think research.

ALZHEIMER’S RESEARCH UK FOR A CURE.
Welcome to think research.

WE STAND FOR A CURE.
Dementia robs us of everything that matters – our memories, our connections and the people we love most. It has no right to take any of this from us but we have every right to stop it. That’s exactly why our charity was created. And we will end the heartbreak of dementia, by finding a cure.

Inside this issue of think research we set out a plan to find this cure, with news on the treatments we’re developing, as well as new diagnostic tests and ways of preventing dementia from happening at all.

It is groundbreaking progress, and a new era for dementia research. But it’s only possible because you’re standing with us. Thank you, from everyone at Alzheimer’s Research UK, and I hope you enjoy the issue.

Hilary Evans, Chief Executive, Alzheimer’s Research UK.

Hilary has been appointed as co-chair of the government’s new Dementia Mission and Alzheimer’s Research UK will now play a crucial role convening industry, the NHS and families living with dementia to transform the lives of everyone affected by this condition. Look out for updates on this important work in future issues.

You can read more about the stories in this issue and our work in 2023 at alzres.uk/think or by scanning the code here.
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This fully recyclable newsletter uses vegetable-based inks and FSC/PEFC certified materials. Its production has also been powered by renewable solar energy.
A BOLD NEW FUTURE FOR OUR SCIENTISTS, SUPPORTERS AND YOU.

By Tim Parry, Director of Communications.

It’s an amazing moment. For years, many thought the diseases behind dementia were unstoppable. But with groundbreaking drugs like lecanemab on the horizon scientific research has proved otherwise. And as a bright new future opens ahead of us, it’s time to believe in a cure for dementia.

Alzheimer’s Research UK is now setting a course to find this cure. It will need our scientists to maintain their pace and dedication. It will require many more breakthrough drugs, for every form of dementia. And it will demand brand new ways of diagnosing and preventing this heartbreaking condition.

But with your help we can do all of this. It’s the beginning of the end for dementia. And together, we can stop the heartbreak it causes forever.
Our ambitious work is already underway. We’re pushing even further into the clinical research space, so that every study you support will create new ways to diagnose, prevent and treat dementia. And through programmes like our Drug Discovery Alliance and EDoN we’re leading a revolution that will stop dementia completely.

It’s a really exciting new era. And we’re entering it with a new purposeful look for our charity (see our new logo below) that reflects our renewed urgency and ambition. We’ll be ramping up our campaigning and visibility – so everyone in the UK knows about our work and its potential. And with fresh government commitment to research and growing public awareness of dementia risk (led by our pioneering Think Brain Health initiative), science is gaining on a cure for dementia from every possible angle.

We look forward to sharing more about our exciting mission in the coming months. And you can find more about our route to a dementia cure on page 8 of this issue.
Like lecanemab, donanemab is an antibody drug designed to target amyloid, a protein that builds up in the brains of people in the early stages of Alzheimer’s disease.

Created by the US pharmaceutical firm Eli Lilly & Company, donanemab has been in development for almost a decade. In 2021, the phase II trial results showed that the drug slowed a decline in memory and thinking among a small group of study volunteers. It also reduced levels of amyloid plaques in the brain.

Such encouraging findings have paved the way for a phase III trial of donanemab, scaling up the study so it could be trialled on many more people. The results of this are (at the time of publication) imminent. And if the news is good, it could be that another new drug for dementia has been found.

“Donanemab’s successes to this point give us real hope for the future, and provide further strong evidence that dementia research is on the right path.

“Of course, proof is everything. But it could be that yet another effective, disease-modifying drug is in the pipeline. That’s a wonderful prospect. And we believe it’s only a matter of time before we have a viable treatment option for people in the UK.”

Dr Susan Kohlhaas, Executive Director of Research and Partnerships.
LEARN ABOUT THE NEXT GENERATION OF TREATMENTS WITH LAB NOTES.

At our Drug Discovery Institute in Oxford, Prof Paul Brennan is developing a new compound that will become the basis of a new drug, designed to repair damaged microglia cells in the brain.

These cells keep our brains healthy by clearing away used proteins such as amyloid. But when they stop working, natural waste builds up and can lead to Alzheimer’s disease.

Excitingly, your support has already helped Prof Brennan’s team to design over 300,000 new chemical compounds – and one will form the basis of a new dementia treatment.

In this month’s Lab Notes, Prof Brennan joins Prof Fiona Ducotterd from our Drug Discovery Institute at University College London and our Executive Director of Research and Partnerships Dr Susan Kohlhaas.

Together they look at all of the treatment development studies that are taking place across all our Drug Discovery Institutes. They also discuss the amazing progress that’s taking place in our laboratories, because of the support you give.

Lab Notes are specially designed and recorded talks and events which give you an insider’s look into our life-changing research. You can watch the latest episode from our Drug Discovery Institutes and catch up with the entire series at alzres.uk/think-labnotes.
TREATMENTS.

Across the globe over 140 potential Alzheimer’s drugs are now being clinically tested, and many are a direct result of the science you’ve helped us to fund. It proves how important you are, and how close research is getting to a full range of treatments that will transform the lives of the people we love.

Drugs for Alzheimer’s and every form of dementia will be the greatest weapon we have. So we’re stepping even deeper into pharmaceutical development from 2023 onwards – by developing new innovations in drug discovery, and doing even more to develop powerful, effective ways of treating the condition.

Central to this will be our Drug Discovery Alliance, a huge multi-site laboratory which brings together teams from the Universities of Cambridge and Oxford with University College London. It’s where we’ll translate everything we’re learning into the design of new treatments. And it’s a testament to the advances we’ve been able to make, because of supporters like you.
Among the genes that put people at a higher risk of Alzheimer’s disease, **SORL1** is one of the most important discovered in our lifetimes. When working normally it influences a host of important brain functions, but when things go wrong it can cause our brain cells to change shape and behave abnormally. This deviation can be linked to Alzheimer’s disease and the resulting dementia.

Our plan is to prevent and repair these problems by studying the DNA of abnormally shaped cells that carry the SORL1 gene. Our research will uncover a huge amount of new information about how dementia can start, and tell us much more about what can be done to both treat and prevent the condition.

And in another step forward in our search for new treatments, we’ll test **experimental chemical compounds** which we’ve designed to correct the differences in abnormal SORL1-carrying cells. Because if we can do so, we’ll get even closer to the discovery of new and disease-modifying drugs for dementia. And that means we’ll be even closer to a cure.

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**DIAGNOSIS.**

Any future treatment will be most effective if given in the earliest stages of someone’s dementia. So we’ll improve dementia diagnosis in the UK – and spot the diseases that cause dementia long before symptoms start.

At the forefront of this is our **Early Detection of Neurodegenerative Diseases (EDoN)** initiative, the largest of its kind. EDoN will collect, share and analyse clinical and digital health data from a ‘toolkit’ of wearable technologies and smartphone apps, in order to detect signs of diseases like Alzheimer’s years earlier than is currently possible.
New diagnostic technologies could provide a cost-effective, non-intrusive way for doctors to identify the initial stages of a dementia-causing disease. And they will help the NHS to provide the right support, treatments and prevention strategies for people who need them. They could also provide a chance for more volunteers to get involved with vital clinical trials.

Studying the brain’s protective wall to develop new diagnostic tools.
By Dr Ben Dickie, University of Manchester.

The blood vessel wall protects our brains and removes natural waste products. But when damaged, it can harm the brain and lead to the memory loss we see in Alzheimer’s disease.

This wall is made of pericytes and other cell types. Pericytes are important because they become lost in the very early stages of Alzheimer’s and we also know that people with fewer pericytes lose their memory at a faster rate. So if we can detect and treat their loss at the earliest possible opportunity, we could find ways to slow – or even stop – some of the damage that Alzheimer’s causes.

Several research groups including ours have been developing MRI techniques that detect damage to the vessel wall. My team and I will now help to determine which scan works best, and whether it’s precise enough to detect early pericyte loss. If successful, our work could provide doctors with a new diagnostic tool, accelerate the development of damage-repairing drugs and protect more people from dementia.
Sadly, many cases of dementia can’t yet be prevented. This is because our age and genetics are central to shaping our risk. But research suggests many of us can help reduce our risk of developing dementia by looking after our brains in the same way we would the health of our hearts.

So Alzheimer’s Research UK is working to improve the public’s understanding of dementia and risk, by giving people clear, practical information about the changes they can make to help protect their brains.

Alongside the educational and community programmes we’re funding, we’ll continue to make waves with Think Brain Health – the only public campaign dedicated to protecting the nation’s brain health.

In the last issue you’ll have read about our Think Brain Health Check-in, a free, digital tool that helps people to explore their own brain-healthy habits. And it provides personalised guidance that could help you to look after your own incredible brain.

More than 200,000 people have now checked in with their brain health. Join them at alzres.uk/think-check-in.
In January we convened our new Policy Insight & Experience Panel. This brings together a diverse mix of volunteers from across the country, all of whom have been personally affected by dementia.

Their experiences, ideas and opinions are now guiding the way we influence government policy, ensuring that the issues which matter most to people affected by dementia are being tackled.

Working alongside our existing network of UK campaigners, the panel also strengthens and amplifies our charity’s voice, ensuring that dementia remains high on the political agenda. And with the government’s Dementia Mission, the announcement of a Major Conditions Strategy (which covers dementia, cancer and more) and a general election on the horizon, there is plenty for our volunteers to be involved with.
THE GIFT OF TIME.

We have a wide range of volunteering opportunities available at Alzheimer’s Research UK, from supporting our government campaigns to cheering on runners at national marathons and events. And whether you can spare loads of time for research or only a few hours, there are many brilliant ways to help.

[link]

‘Everyone is working towards the same goals, and the shared vision is incredibly empowering.’

Kathy Connor,
a policy volunteer since 2019.
Twice a year, our Grant Review Board brings together leading dementia experts to review research applications, submitted to Alzheimer’s Research UK from scientists across the UK. We then allocate funding to the proposals which have the most potential.

And our criteria is very clear. Every approved study must ultimately benefit people affected by dementia, by leading to improvements in dementia diagnosis, to new ways of preventing the condition or to effective treatments that will transform the lives of the people we love.

Here, we explore just one of the 23 new studies you’ve helped us to fund. To read about the others, head to alzres.uk/think.
The loss of nerve cells and other types of brain cells is a key feature of diseases that cause dementia. Importantly, the loss happens long before recognisable symptoms of dementia appear. And it could be why many prospective drugs fail in clinical trials, because they aren’t being administered early enough in the disease process.

But research into DNA has revealed something which could be crucial to any drug’s future success.

Sitting above the DNA sequence in our cells’ genome is a secondary layer of information known as the epigenome. This acts as a sequence of switches, dictating which genes in our bodies get turned on and off. These varying switches play a critical role in determining how cells behave throughout our lives and can be used as molecular barcodes to identify specific cell types found in the brain.

My team and I are using these molecular barcodes to develop a blood-based test to monitor the identity of the remnants of dead nerve cells found in the blood. If this biomarker blood test proves successful, it could allow us to spot diseases including dementia with Lewy bodies, frontotemporal dementia, or Alzheimer’s disease at a far earlier point in the disease’s progression.

What’s more, the test could be of considerable use in the development of new treatments – helping researchers and pharmacists to target the disease long before any widespread loss of brain cells occurs.
When Jean Richmond passed away in 2015, her husband kindly gifted money left in Jean’s Will to dementia research. And because of this profound generosity we’re making more progress than ever, having invested in a fascinating piece of technology called the **Olympus VS110.**

**SCALING UP OUR STUDIES AND MAKING LIFE-CHANGING PROGRESS.**

Studying brain tissue is essential if we’re to understand the molecular processes behind dementia but it’s a complex and often frustrating process. The brain is one of the most inaccessible organs and preparing thin slices of tissue for microscopic examination is both specialist and time-consuming.

The Olympus slide scanner transforms this work. It scans donated tissue then creates incredibly precise digital images for scientists like me to use. Multiple images can then be shared across the UK (and even the world), allowing researchers to analyse the same section of a particular brain, at the same time. And the Olympus makes our work at least twenty times faster than before.

**A PROFOUND AND POSITIVE IMPACT ON DEMENTIA RESEARCH.**

By studying donated brains, we have researched whether bouts of illness, such as urinary or chest infections, can make Alzheimer’s worse. The Olympus has allowed us to study more than 1,000 sections of donated tissue, finding clues that such infections can indeed be linked to accelerated cognitive decline. This will now lead to new studies, as we learn how best to manage illness in people with the disease.
Jean and her family have transformed our research. A gift in your own Will could do the same.

Your support could be vital in helping to find a cure for dementia. And a gift in your Will, whether large or small, can offer real and tangible hope to future generations. To find out more about the impact you could have, request a free gifts in Wills guide at alzres.uk/think-wills.

The Olympus doesn’t just help with research into Alzheimer’s disease. It’s also providing valuable insight into brain inflammation, in people with dementia with Lewy bodies. And my colleagues can now use the scanner to dig deep into the workings of a potential drug which didn’t quite clear trials, but which could still be refined and vastly improved.

All of this has been made possible by Mr and Mrs Richmond’s generosity. In fact, one in three studies across the Alzheimer’s Research UK network can only be funded because of gifts in Wills. And each takes us closer to the groundbreaking new preventions, diagnoses and treatments that will one day cure dementia.
Our Dementia Research Infoline answers your questions about research, dementia symptoms, and other very important matters. We also share trustworthy information here in think research. In this issue we look at the new drugs lecanemab and donanemab, which have been designed to treat dementia.

Q: What goes wrong in Alzheimer’s disease?

A protein called amyloid plays a role in the healthy immune system. But when it’s not naturally cleared from the body – as all used proteins should be – amyloid can become harmful, misfolding to form amyloid-beta (Aβ1-42). This forms into dense, toxic ‘plaques’ which kill neurons in the brain in a process known as the amyloid cascade hypothesis, which is widely thought to contribute to Alzheimer’s disease. And it could start up to 20 years before dementia symptoms show.

We don’t precisely know how the process starts. But a number of factors could be at fault, including DNA mutations, missing enzymes (which would usually stop amyloid folding into its harmful beta form) or damage to the brain and body.
**Q: What have the new drugs been designed to do?**

The ‘mab’ in **lecanemab** and **donanemab** stands for ‘monoclonal antibody’ – another protein, which binds to amyloid-beta and helps the body to expel it. This is just as the body would remove harmful germs such as bacteria using natural antibodies.

**Q: Are they effective?**

Phase III clinical trials have shown that **lecanemab** removes amyloid and improves people’s cognitive abilities over an 18-month period. But it’s only been shown to work for people with early stage Alzheimer’s disease, and it doesn’t work for everyone. We still don’t know about its long-term effects (or side effects) and are eagerly awaiting results from similar clinical trials for **donanemab**.

Of course, our hope is that both drugs will become available in the UK, if approved by regulators here. But we’re on a long road to a cure for every form of dementia, and many more treatments still need to be developed. We also need to improve diagnosis, identifying biomarkers (such as amyloid beta plaques) far earlier than is currently possible. That way drugs like these can be given when they are at their most effective.
You can volunteer for dementia research studies and play an important role in the search for new treatments.

People with and without dementia can take part in this vital research. When you sign up, you’ll be matched to studies you might be suitable for and can choose which ones you take part in. By doing so, you will be helping scientists to understand more about the diseases that cause dementia - as well as how to diagnose and treat them.

It’s quick and easy to register to Join Dementia Research. Call our friendly team on 0300 111 5 111 (9am-5pm, Mon-Fri), sign up at alzres.uk/think-jdr or scan this QR code.

Correct Answer - Box D corresponds to the flat pack TEA-TIME TEASER.

(See side of page for answer.)