	\$2,143,000
Funded Research	\$250,000	\$1,238,000	\$8,424,000

Research Update

Research funded during the second quarter of 2009.

Project	Researcher	Distribution Amount
Abeta as an Anti-Microbial Agent This project will further explore evidence that the Abeta peptide, acknowledged to be implicated in the cause of AD, may be an anti-microbial agent. The work is a collaboration between Dr. Robert Moir, Dr. Rudy Tanzi, Dr. Charlie Glabe, and infectious disease expert Dr. James Kirby (Harvard Medical School).	Drs. Rudy Tanzi and Rob Moir, Massachusetts General Hospital Dr. Charlie Glabe, University of California at Irvine	\$250,000

Our New Blog!

As we make progress toward a cure, we're dedicated to keeping you informed about the latest advances and treatments. Our new blog, located on our website, features:

- Updates on the latest scientific advances in plain English – no PhD required!
- Posts from the organization's founders and our President and CEO Tim Armour.
- Interviews and video posts from the research teams we support, giving you an inside look at where your donations go.
- News from our researchers about the work bringing us closer to a cure.
- How families and caregivers are joining in the fight to end Alzheimer's.

Check it out: <http://curealzfund.org/Blog>

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.

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Mission

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

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 501(c)(3) public charity with federal tax ID # 52-2396428.

Our Researchers *and* Rock Stars

Nationally recognized Cure Alzheimer's Fund researchers Dr. Rudy Tanzi and Dr. Sam Gandy add another distinction to their scientific careers as they join rock celebrities, including Grammy Award-winning singer Sheryl Crow, Josh Groban, hip-hop artist and *X-Men Origins: Wolverine* singer and co-star will.i.am and Aerosmith's Joe Perry, for a designer menswear photo shoot as "Rock Stars of Science" in the June issue of *GQ* magazine.

The scientists traded in their white lab coats and donned trendy menswear for a photo shoot that the organizers of the project—the Geoffrey Beene Gives Back® Alzheimer's Initiative, a philanthropic wing of the Geoffrey Beene menswear label—hope will help heighten the public's awareness of these researchers and their work while showcasing the need for greater science funding. *The Boston Globe* wrote an editorial in support of the campaign, emphasizing again the hope that this campaign will change a "recognition gap" as described by a 2008 survey by the Chicago Museum of Science and Industry that found only 4 percent of Americans can name a living scientist. The campaign also has a website, www.rockstarsofscience.org.

The scientists traded in their white lab coats and donned trendy menswear for a photo shoot ...



(Top photo, L to R) Rudy Tanzi,
Joe Perry, Francis Collins



(Photo on right, L to R)
Ronald Petersen, will.i.am,
Steven Dekosky, and Sam Gandy