

# Rocky start for Alzheimer's drug research in 2018

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An Alzheimer sufferer models a creation by designer Guio Di Colombia during the Walkway Inclusion fashion show in Colombia last November

The year 2018, barely underway, has already dealt a series of disheartening blows to the quest for an Alzheimer's cure.

Within the first three weeks, pharmaceutical giant Pfizer abandoned the costly and frustrating field of dementia drug development, and two promising treatments stumbled in patient trials.

Alzheimer's support groups are putting on a brave face, but the collective disappointment is palpable as the global cost of caring for some 50 million dementia sufferers is set to reach \$1 trillion (819 billion euros) this year.

"It's very fair to say that progress is slow," David Reynolds, chief scientific officer at Alzheimer's Research UK, a charity, told AFP.

"Companies have put a lot of time, effort and money in over the last 25 years, and there haven't been any new medicines launched in this area for 16 years now."

Experts say it takes 12-15 years, on average, and more than \$2 billion to develop a single drug.

According to the Alzforum website, which gathers data on candidate drugs, fewer than 300 have made it to Phase II drug efficiency trials so far.

Only five have ever been approved to treat symptoms such as memory loss associated with Alzheimer's, first identified more than 100 years ago.

With a clinical trial failure rate of over 99 percent, there is still no licenced drug that slows the condition's progression, or cures it.

Today, about 100 candidate dementia drugs are enrolled in trials, compared to over 1,000 for cancer, according to Reynolds.

One reason is that "pharmaceutical companies ultimately are companies. They are beholden to their investors," he said.

"A return on investment is really: How much time and money do you put into getting a new medicine versus how much money can you make once you've actually got it? In this area, success has been very difficult to come by."

## **Mysterious brain**

The stakes are high.

According to the World Health Organization (WHO), some 10 million people per year are diagnosed with dementia, with Alzheimer's disease accounting for about two-thirds of cases.

By 2030, the number of sufferers is projected to reach 82 million globally, and by 2050 some 152 million.

The medical, patient-care, and economic costs are enormous.

A heavy burden falls on family members, the majority of care providers worldwide. Many have to give up their jobs.

Alzheimer's affects mainly older people—about one in four over-85s is a sufferer. And numbers have soared as lifespans have lengthened thanks to medical advances in other fields.

With cardiovascular disease and cancer the biggest killers in the 1960s and '70s, that is where most of the research money went.

"In dementia, that investment wasn't there. So the amount of knowledge... about the disease is at a much, much earlier stage, and

arguably the brain is a much more complicated organ" than the heart, said Reynolds.

To this day, scientists don't know exactly what causes Alzheimer's, leaving drug developers stumped.

On January 6, Pfizer announced an end to its "discovery and early development efforts" for Alzheimer's and Parkinson's dementia drugs.

Two days later, Danish company Lundbeck reported its idalopirdine compound did not "decrease cognitive loss" in patients, and on January 12, biotech firm Axovant announced the end of the road for its offering, intepirdine.

## **Slow, but not backwards**

Experts say every failure of a drug reveals something new about Alzheimer's disease, which is thought to be associated with a buildup of protein "plaques", and "tangles" in the brain.

One important recent realisation was that an effective treatment may have to begin long before symptoms appear as protein build-up likely starts decades before disease sets in.

This, in itself, presents a research challenge.

"How do you find these patients?" when they are in middle age and symptom-free, explained French neurology professor Bruno Dubois. "How long do you treat them?"

Drugs in development today are targeting several tracks.

Some use antibodies to mop up proteins in circulation, or enzymes to

inhibit their production.

Another experimental approach is vaccination: training the body to produce its own antibodies to attack disease-causing proteins.

"We are not moving backwards," insisted Reynolds.

Yet, he was "by no means certain" that a goal set by the G8 in 2013 to develop a cure or treatment for dementia by 2025 can be met.

"Even knowing the obstacles, we have never been as optimistic as we are today," added James Hendrix, a director at the US-based Alzheimer's Association, one of several non-profit research funders.

"We will not slow down in our fight against this terrible disease," he vowed.

"We are steadfastly committed to both advocating for further increased federal funding for Alzheimer's and dementia research, and increasing our own level of research funding to get us to where we ultimately need to be—a world without Alzheimer's disease."

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