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# Alzheimer's cure behind the boom in brain science



Finding a cure for Alzheimer's Disease has never been more urgent. In Australia, it is the second leading cause of death. David Rowe



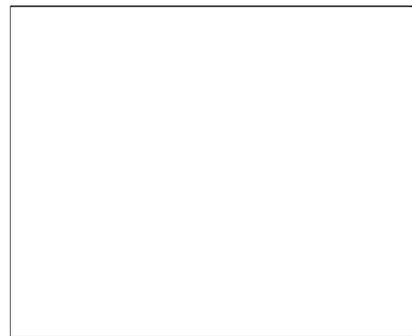
by **Tony Boyd**

When a bunch of prominent, astute Australians backed a \$10million share issue by a Sydney-based biotech company, they joined the global rush to punt on treatments or cures for Alzheimer's Disease.

The investment by these high net worth individuals in Actinogen was a pittance compared to what is being spent by international pharmaceutical companies.

This week Biogen Inc, a US company that focuses on neurology, oncology and immunology, said it would need to invest \$US2.5 billion to commercialise an experimental Alzheimer's treatment. CEO George Scangos told a medical conference in Boston, the money would cover phase three clinical trials and the construction of a new drug factory. The phase three clinical trials will begin later this year.

Biogen is one of many members of big pharma seeking the blockbuster drug which will inevitably be worth multiple billions of dollars. Big pharma in the US spends about \$US5 billion a year on Alzheimer's research and development.



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Finding a cure for Alzheimer's Disease has never been more urgent. In Australia, it is the second leading cause of death. David Rowe

Finding a cure for AD has never been more urgent. In Australia, it is the second leading cause of death. There are about 320,000 sufferers and that is expected to rise to 1 million by 2050. The medical costs of the disease are rising each year, and that does not include the cost of millions of hours of unpaid care provided by family members and friends.

The human tragedy that is AD usually manifests first with evidence of cognitive impairment including memory loss, language difficulties and loss of abstract reasoning. It is usually diagnosed in patients in their 60s. A quarter of 85 year olds and half of 95 year olds develop the disease, according to Actinogen.

Exponential growth in the disease over the past decade has not been accompanied by the development of approved drugs. In fact, not a single new drug for Alzheimer's has been approved in the past 10 years in the United States, according to a report published this week by the Massachusetts Institute of Technology. About 5 million Americans suffer from AD and that is projected to double in coming decades.

The MIT report titled Why Declining Investment in Basic Research Threatens a US Innovation Deficit lamented the fact that US federally funded research into Alzheimer's was woefully inadequate.

It said that many basic questions remain unanswered: very little is known about what causes AD, how and when it begins, how it progresses and whether it can be slowed, arrested, or reversed. "The foundational knowledge is simply missing," the MIT report said.

It championed the need for a mammoth investment in basic research similar to the US government's declared "War on Cancer" in 1971. That was extremely successful but the benefits took a long time to come through the pipeline in the form of drugs.

But in the past two years, the US Federal Drug Administration approved 19 new cancer drugs.

MIT says if the US wants similar progress on AD the country will have to expand research in neurobiology, brain chemistry, and the science of ageing.

Actinogen chairman Martin Rogers rejects the suggestion that not enough is being spent on basic research. He says it's just that all previous efforts have failed. He quotes a 0.4 per cent success rate in dementia research.

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He says most of the R&D for developing new drugs is targeting plaquing in the brain by amyloid beta. Plaquing is caused by preventing the formation of amyloid beta, or removing/dissolving amyloid beta.

The drug being developed by Biogen, BIIB037, reverses build-up of beta amyloid in the brain and, according to the company, also reduced cognitive decline

But the largest current selling drug is from Pfizer, called Aricept, with peak sales of \$US7 billion. Aricept is a cholinesterase inhibitor.

Actinogen's drug, Xanamem, works by inhibiting the stress hormone cortisol in the brain.

Rogers believes the solution for AD patients will be a cocktail of the current and future drugs in development.

MIT says there are many fascinating opportunities that could provide an alternative to drugs, the first of which appeals to Chanticleer.

"One might simply be to slow the ageing process itself, by altering what appears to be an internal "clock" that drives the process," the report said.

"There are strong but imperfectly understood links between nutrition and human development beginning in-utero and continuing throughout life, and it is well established that sharply restricted, low-calorie diets can slow the aging clock.

"If we understood the links better, could drugs or sophisticated nutritional interventions be found that have the same effect?

"In fact, drugs that activate a particular group of genes known as sirtuins are showing promise in extending lifetimes and mitigating age-related diseases in animal models, but they need further investigation and exploration of their impact on Alzheimer's.

"Another opportunity might come from exploring in detail how brain cells communicate with each other—in effect mapping and understanding the brain's neural circuitry and comparing the circuit diagrams of healthy versus AD patients.

"For some other brain diseases—severe depression, Parkinson's disease—electrical stimulation of the brain has proved helpful. If we understood how the neural circuitry was affected by Alzheimer's, might a similar non-invasive electrical stimulation approach be of use?"

The complexity of the challenges posed by the disease and the huge amounts of money needed to find new treatments or a cure would tend to work against an Australian biotech.

However, Australia has a number of advantages. Rogers says America is an expensive place to run a clinical trial but America does produce half of the world wide health care sales and it has the most productive regulator in the FDA.

He says Australia's 45 per cent cash rebate on R&D expenditure for companies with turnover of less than \$20 million makes it attractive to do the phase two Alzheimer's trial that Actinogen Medical is currently undergoing with Xanamem, in both Australia and the US.

The Actinogen clinical trial will involve 200 patients. That will be funding from the recent \$11 million capital raising which was handled by KTM Capital and Forrest Capital.

But a hard-headed biotech analyst at Canaccord Genuity, Matthijs Smith, reckons Actinogen will struggle to commercialise its drug.

He refers to other companies that have promised much and not delivered to back up his argument that money pointed in the direction of AD carries very high risks. One example is Prana Biotechnology, which is now listed in the US.

Smith says the world is littered with failed AD drug trials including several failed attempts by Eli Lilly. It is believed there have been more than a 100 clinical trial AD failures.

However, Smith says the continuing boom in clinical trials provides growth opportunities for companies that can streamline the testing process.

A problem with AD is that once the patient is suffering from the disease it is too late for the drug treatment to assist. The earlier the cognitive impairment can be identified the better.

That leads Smith into recommending investors seriously consider an Australian listed company called Cogstate. It told the market this week that the total value of sales contracts signed in the fiscal year to date is \$US21.9 million, making this the most successful financial year for sales contracts. The sales are up from \$US9 million during the previous financial year.

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