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Issue 47 | Spring 2023



Christine O'Connell:  
living well with  
breast cancer

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Our mission is to make the discoveries that defeat cancer.

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Written and produced by The Institute of Cancer Research, London  
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## Editorial

Transforming the lives of people with cancer has always been at the heart of what motivates us here at The Institute of Cancer Research. It continues to be front and centre of our minds as we set in motion our recently-launched five-year strategy *Defeating Cancer*, which you can read more about on page 9.

This drive has underpinned our scientific discoveries and achievements throughout our history, leading to better diagnosis and treatments and ultimately real benefits for people with cancer. A recent example of this was a landmark moment in the treatment of advanced breast cancer with a new targeted drug, capivasertib. This exciting new drug was born from our cutting-edge science and pioneering programme of clinical trials, in collaboration with our partners. On pages 12-13, we tell the remarkable story of its development.

But we couldn't achieve any of our successes without you, our supporters and donors, who are with us, supporting our research every step of the way – some quite literally.

One of our supporters, Christine O'Connell, is living well with breast cancer thanks to a targeted treatment. Christine is so passionate about supporting us in finding new treatments that she is funding a PhD studentship to help us train the cancer research leaders of the future. She shares her motivations with us on page 14.

Thank you all for your continued support as we move forward in this next phase of our journey. Together we can carry on making the discoveries that defeat cancer.

**Professor Kristian Helin**  
Chief Executive  
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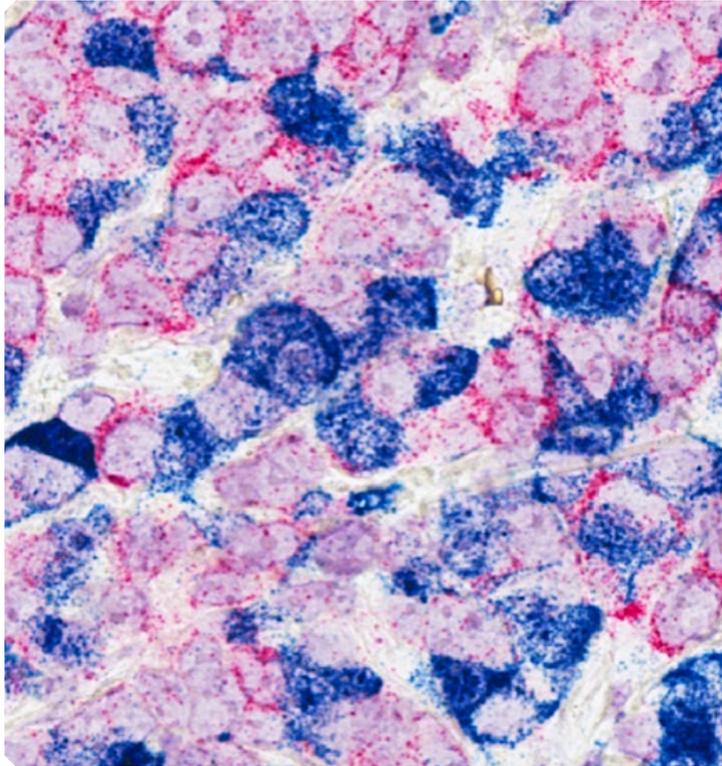
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# Landmark moment for treatment of advanced breast cancer

A new type of targeted medicine pioneered by our scientists has shown 'remarkable' benefits for people with advanced breast cancer in a major phase III clinical trial.

Capivasertib, which blocks activity of the cancer-driving molecule AKT, was found to be effective across all patients in the trial and can double the length of time people live before their cancer comes back.

Trial leader Professor Nick Turner, Professor of Molecular Oncology at the ICR, said: "This has been one of the most effective drugs we've seen in clinical trials in my career, and it's really exciting that it will hopefully become a future treatment option for patients with breast cancer."



Breast cancer cells (Credit: Min Yu)

Read more on pages 12-13

## Blood tests could offer smarter treatment for children's cancer

Our scientists have developed a simple blood test that could guide the treatment of children with the cancer rhabdomyosarcoma.

Professor Janet Shipley, Professor of Molecular Pathology, led an international

study showing that 'liquid biopsy' blood tests could pick up signs that a cancer has returned, assess the severity of the disease, and help guide choice of drugs. The results are already being taken forward into a large collaborative clinical trial.

Professor Shipley said: "Liquid biopsies have the potential to transform how we monitor and treat children with rhabdomyosarcoma. We hope that they can become a less invasive alternative to tissue biopsies."

## Modified cold sore virus shows promise against advanced cancers

Our researchers have discovered that injecting a genetically modified version of the herpes simplex virus into tumours may be effective in treating advanced cancers.

The virus replicates inside cancer cells, bursting them from within, and rallies the immune system to attack what's left. A quarter of the patients in the study responded well, including one with salivary gland cancer who saw his tumour disappear completely.

Professor Kevin Harrington, Professor of Biological Cancer Therapies, who led the study, said:

"It is rare to see such good response rates in early-stage clinical trials. I am keen to see if we continue to see benefits as we treat increased numbers of patients."



Professor Kevin Harrington



Phospho Biomedical Animation

## 'Dark matter' shaping cancer behaviour unveiled

Our scientists have led research that shows cancers can evolve to be more aggressive without relying only on DNA mutations.

A pair of studies together revealed that cancer's gene activity can be influenced by changes to the structure of DNA caused by behaviour or the environment, without altering the genetic code itself. Scientists describe these 'epigenetic' changes as cancer's 'dark matter' because they have important effects on how cells behave but are hard to see.

## £1m pledge to help unravel mystery of shape-shifting childhood cancer

Our scientists have embarked on a pioneering project to prevent or treat relapse in the most common type of sarcoma found in the soft tissues of children – thanks to a generous £1million donation by children’s cancer charity Alice’s Arc.

The project, which is co-led by Professor Janet Shipley and Dr Alejandra Bruna, will examine how chameleon-like rhabdomyosarcoma cells can ‘shape-shift’ without undergoing any genetic changes.

The amazing work of Alice’s Arc was inspired by Alice Wakeling, who died from rhabdomyosarcoma aged seven. The charity has built a network with other families affected by the disease across the UK, and fundraised in those communities to support our work.

Alice’s mother Sara said: “New treatments are urgently needed. Discovering more about the biological mechanisms that drive this disease creates a sense of hope for families. Alice’s Arc is delighted to be funding the project.”



## Improving early diagnosis for people at risk of bowel cancer

We’re delighted to receive funding from St Mark’s Hospital Foundation and 40tude for research to improve the detection and prevention of bowel cancer.

The work, led by Professor Trevor Graham, Director of the ICR’s Centre for Evolution and Cancer, aims

to develop a blood test to spot early signs of cancer in people with inflammatory bowel disease. It could open up opportunities to prevent bowel cancer in people with a high genetic risk.

Jason Bacon, Chief Executive of St Mark’s Hospital Foundation and

Academic Institute, says: “Our partnership with the ICR is vital to the success of these projects, which advance our understanding of the cancer risk from inflammatory bowel disease and inherited familial cancer conditions such as Lynch Syndrome.”

## Carols from Chelsea celebrates 20th anniversary

Famous faces and glamorous guests packed the stunning Wren Chapel at the Royal Hospital Chelsea, as we celebrated two decades of our annual Carols from Chelsea service and raised more than £110,000 for our research.

The programme featured readings from actors Eddie Redmayne, Emilia Fox, Sophie Winkleman and Victoria Smurfit, as well as news presenter Mark Austin. They were joined by Mike Shaw, who paid tribute to his daughter Abbie who died of neuroblastoma aged five. Abbie’s Fund, which was set up in her name, now supports our research into childhood cancer.

Thank you to the organising committee, and especially to the Chair, Diana MacKenzie-Charrington, who is stepping down after seven successful years in the role.



Carols from Chelsea at the Wren Chapel

## Christmas appeal raises more than £120,000 for tomorrow’s cancer leaders



Iona Black, PhD Student

We are hugely grateful to everyone who has supported our Christmas fundraising appeal to help us train the next generation of cancer researchers. You have helped raise more than £120,000 so far.

To continue discovering smarter, kinder treatments for people with cancer, we need the very brightest cancer scientists and clinicians. That’s why we’ve asked for your support, to give talented scientists the best possible start to their career.

Thank you to everyone who has donated so far, and there is still time to do so if you haven’t already. If you can, please support our appeal to help more patients survive cancer:

[icr.ac.uk/next-generation](https://icr.ac.uk/next-generation)

## Record number of participants join Terry Fox Run UK



Signing the wall at the 2022 UK run

**More than 1,300 people joined runs and walks across the UK last October to raise money for our research, in memory of Canadian hero Terry Fox.**

In 1980, Terry ran 3,339 miles across Canada over 143 days after losing his leg to a rare bone cancer. Since his death, thousands of fundraising runs have been held worldwide in his name. All funds raised in the UK go towards our research.

The 2022 UK run was bigger than ever, and Terry's brother, Darrell, joined the event in London at Regent's Park.

Darrell also visited our Centre for Cancer Drug Discovery to learn more about our scientists' work, and was honoured at a special reception at Canada House.

## Events calendar

Are you ready for a challenge? If you would like to join #teamICR and raise money for our vital research, we have places available in the following events. For more information visit [icr.ac.uk/sports](https://icr.ac.uk/sports) or email [sports@icr.ac.uk](mailto:sports@icr.ac.uk)

### Upcoming events

- Terry Fox Run UK  
**Sunday 17 Sept 2023 TBC**
- Royal Parks Half Marathon  
**Sunday 8 Oct 2023**
- TCS London Marathon  
**Sunday 21 April 2024**

## Rudy's legacy

This year marks the 10th anniversary since Rudy Menon died from gliomatosis cerebri, an inoperable brain cancer, on his 26th birthday.

His family holds an annual fundraising walk in Rudy's memory and has raised more than £400,000 towards our research.

This has helped them support two studentships to advance our understanding of the disease. The first student, Shauna Crampsie, is now in the final stage of her PhD in Professor Chris Jones's lab, and a second student will start there in the autumn.



The pain of losing a child, a sibling, a friend is something we know. If we can save one Rudy, that's our mission now and the reason we're funding this vital research.

**Rudy's mother Vidhu**



## Our new ICR strategy: *Defeating Cancer*

We recently launched our five-year strategy to transform the lives of cancer patients – setting out our vision to defeat cancer through world-class research and education, and by growing our impact on society.

We have created an exciting plan resting on our understanding of cancer as a complex ecosystem of cells and signals.

We see cancer research as an ecosystem too, and our strategy aims to defeat cancer by drawing on three key elements:

- 1. World-class cancer research** – Unravelling cancer's ecosystem, overcoming drug resistance, and advancing diagnosis and treatment.
- 2. Inspiring tomorrow's leaders** – Empowering our students and early-career scientists and clinicians to become tomorrow's leaders.
- 3. Growing our impact for patients** – Maximising the chances of our findings reaching patients.

These pillars will be underpinned by our excellent organisation – a strong foundation which enables close collaboration to support our science and a sustainable future.



We have identified some key priorities where your support can make a difference:

Our new Centre for Cancer Drug Discovery will help us to develop smart new cancer drugs that target the tissue environment to treat the disease.

Our Centre for Translational Immunotherapy aims to develop exciting treatments to stimulate the immune system to fight cancer.

Our Centre for Evolution and Cancer will help us overcome cancer's deadly ability to evolve and become resistant to treatment, to keep one step ahead of the disease.

But driving forward our research is only possible with your continued support.

Every donation we receive is vital to provide sustainable funding and help us plan and fund research where the need is greatest across our projects.

Whether it is a small, regular donation or a gift in your Will, contributions which sustain us into the future deliver a big impact on our research.

To make a regular donation please visit [icr.ac.uk/regular-donation](https://icr.ac.uk/regular-donation) or find out more about our strategy at [icr.ac.uk/strategy](https://icr.ac.uk/strategy)

# Dr Stephen-John Sammut

Dr Stephen-John Sammut joined us in November 2022 as a Clinician Scientist and leader of the Cancer Dynamics team. His research uses artificial intelligence to forecast how cancer is likely to respond to treatment, and to spot early signs that the disease is becoming resistant to drugs.

**Joined the ICR**  
November 2022

#### Specialist subjects

Machine learning, biomarker technologies, personalised medicine

#### Interests

Outside of the lab, Stephen-John enjoys cooking and gardening. He especially enjoys making pizza in woodfired ovens – in true Mediterranean style.

“ ”

What if we could predict which patients will respond well to treatment before we even start? That's where I come in.

Dr Sammut was previously at the University of Cambridge, where after completing his medical oncology training he was awarded a postdoctoral lectureship in breast cancer and a PhD in breast cancer genomics at the Cancer Research UK Cambridge Institute.

He is developing 'machine learning' methods that teach computers to predict cancer's response to treatment by feeding them data about the wider tumour ecosystem. He also uses data acquired from cancers during chemotherapy to stay ahead of drug resistance, and to detect it if it emerges during treatment.

Dr Sammut says:

“Unfortunately, in the clinic we are unable to predict response to cancer treatments. While some patients see exceptional results and are cured, many are less fortunate. But what if we

could predict which patients will respond well to treatment before we even start? That's where I come in.”

Last year, Dr Sammut published his advances in personalised breast cancer medicine in a landmark paper in *Nature*, which was cited as one of the top 10 cancer research publications by the European Association for Cancer Researchers in 2022.

He says: “The ICR is truly passionate and committed to making a difference to the lives of the cancer patients I see in the clinic, and this is one of the main reasons why I work here. The ICR's association with The Royal Marsden allows for unparalleled translational science, meaning the latest research advances can be quickly translated into tangible benefits for our patients.”



# Capivasertib: an ICR success story

**A drug called capivasertib is poised to become an exciting new treatment for people with breast cancer. It's an achievement born from the ICR's cutting-edge science and our pioneering programme of clinical trials.**

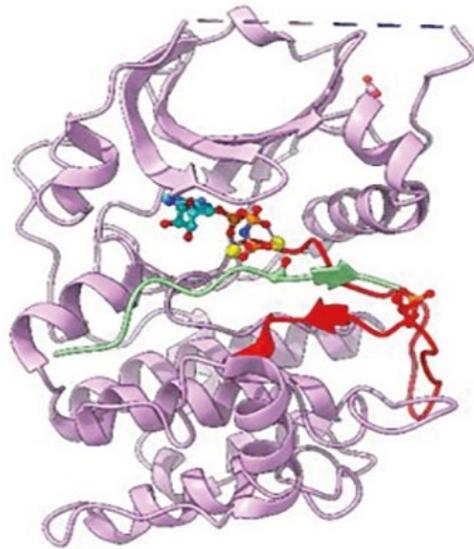
In December last year, the ICR's researchers unveiled some 'remarkable' results from a late-stage clinical trial – showing that a new drug called capivasertib was effective for patients with the most common form of breast cancer.

It takes years of research to create a new cancer treatment, and the ICR has been involved every step of the way in the success of capivasertib – from the early fundamental science and later drug discovery, right through to the cutting-edge clinical trials.

Capivasertib is a new type of drug called an AKT inhibitor. It blocks the activity of the molecule AKT which helps cancer cells survive, grow uncontrollably and resist the effects of some treatments. There is evidence that AKT plays an important role in a range of cancers, including breast, lung, ovarian and prostate cancers.

## Understanding AKT

Much of our understanding of AKT stems from research at the ICR. In 2002, Professor David Barford and his team revealed the crystal structure of AKT, using a technique called X-ray crystallography.



AKT Inhibitor. Credit: David Barford

They also provided important clues to how it's switched on in cells – showing that part of the protein called the ATP binding pocket is crucial for its activity in cancer.

## Finding AKT inhibitors

Professor Michelle Garrett, who led the ICR's Clinical Pharmacodynamic Biomarkers Group, and Professor Paul Workman, who was Director of the Cancer Research UK Centre for Cancer Therapeutics, worked together using a technique called fragment-based drug discovery to identify AKT inhibitors.



This has been one of the most effective drugs we've seen in clinical trials in my career, and it's really exciting that it will hopefully become a future treatment option for patients with breast cancer.

**Professor Nick Turner**

Working with the company Astex Pharmaceuticals, they found small molecules that could fit into the ATP binding pocket, and then built larger compounds with the right shape and chemical properties to block AKT activity. They developed several AKT inhibitors, including the precursor of capivasertib, which showed promising activity against a range of cancers.

AstraZeneca then licensed these AKT inhibitors and developed one of them further into the drug capivasertib, which was first unveiled in 2010.

## Clinical trials

Our researchers have continued to be closely involved in the development of capivasertib, playing a major role in running clinical trials of the new drug. Professor Udai Banerji, Deputy Director of the Drug Development Unit at the ICR and The Royal Marsden, ran the first trial of capivasertib in patients. This found early evidence that it could shrink tumours in patients with breast, ovarian and cervical cancer.

Then Professor Nick Turner, Professor of Molecular Oncology at the ICR and Consultant in Medical Oncology at The Royal Marsden, led the phase III CAPitello-291 trial, which used capivasertib alongside hormone therapy to treat oestrogen receptor positive, HER2 negative breast cancer – the most common form of the disease.



Professor Nick Turner

In initial trial findings, presented at the San Antonio Breast Cancer Symposium in the US, the drug doubled the time it took for cancer to progress. Excitingly, it worked in patients whether or not they had defects in the AKT signalling pathway.

We hope that capivasertib will be licensed later this year for the treatment of oestrogen receptor positive, HER2 negative breast cancer.

And its story does not end there – the drug is also being tested in later-stage clinical trials for hormone-resistant advanced breast cancer, triple-negative breast cancer and PTEN-deficient prostate cancers.

Our pioneering research, in collaboration with clinical and commercial partners, looks set once again to have a transformative impact on the lives of patients.

**To continue to make discoveries to help people with cancer, we rely on the generosity of supporters and donors like you, to sustain our work into the future. Help us make the next big discovery by giving a regular gift today: [icr.ac.uk/regular-donation](http://icr.ac.uk/regular-donation)**

## “The ICR’s research gives me hope”

Christine O’Connell was 40 when she was diagnosed with breast cancer. After months of treatment, she thought her cancer was behind her. But six years later, she had a seizure while out on her bike and was told it had returned and spread to her brain. Here she explains why our research is so important for people with cancer like her.

“I was in total shock when I found out I had secondary breast cancer. Fortunately the drug palbociclib had been approved for use on the NHS just months before. The trials in the UK had been led by the ICR. I’ve now had more than 60 treatment cycles with the drug and my cancer is stable.”

This means I can take a pill every day and continue to do the things I love, like cycling, which has been my lifeline.

I am proud to say that through the One More City campaign which I set up, we have raised more than £250,000 for research into new treatment options for people with stage 4 breast cancer.

Our goal is to cycle from one city to another, setting off each year from the city we finished in the year before.

We’re now riding to fund a second studentship at the ICR. By funding a PhD, we’re contributing more than just a piece of equipment – we’re helping to give someone a



Christine O’Connell  
(Credit: Richard Lewisohn)

future, someone who will become a great scientist and a long-term asset in our mission to defeat cancer.



One More City cycling team (Credit: Saskia Martin)

## Scientists behind breast cancer gene discovery honoured with new plaques

The team of 41 scientists involved in the landmark discovery of the BRCA2 gene in 1995 have been celebrated with two commemorative plaques, installed at our labs in Chelsea and Sutton.

Mutations, or faults, in the gene can cause breast, ovarian, prostate and pancreatic cancer. The discovery was a major scientific breakthrough which led to genetic tests for cancer and underpinned the development of new treatments – transforming the lives of many thousands of people worldwide.

Professor Andrew Tutt, Professor of Breast Oncology at the ICR, said: “The discovery of BRCA2 was an incredibly important moment, and its impacts continue to be felt decades later. In the shorter term, it allowed families with a history of breast cancer to receive genetic testing and be assessed for future risk. But it also spurred decades of research at the ICR into identifying cancer’s weaknesses which culminated in the development of PARP inhibitors – cutting-edge, targeted drugs for patients with cancers caused by faults in this gene.”

Read more: [icr.ac.uk/brca2discovery](http://icr.ac.uk/brca2discovery)

I know at some point my treatment will stop working, and my cancer will progress because it will have developed a resistance to the drug.

At that point, I hope there will be more new treatments in the pipeline that will buy me more time.

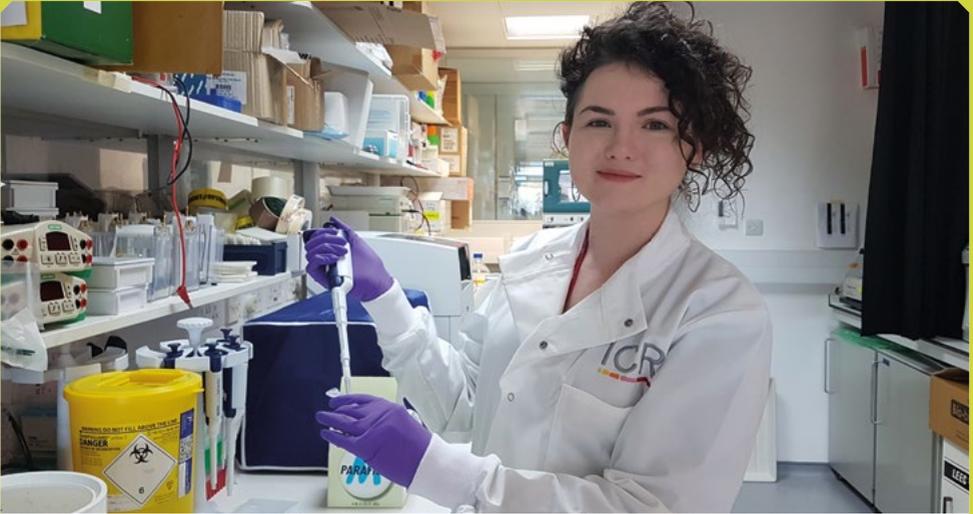
That’s why it’s so exciting to hear about new potential treatment options like capivasertib. This new drug, which the ICR helped discover, offers fresh hope to patients like me.”

“““

It gives us hope to know the ICR is working to make sure that when one treatment fails, there’ll be something else available.



Some of the scientists behind the discovery



Shauna Crampsie, PhD student

## Leaving a legacy

Leaving a legacy is one of the most significant contributions you can make to fund our life-changing cancer research. 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 will 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. Most people who use this service leave a gift in their Will to us, to become a part of the journey to defeat cancer.

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.

**Visit [icr.ac.uk/legacy](https://www.icr.ac.uk/legacy) to find out more.**