ICR The Institute of Cancer Research

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Dr Ben O'Leary: Delivering a new era of smarter therapies for head and neck cancers

Inside this issue

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Editorial

Our mission to defeat cancer would not be possible without the continuous commitment of both our staff and our supporters, whose inspiring efforts lead to inspiring science.

In recent months, staff members have climbed mountains not only figuratively for the ICR – through their dogged pursuit of scientific answers – but also literally. Dr Rachael Natrajan cycled the Italian hills between Venice and Rome, while Professor Helen McNair trekked to the K2 Himalayan basecamp. Several employees also joined more than 100 walkers in the hilly Lake District for Climb of Life – now in its 18th year supporting us. *See pages 6–7 for our latest fundraising news.*

We also continue to be in awe of the generosity of our supporters. The Doing it for Daniel Foundation donated £21,000 to fund vital research by Professor Chris Jones in paediatric brain tumours – particularly diffuse midline glioma, the terminal brainstem cancer that affected Daniel. We are eternally grateful for their support. *Read more about Daniel on pages 8–9.*

In the labs, our scientists are making progress against many different cancer types. Head and neck cancer, which has seen few curative advances, is the focus for Dr Ben O'Leary, who was recently appointed to lead the Evolution and Translational Genomics Group. *Read about Dr O'Leary on pages 10–11.*

We are also seeing encouraging developments in blood cancer due to the groundbreaking research advances made by our scientists. *See pages 12–14 to learn more.*

As ever, we remain at the forefront of cancer research – thanks to our staff, students, supporters and partners. Together, through passionate fundraising efforts and the unwavering determination of our scientists, who challenge conventions to drive breakthroughs in drug discovery and development, I believe we can defeat cancer.

Professor Kristian Helin
Chief Executive, The Institute of Cancer Research

“I hate running, but I hate cancer too”

Alex Naim with his medal for completing the Royal Parks Half Marathon

Alex Naim, 27, a solution engineer living in London, completed the Royal Parks Half Marathon and raised more than £11,000 for our vital research – even though running is one of his least favourite pastimes. Here, he shares his experience.

“In summer 2023, I was diagnosed with testicular cancer. Thankfully it was caught early, and I feel lucky – I know some people go through things that are so much worse.

“It started when I found a lump under my skin, and just two and a half weeks later, I had my first surgery.

“The initial results came back unclear, so I had to wait two weeks for further tests that confirmed it was cancer, and then another two weeks to go back into surgery again.

“I was told it was 'non-seminoma', which is the more aggressive type of testicular cancer, so doctors said I had to have chemo too because they also found it in my lymph vessels.

“My treatment only lasted a month, thankfully, but it was a very hard time. I knew it was going to be fine overall because it was caught early, but it was still a really difficult thing to go through.

“I’m someone who hates running – I really hate it, and that didn’t change while I was training for the Royal Parks Half.

“But I also hate cancer, so what better way to raise money than doing something difficult?

“I wanted to celebrate my recovery and first year in remission, and to raise money to help eradicate this nasty disease.

“I’ve been really surprised by the response I’ve had. With my employer contributing through match funding, I’ve raised more than £11,000. Family and friends have been so supportive, as has the wider community on Instagram. There are a lot of people who care, and it’s amazing to see.”

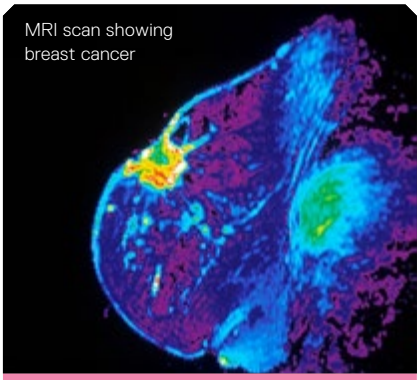
“I wanted to celebrate my recovery and first year in remission, and to raise money to help eradicate this nasty disease.”

Improved breast cancer diagnostic tools on the horizon

Our scientists are developing tools that will help to identify women at high risk of breast cancer, even if they do not have a family history of the disease.

The Breast Cancer Now Generations Study is one of the world's largest and longest-running studies into the causes of breast cancer. Over the past 20 years, it has contributed to the discovery of hundreds of genetic changes linked to breast cancer and shed light on the major associated lifestyle and hormonal factors.

Study co-leader Professor Montserrat Garcia-Closas said: "We're going to develop better breast cancer risk assessments by building on the discoveries made over the last two decades into the genetic, social and environmental factors that cause breast cancer. This will help women receive more personalised and effective care."



MRI scan showing breast cancer

"We're going to develop better breast cancer risk assessments by building on the discoveries made over the last two decades.

New drug target discovered for aggressive form of prostate cancer

Our scientists have discovered that a protein linked to prostate cancer is associated with more aggressive forms of the disease.

In new research led by Professor Johann de Bono and Dr Adam Sharp, the team has shown that the BCL2 protein is present in high levels in a type of advanced prostate cancer that has stopped responding to hormone therapy.

It is now hoped that BCL2 could be a new target for treatment and be used to help predict who will become resistant to hormone therapy.

A prostate cancer clinical trial testing the BCL2 inhibitor venetoclax – a drug approved for some types of leukaemia – along with the hormone therapy enzalutamide has already begun.

World's first trial to test multiple treatments for brain cancer

We are excited to be leading a pioneering research study aiming to speed up the development of new treatments for glioblastoma, an aggressive form of brain cancer.

The 5G (next-Generation aGile Genomically Guided Glioma platform) study is the world's first adaptive clinical trial for people with brain tumours. It will allow brain cancer patients to access drugs that are precisely targeted to their disease and swap to different treatments if needed.

Every patient on the trial will have their genome sequenced, enabling researchers to target their disease with greater precision than ever before. The drug or drug combination each patient receives will be based on the genetic makeup of their tumour.

Powerful new therapy doubles progression-free survival in advanced breast cancer

Professor Nicholas Turner

15 months The average time the patient gains without disease progression

A trial led by Professor Nicholas Turner has shown that a powerful three-drug therapy for aggressive advanced breast cancer could halt the progression of the disease by an average of 15 months – more than twice as long as a combination therapy currently available on the NHS.

The new therapy consists of two targeted drugs called inavolisib and palbociclib, along with the hormone therapy fulvestrant. It is suitable for women with PIK3CA-mutated HR+, HER2-breast cancer.

Following this landmark study, the new therapy combination was granted FDA approval in the United States. It is hoped that it will soon be approved in the UK and become the standard of care in women with this form of breast cancer.

Big step forward for Climb of Life

Blustery winter weather didn't stop 110 intrepid walkers from heading to the Lake District to take part in Climb of Life in November – raising more than £100,000 for our life-changing cancer research.

Graeme Chapman MBE, who set up Climb of Life 37 years ago, has been raising money to support our research since 2007. The annual fundraising event has now raised an incredible £1.5m for the ICR.

He said: "My father died of pancreatic cancer, and there were friends that were close to me that had cancer. The ICR impressed me because of the scientific work that they were doing. It's been a great partnership ever since."

Some of the Climb of Life walkers

Terry Fox runs raise thousands for research

Hundreds of people laced up their trainers for the UK Terry Fox runs last autumn. The fundraising events, which exclusively support our research, were set up in memory of Canadian hero Terry Fox.

Terry famously ran a 'Marathon of Hope' across Canada using a prosthetic leg, having lost his right leg to osteogenic sarcoma. He completed one marathon a day, raising money to help other cancer patients.

ICR staff at the London Terry Fox run

More than 1,000 participants across events in London, Hampshire, Glasgow, Edinburgh and Wrexham were encouraged to run, jog, cycle, walk or roll up to 10km. They raised more than £120,000 for our research, making 2024 the Terry Fox Run's best year yet in the UK.

Taking fundraising to new heights

Professor Helen McNair embarked on the challenge of a lifetime when she trekked to the basecamp of K2 in the Himalayas – all to raise money for our research and for the Royal Marsden Cancer Charity.

Helen, Professor in Translational Therapeutic Radiography at The Royal Marsden and the ICR, walked for up to eight hours a day over two weeks to complete the epic endeavour, reaching heights of 5,000m and raising £4,000 in the process.

Helen said: "The trip was organised by my friend, Francesca Godwin-Austen, who had planned to complete the challenge with her late husband, Jonathan.

Professor Helen McNair in the Himalayas

"He was a descendant of the 19th-century surveyor after whom the Godwin-Austen glacier at K2 is named. Jonathan sadly died from bowel cancer before they could go.

"We had amazing views because of clear skies. We were very fortunate. I was surprised I wasn't stiff in the mornings, and although tired when we got to camp, always recovered."

Helping us advance our ovarian and breast cancer research

A huge thanks to everyone who has supported our Christmas fundraising appeal. The campaign, which is helping women with cancer live longer, better lives, has highlighted the work our scientists are doing to develop smarter, kinder treatments for ovarian and breast cancer.

Each year in the UK, 7,500 women are diagnosed with ovarian cancer, and a further 56,400 are told they have breast cancer. While survival rates have improved, thousands are still dying every year.

We have already raised more than £120,000 to fund our life-changing research.

If you would like to make a donation, please visit:
ICR.ac.uk/GiftOfResearch

With your support we have raised more than

£120,000

“Every child with brain cancer should have a chance at life”

Daniel Caplan was 16 when he was diagnosed with an aggressive brain tumour. He passed away seven months later. Last May, to mark what would have been his 21st birthday, his parents Alison and Brian generously donated £21,000 to fund our research. Here, Alison explains why she hopes her son’s legacy will improve treatments for young people with cancer.

“Daniel was vibrant, popular and full of life. He loved music, football and having fun with friends, and he planned to study International Business at university.

“But in May 2020, just before his 17th birthday, he began to complain of headaches. We also noticed he was dragging his right foot.

> **“Daniel was vibrant, popular and full of life. He loved music, football and having fun with friends.**

He was immediately sent to hospital

“We knew this wasn’t right and took him to the GP. He was immediately sent to hospital where he had a CT scan, and that night, we were told a mass had been found on his brainstem.

“A further MRI scan revealed a 5cm tumour and doctors suggested Daniel undergo a biopsy. The risks were explained to us, but we all agreed it was necessary.

“Afterwards, Daniel’s mobility declined and his motor skills were badly affected. But he was able to come home while we waited for the results.

It was the worst possible diagnosis

“Returning to hospital the following week, we were told Daniel had an aggressive brain tumour called diffuse midline glioma, or DMG, a terminal brainstem tumour mostly affecting children. It’s also known as DIPG.

“We had spent the week researching brain tumours so were aware we were being given the worst possible diagnosis. But when we asked about treatment options, it was hard to believe there weren’t any.

“Daniel started palliative radiotherapy, with the intention of slowing the tumour’s growth. But we felt a sense of hopelessness from the moment he was diagnosed. We knew he was dying.

During his illness he was the bravest boy

“We secured experimental drugs from overseas and Daniel was accepted on a clinical trial, but his cancer progressed so quickly he couldn’t take part.

“During his illness he was the bravest boy. He was so positive and didn’t like to think too deeply about what was happening. In his last three months, he could not get up, so we had a hospital bed installed in our bedroom.

“Daniel wanted us to care for him at home. A nurse came to

administer morphine, steroids and anti-seizure medication, but we looked after him.

"He died on 30 November 2020, seven months after his diagnosis.

He wanted to raise money for research

"Daniel always hoped he would get better but understood the odds were against it. He wanted to raise money for brain tumour research, particularly for his type of tumour, to give others the chance of treatment he didn't have.

"So, to keep his memory alive and honour his wishes, we set up the Doing it for Daniel Foundation. Initially, our aim was to provide gifts for children who had been diagnosed with cancer. Daniel loved the beach, so we also bought a beachside property so children with cancer and their families could have some respite by the sea.

We want to see new treatment options

"However, we also wanted to focus on research. Our hope is that children diagnosed with Daniel's type of cancer could have a treatment option that would give them a chance and, if it could not save them, a decent quality of life for the time they have left. We want to see a time when a DIPG diagnosis is not a death sentence.

"We had followed Professor Chris Jones' work in this field for some time and wanted to make a contribution to his research. We are proud to have achieved this and hope it will make a difference, so no other family will have to go through what we have experienced."

Alison Caplan with her son, Daniel

Unlocking resistance: a new vision for head and neck cancers

In July 2024, we were thrilled to appoint Dr Ben O'Leary to lead the newly formed Evolution and Translational Genomics Group. Situated in our Centre for Evolution and Cancer, the recently established team is primarily investigating how head and neck cancers – which include those affecting the throat, mouth and voice box – evolve and develop resistance to treatment. Dr O'Leary aims to unlock this mystery to shape a new era of smarter, more effective therapies.

Cancers of unmet need

Due to their often aggressive nature and the lack of understanding about how they develop resistance to therapy, head and neck cancers are among the most challenging cancers to treat. Combined, they represent the fourth most common cancer in UK men, but there has been little progress in curative treatment over the past 30 years. Once the cancer recurs, which happens in 40 per cent of high-risk cases, survival rates drop to an average of just 12 months, showing the urgent need for continued innovation in this area.

How these cancers evolve before, during and after treatment is the focus of Dr O'Leary's work. His team is currently exploring why some tumours respond well to radiotherapy while others start with or develop resistance. This knowledge will prove critical for improving existing treatments – such as surgery, radiotherapy and immunotherapy – and developing newer strategies, such as combination treatments.

An era of smarter treatments

The Evolution and Translational Genomics Group is also developing new technologies to predict treatment outcomes. For instance, analysing tumour DNA circulating in the blood – derived from dying cancerous cells – can provide insight into how cancer evolves, its behaviour

Dr Ben O'Leary in his lab

under radiotherapy and why some patients' tumours do not respond to certain treatments.

Dr O'Leary said: "Imagine being able to confidently decide the suitable course of action for a patient. If we can predict what radiotherapy will or will not cure, we can spare patients from major surgery, possibly preserving their speech. Equally, we can avoid using radiotherapy where it won't work."

> "If we can predict what radiotherapy will or will not cure, we can spare patients from major surgery, possibly preserving their speech.

The team's approach focuses on exploring how combining radiotherapy with immunotherapy could enhance patient outcomes. Uncovering why certain treatments succeed or fail in certain individuals could lead to more targeted and effective combination therapies.

Forward vision

Dr O'Leary emphasised the momentum behind his lab's groundbreaking research:

"The team is coming together well. We share an optimistic vision for smarter oncology treatments, especially for cancers of unmet need. Our work is about tailoring treatments to each patient, avoiding unnecessary interventions and improving outcomes wherever possible. It's incredibly rewarding to know that our science is so closely tied to making a real difference for patients."

From engineering to oncology

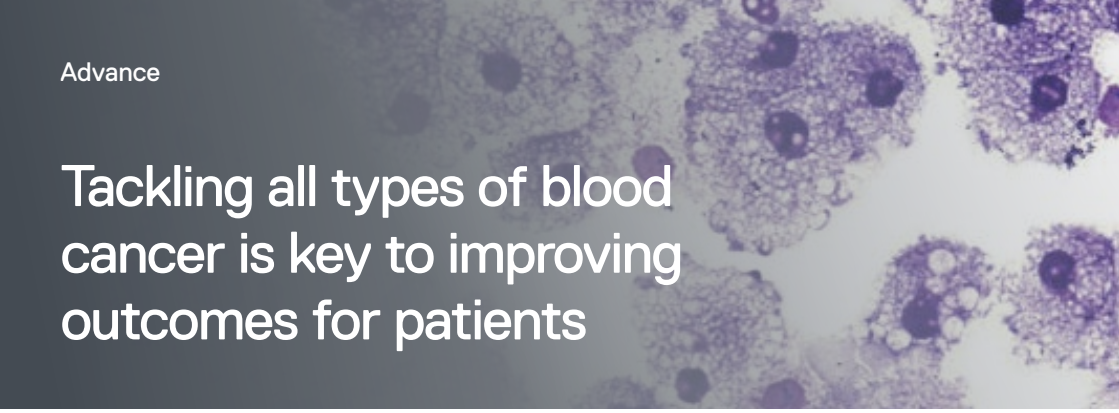
A career at the ICR was not what Dr O'Leary envisioned during his bachelor's degree. After beginning his academic career studying aerospace engineering, a prospective master's degree project investigating fluid transfer flow in the liver sparked intrigue, and a new career trajectory within biological sciences followed.

Leaving engineering behind, Dr O'Leary worked as a care assistant at Great Ormond Street Hospital, which solidified his ambition to pursue medicine.

After completing his medical training at King's College London, he was drawn to oncology because of its unique blend of compassionate care and scientific rigour. Academic training followed at the ICR and The Royal Marsden with a PhD in circulating tumour DNA research, setting the scene for his focus on head and neck cancer evolution and treatment resistance.

Dr O'Leary's dedication and innovative approach will inspire his team to make a transformative impact on the ongoing fight against head and neck cancer.

Tackling all types of blood cancer is key to improving outcomes for patients



Blood cancer is an umbrella term for cancers of the blood, bone marrow and lymphatic system. A new diagnosis occurs every 14 minutes, making it the fifth most common cancer in the UK. It also has the third highest mortality rate.

Despite these statistics, blood cancer receives less attention at a national level than common solid tumour cancers, such as breast, prostate and colorectal.

This is largely because different types of blood cancer are reported on separately. Individually, each causes fewer cases and deaths than blood cancer would overall, masking the disease's real impact.

> A new diagnosis occurs every 14 minutes.

Blood cancer poses some unique challenges

Nonspecific symptoms, including unexplained weight loss, bruising and fever, mean blood cancer often goes undiagnosed until it has progressed. Also, while solid tumours have fixed positions initially, blood cancer circulates the body. Some standard cancer treatments – including surgery – are therefore not suitable.

Undaunted by these hurdles, our scientists are working hard to find better ways to diagnose and treat blood cancer. Their projects span multiple blood cancers, including the three main types: leukaemia, lymphoma and myeloma.

Identifying an untapped vulnerability in leukaemia

A team led by Professor Kamil Kranc, Professor of Haemato-Oncology, has developed a new treatment approach for acute myeloid leukaemia (AML), an aggressive blood cancer lacking treatment options.

In a recent preclinical study, scientists showed that blocking enzymes called PHDs causes protein level changes that stop AML from starting or progressing. They then generated a PHD inhibitor called IOX5, which uses a unique mechanism to selectively block PHDs. The next step is to progress this compound to clinical trials. Encouragingly, existing anaemia drugs that block PHDs have also been shown to be effective, so multiple new leukaemia treatments could be on the horizon.

Focusing on lymphoma at the drug discovery stage

Several of our teams have helped develop a compound with the potential to treat B-cell lymphoma and other cancers. Dr Rob van Montfort's Hit Discovery and Structural Design Group first discovered new small

molecules able to block a protein called BCL6. BCL6 binds to and helps switch off target genes involved in cell cycle regulation, promoting cancer growth.

Professor Swen Hoelder, Head of Chemistry, and his colleagues in our Centre for Cancer Drug Discovery then created a potent compound that binds to BCL6 and tags it for destruction – a process called protein degradation. This compound successfully inhibited lymphoma cell growth. The team now plans to test it in further preclinical studies.

A potentially practice-changing trial in myeloma

Our researchers co-led MUK Nine OPTIMUM, a first-of-its-kind myeloma trial that compared patient outcomes across two clinical trials rather than using a control group. All the patients had ultra-high-risk myelomas, which have certain genetic changes that make them more aggressive.

The first trial, Myeloma XI (MyXI), used the standard of care – a quadruple therapy – while the second, OPTIMUM, tested a combination of five drugs, three of which were not part of the standard treatment.

Professor Martin Kaiser

The study showed that the OPTIMUM participants were, on average, more likely to have a good outcome. At a 30-month follow-up, 77 per cent had stable disease that was unlikely to progress soon, compared with 39.8 per cent of the MyXI participants.

The scientists, led by Professor Martin Kaiser, Group Leader in Myeloma Molecular Therapy, hope the new drug combination can be made available to high-risk patients with myeloma.

A promising future

Although overall blood cancer survival rates increased by 14 per cent between the 1994–2007 and 2008–2021 periods, some types – such as AML – are still very deadly, meaning much work remains to be done.

Fortunately, cancer research is arguably more dynamic than ever before, with discoveries being made at an unprecedented rate and the understanding of cancer increasing daily.

We remain at the forefront of this research, with our scientific breakthroughs helping develop new diagnostic tests and treatments. We are determined to give blood cancer the attention it needs so that we can improve patient outcomes and save thousands more lives.

Regular gifts sustain our life-saving research into the future. To make a monthly donation, visit: ICR.ac.uk/monthly

"We hope research will bring kinder treatments for children"

Polly Osborn's son Jesse was two when he was diagnosed with B-cell acute lymphoblastic leukaemia, a blood and bone marrow cancer, in November 2023. Last July, to celebrate the end of his treatment, his family organised the Great Cousin Run, raising close to £15,000 for our research. Here, Polly explains how important this research is for children like Jesse.

"Jesse was a normal, active toddler when he started suffering with frequent infections. Compared with his identical twin, he didn't seem well.

"I noticed a bruise on his face that didn't go away and tiny spots on his leg. They were small and easy to ignore, but something told me to take them seriously.

"When Jesse was diagnosed with leukaemia, his prognosis was good. But it was still an enormous shock to hear my child had cancer.

"He started chemotherapy, but within weeks developed liver problems, caused by a rare reaction to his drugs. Admitted to the High Dependency Unit, he lost function in his arms and legs and could barely hold up his head.

"After nine days, he started improving. But he had virtually no mobility and had to learn to walk all over again. His drug regimen was changed, and he completed the intense stage of his treatment last summer.

"To mark this milestone and celebrate his remission, we organised the Great Cousin Run, which saw Jesse's cousins run between 1km and 10km. The gruelling treatment had taken its toll, but Jesse was able to join in, running the last 100m with their help. It was emotional to see him cross the finish line, a feat only made possible thanks to years of ICR research and the support of his wonderful medical team.

"Jesse's experience illustrates the importance of developing kinder treatments for cancer that don't just focus on the end result but also on achieving it more safely. Research into more options to treat the most advanced cancers gives us hope. But there's still a long way to go."

Polly Osborn and her son, Jesse

> "We've met other families whose children have not had such a good prognosis. But with the worst hopefully behind him, we now feel positive about Jesse's future.

“Thinking about what I was raising money for kept me going”

Dr Rachael Natrajan embarked on a 400-mile cycling adventure that raised more than £80,000 for our research.

Having run marathons and jumped out of planes, Rachael Natrajan, who leads the Functional Genomics Group in the Breast Cancer Now Toby Robins Research Centre at the ICR, embraces challenge. But she stepped out of her comfort zone when she joined One More City to cycle from Venice to Rome in four days.

One More City is a cycling event started in 2017 by Christine O'Connell, who rode to Paris to raise money for breast cancer support services following her own diagnosis in 2013. Afterwards, Christine learned that her cancer had returned, spreading to her brain and bones.

Since then, Christine and her team have completed eight rides through seven countries, raising more than £400,000 for research into secondary breast cancer. In 2020, One More City became an ICR charity partner, committing to working with us to improve the lives of people with this condition.

Having funded a PhD student at Imperial College London and two PhD students at the ICR, Christine now hopes to raise £250,000 over three years to fund an ICR clinical research fellow.

Rachael’s motivation to help was not just professional:

“I lost my mum to secondary breast cancer. It was horrific watching her go through it. Her cancer came back very aggressively 18 months after her initial diagnosis. At the time, chemotherapy was her only option. She didn’t want to go through that again. Her prognosis was poor and she wanted some quality of life, but it was extremely hard to watch her die.”

Rachael’s mum inspired her career in cancer research and, along with some encouragement from Christine, became the driving force behind her taking on the cycle ride.

With only three months training, it was anything but easy. However, when things got tough, Rachael was encouraged by those around her.

“Christine was a phenomenal inspiration. During those moments where I felt like giving up, I reminded myself what she’s been through and what she’s still going through – that spurred me on. She’s remarkable.”

Dr Rachael Natrajan cycling. Credit: Vincent Engel

“Leaving a gift in your Will to The Institute of Cancer Research is to leave a legacy of hope.”

Tina Regan, 68, has been touched by cancer personally and seen the devastating impact it has had on her immediate family. That is why she has pledged to leave a gift in her Will to fund our groundbreaking research.

“I knew I could make an impact by leaving a donation that would fund cancer research. New drugs and treatments don’t come out of thin air – we need continued developments to make that happen.

“In my lifetime, I have seen the statistics change from one in four being affected to one in two. Anything that can be done to try to prevent this disease or find kinder ways of treating it is so important.”

Leaving a legacy is one of the most significant contributions you can make to help us defeat cancer. These incredible gifts help our scientists to drive forward their research and take on new challenges, with the support of long-term funding.

Our free online guide contains all the information you need to write or update your Will. We have partnered with expert solicitors to provide our Will for Free service, which means you can make or update your Will, and we will cover the cost.

We are so grateful to everyone who has left us a gift in their Will and those who have pledged to do so, to sustain our work into the future.

Find out more at icr.ac.uk/legacy

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