

Unleashing innovation: a new era for dementia

Dementia, the looming health crisis of our time, has long lacked effective treatments. But now, recent drug breakthroughs and the pioneering Dementia Discovery Fund offer hope for a brighter future.

By Laurence Barker and Jonathan Behr

An urgent need

Dementia is the definitive health crisis of the 21st century. Over 55 million suffer from it worldwide¹. In the UK it claims more lives than either heart disease or the most deadly cancer², with other nations rapidly catching up. Its economic cost is projected to skyrocket to nearly \$ 3 trillion by 2030³, and beyond. Solving this crisis would transform society and likely yield remarkable investor returns.

Beyond the staggering numbers lies a painful reality. Each data point represents an individual losing their memories, sense of self, bodily functions, and ultimately, their lives.

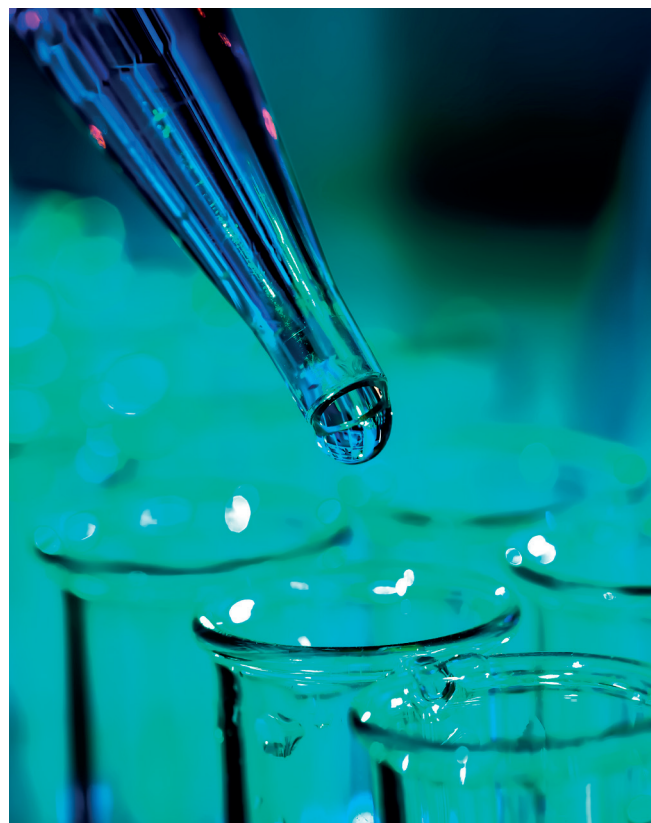
And – cruellest of all – dementia has no cure. Until very recently, there was no treatment available to even slow down, let alone halt,

cognitive decline. That may finally be set to change, however.

Breaking the deadlock

The new drugs aducanumab, lecanemab and donanemab bring hope in the battle against Alzheimer's disease (AD), the most common form of dementia. Phase-3 trial results demonstrate their potential to slow cognitive deterioration in early-stage AD.

Amidst accelerating innovation, the development of these drugs has benefited from an ongoing shift towards smaller, more targeted clinical trials. The FDA's recent accelerated approvals of treatments for neurodegenerative conditions – two for AD⁴ and two for amyotrophic lateral sclerosis (ALS) – reflects this change, signalling a dramatic de-risking of dementia R&D.



This benefits drug developers, investors, and crucially dementia patients themselves.

While these new drugs are cause for celebration, their clinical benefits are modest. None are cures for dementia.

This shouldn't come as a big surprise. The brain is exquisitely complex. There are myriad ways in which its systems can start to misfire or break down, leading to a wide variety of dementias and other neurodegenerative conditions – including AD, Parkinson's disease, Lewy body dementia, frontotemporal dementia, ALS, and Huntington's disease. The aforementioned AD drugs were developed against a decades-old hypothesis, highlighting the pressing need for investment in new therapies that leverage our current

understanding of brain disease.

The Dementia Discovery Fund (DDF)

Established in 2015, the DDF is the world's largest family of dementia-focused venture capital funds. With our first circa \$ 350 million impact fund, our mission is clear: to invest in and build the early-stage biotech companies most likely to develop transformative treatments for neurodegenerative diseases. We prioritize both patient impact and financial returns, collaborating with diverse limited partners, including eight major pharmaceutical companies, industry leaders, government entities, advocacy organizations, philanthropists, and dementia charities. This collective expertise empowers us to effectively confront the complexities of dementia research and development.

The DDF takes a ‘deep’ and ‘diverse’ approach to dementia. We delve into the cutting-edge science, collaborating with foremost researchers and drug developers, in both industry and academia, many of whom sit on our scientific advisory board or are engaged as venture partners. And our portfolio of 18 active companies confronts all the most prevalent forms of dementia and neurodegenerative conditions, employing diverse approaches targeting multiple disease mechanisms.

We reject the idea of a trade-off between social impact and financial returns. Our ‘dual-bottom line’ commitment is accomplished by adding rigorous impact criteria to the usual financial investment criteria, which overall creates a high hurdle for investment. In this vast, untapped market, any effective treatment should generate substantial returns. Crucially, we’re convinced our companies are poised for success.

Lessons from cancer

Our optimism partially stems from the huge strides made in cancer care. We believe this rests on two key lessons – both at the heart of the DDF strategy – which must now be applied to dementia.

Lesson 1: Precision Medicine

Advances in DNA sequencing, scanners, molecular biomarkers, AI and big data have enabled precise diagnosis of cancers and treatment regimes tailored to specific patient groups.

Dementia drug development must follow this approach. In the past,

trial patients were selected solely on the basis of clinical symptoms, ignoring the wide range of underlying disease causes. This led to expensive clinical trials with high failure rates.

Therini Bio, a DDF portfolio company, takes a far more precise approach. Its lead candidate drug targets fibrin, a blood protein that causes inflammation in the brain when it leaks from blood vessels. By measuring fibrin levels in brain fluid, they focus their clinical trials on the patients most likely to benefit from their novel treatment.

Lesson 2: No Cure in a Single Drug

Recent advancements in cancer treatments have shown that potent single therapies, including immunotherapies and targeted kinase inhibitors, can be transformative for some patients but not for the majority. Much of the broader progress in cancer care has come from combining multiple individual therapies, in sequence or in parallel.

A similarly multi-faceted approach is crucial for dementia. Lecanumab, aducanumab, and donanemab, for example, target amyloid beta, a protein that can form toxic plaques in the brains of AD sufferers. However, clearing amyloid plaques alone is insufficient. We think it will be necessary to use other treatments in combination, including those being developed by DDF portfolio companies.

DDF portfolio company QurAlis applies a similar logic to ALS, the most common form of motor

neuron disease, and to frontotemporal dementia. Its multiple candidate drugs, now in clinical trials, were developed using cutting-edge molecular methods to rectify different individual cellular deficits triggered in ALS patients. These drugs should have a powerful impact on their own and will potentially work synergistically, when delivered in combination. At DDF, we seek complementary approaches and potential synergies across our portfolio.

A time for action

Every three seconds, someone, somewhere is diagnosed with dementia. The chances are you already have a close colleague, friend or loved one who has suffered from these cruel diseases. For too long dementia R&D has been underfunded. This is finally changing.

The latest Alzheimer’s drugs have shown that the dam can be breached. Now it’s time to open the floodgates and release a new flow of treatments. Investing in innovative research and drug development is a tangible way to both make a difference and a return.

Together, we can transform the landscape of dementia care and bring hope to millions of lives. ■



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SUMMARY

Dementia lacks a cure. It affects millions, with soaring economic costs.

New breakthrough dementia drugs provide crucial grounds for hope.

The Dementia Discovery Fund pioneers impact investment in transformative dementia treatments.

Precision medicine, combination therapies and new regulatory flexibility are accelerating and de-risking dementia R&D

The next decade promises several new treatments, bringing significant benefits to patients.

The time to invest in dementia R&D is now.

- 1 For dementia prevalence statistics, see <https://dementiastatistics.org/statistics/global-prevalence/>
- 2 UK Office for National Statistics, see <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/deathregistrationsummarystatisticsenglandandwales/2022>
- 3 World Health Organisation, see <https://www.who.int/news/item/02-09-2021-world-failing-to-address-dementia-challenge>
- 4 In 2021-2 FDA approved lecanumab and aducanumab. A similar drug called donanemab is currently undergoing assessment for approval.