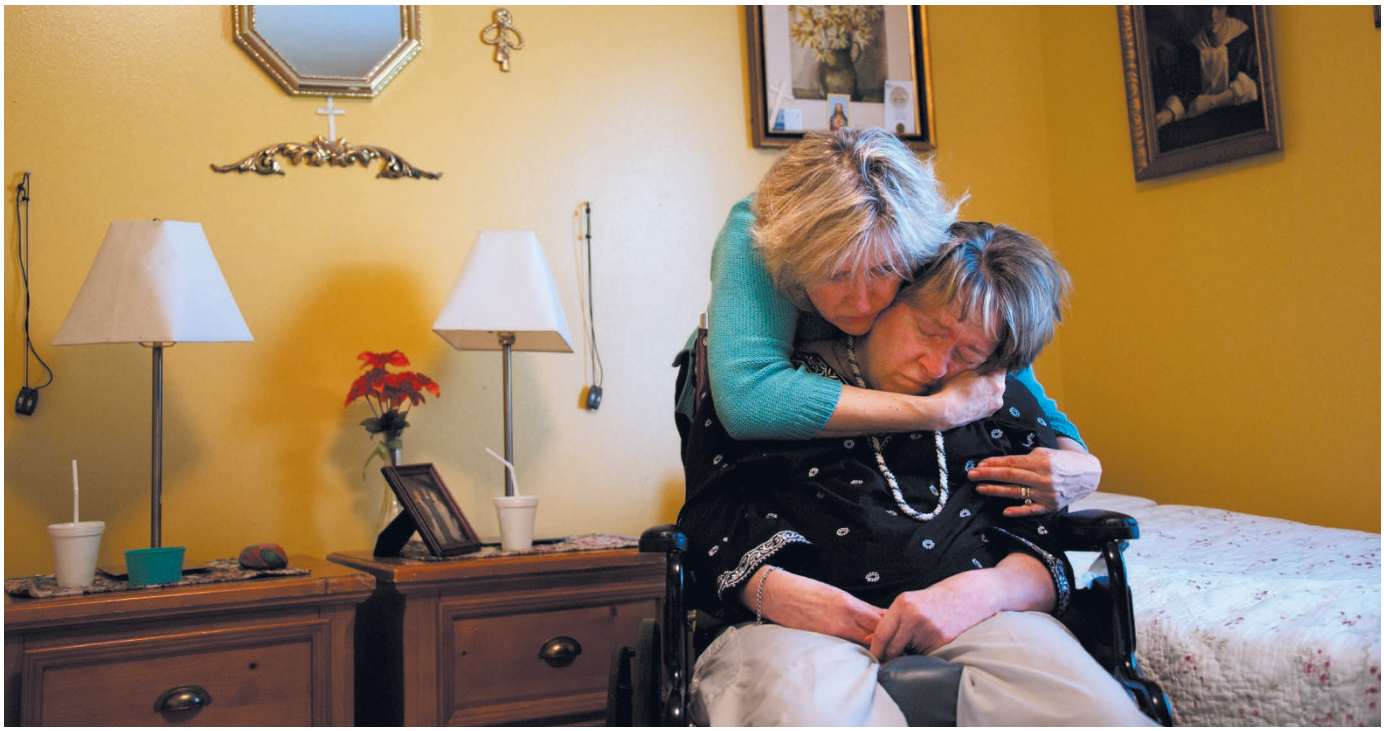
NEWS IN FOCUS



JODI COBB/NATIONAL GEOGRAPHIC CREATIVE

A woman comforts her twin, who has Alzheimer's disease — the underlying cause of the condition is still a matter of debate.

PHARMACEUTICALS

Leading Alzheimer's theory survives drug failure

Solanezumab flopped in a large clinical trial, but the drug or others like it could yet succeed.

BY ALISON ABBOTT & ELIE DOLGIN

A drug that was seen as a major test of the leading theory behind Alzheimer's disease has failed in a large trial of people with mild dementia. Critics of the 'amyloid hypothesis', which posits that the disease is triggered by a build-up of amyloid protein in the brain, say the results are evidence of its weakness. But the jury is still out on whether the theory will eventually yield a treatment.

Proponents of the theory note that the failure could have been due to the particular way in which solanezumab, the drug involved in the trial, works, rather than a flaw in the hypothesis. And other trials are still ongoing to test whether solanezumab — or other drugs that target amyloid — could work in people at risk of the disease who have not shown symptoms, or even in people with Alzheimer's.

"I'm extremely disappointed for patients, but this, for me, doesn't change the way I think about the amyloid hypothesis," says Reisa Sperling, a neurologist at the Brigham and Women's Hospital in Boston, Massachusetts.

She is leading one of several trials to test whether drugs that aim to reduce the build-up of amyloid 'plaques' can prevent Alzheimer's in people at risk of the disease.

Solanezumab is an antibody that mops up amyloid proteins, which can go on to form plaques in the brain, from the blood and cerebrospinal fluid. Eli Lilly, the company that developed the drug, announced on 23 November that it would abandon it as a treatment for people with mild dementia. The outcome adds to a long list of promising Alzheimer's drugs that have flopped in the clinic, many of which, like solanezumab, targeted amyloid. ▶

The Lilly trial tracked more than 2,100 people diagnosed with mild dementia due to Alzheimer's disease for 18 months. Half received monthly infusions of solanezumab, the other half a placebo. Analysis of people with comparable symptoms in earlier studies of solanezumab had seemed encouraging, but the latest trial indicated only a small cognitive benefit, not enough to warrant marketing the drug (see 'Market reaction').

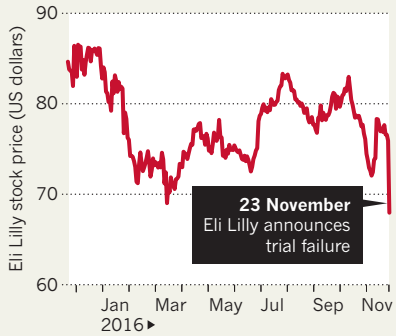
PREVENTION HOPE

Lilly has also been running prevention trials to see whether solanezumab might help people at especially high risk of the disease. The company says it will now discuss with its trial partners whether to continue with those.

Sperling's trial is one of these, and tests solanezumab in people who have elevated amyloid levels in the brain but have not shown any symptoms of dementia. Researchers at Washington University in St Louis, Missouri, are also testing solanezumab, and a similar antibody made by drug company Roche, in people who are currently healthy but are genetically at high risk of developing Alzheimer's. Meanwhile, the Banner Alzheimer's Institute in Phoenix, Arizona, is testing the effects of three therapies that target amyloid production, one of which is an antibody, in people at high genetic risk of Alzheimer's. The Lilly outcome "doesn't disprove the amyloid hypothesis, and it really increases the importance of these longer prevention trials", says Eric Reiman, the Banner institute's executive director and leader of the trials.

MARKET REACTION

When company Eli Lilly announced that an Alzheimer's drug based on the amyloid hypothesis had flopped in a clinical trial, its stock plummeted.



SOURCE: NYSE

Lilly's result may say more about the characteristics of solanezumab than about the accuracy of the underlying amyloid hypothesis, says Christian Haass, head of the Munich branch of the German Centre for Neurodegenerative Diseases. The antibody targets soluble forms of amyloid, he points out, so it "could be trapped in the blood without ever reaching the actual target in the brain in sufficient quantities".

Biogen, a company based in Cambridge, Massachusetts, is testing a different antibody called aducanumab, which targets amyloid plaques in the brain. In early clinical testing, the antibody showed signs of clearing amyloid and alleviating memory loss in people with mild Alzheimer's disease; results from phase III trials are expected in 2020.

"Until the aducanumab data read out, we have not truly put amyloid to the test," says Josh Schimmer, a biotechnology analyst at financial-services firm Piper Jaffray in New York City.

Still, the negative trial findings have emboldened critics of the amyloid theory, who are weary of its failure to yield a treatment. "The amyloid hypothesis is dead," says George Perry, a neuroscientist at the University of Texas at San Antonio. "There's no sign of anybody getting better, even for a short period, and that suggests to me that you have the wrong mechanism," adds Peter Davies, an Alzheimer's researcher at the Feinstein Institute for Medical Research in Manhasset, New York.

No matter what Lilly decides about its other solanezumab trials, the company isn't giving up on Alzheimer's. It is testing an inhibitor of an enzyme involved in the synthesis of amyloid in partnership with AstraZeneca, and is progressing with a handful of candidate therapies aimed at other targets. ■

POLITICS

Bonus funds excite UK scientists

Government announces extra £4.7 billion for research and development up to 2021.

BY ELIZABETH GIBNEY

British scientists are not used to hearing about large increases in national research spending. So when Prime Minister Theresa May promised on 21 November that her government would invest an extra £2 billion (US$2.5 billion) per year in research and development (R&D) by 2020, scientists gave her speech a cautious welcome.

But the funding hike seems to be no financial sleight of hand, according to Treasury documents released on 23 November after Chancellor of the Exchequer Philip Hammond gave an address on the nation's finances. The government expects to spend an extra £4.7 billion on R&D between now and 2020–21, it says, and the final year's £2-billion boost will represent a rise of around 20% in total government R&D spending. Still, it remains unclear how the cash will be allocated, and how much will fund basic, blue-skies research.

"It is a real boost to see UK strength in science being championed by the prime minister and backed with what is the most significant investment in R&D I can remember," said Sarah Main, director of the London-based Campaign for Science and Engineering.

INDUSTRIAL CHALLENGES

Some of the money will go directly to applied R&D through a new Industrial Strategy Challenge Fund, modelled on the US Defense

MORE ONLINE

TOP NEWS

Living cells bind silicon and carbon for the first time go.nature.com/2fgot89

MORE NEWS

- External brain stimulation goes deep go.nature.com/2gepapp
- Peer-review 'heroes' do lion's share of the work go.nature.com/2fhosc6
- Tracking the transition: science agencies under Donald Trump go.nature.com/2gdtbho

NATURE PODCAST

CRISPR's rival stumbles; Pluto's icy heart; and is mitochondrial replacement ready for the clinic? nature.com/nature/podcast

ARNALDUR HALLDORSSON/ BLOOMBERG VIA GETTY