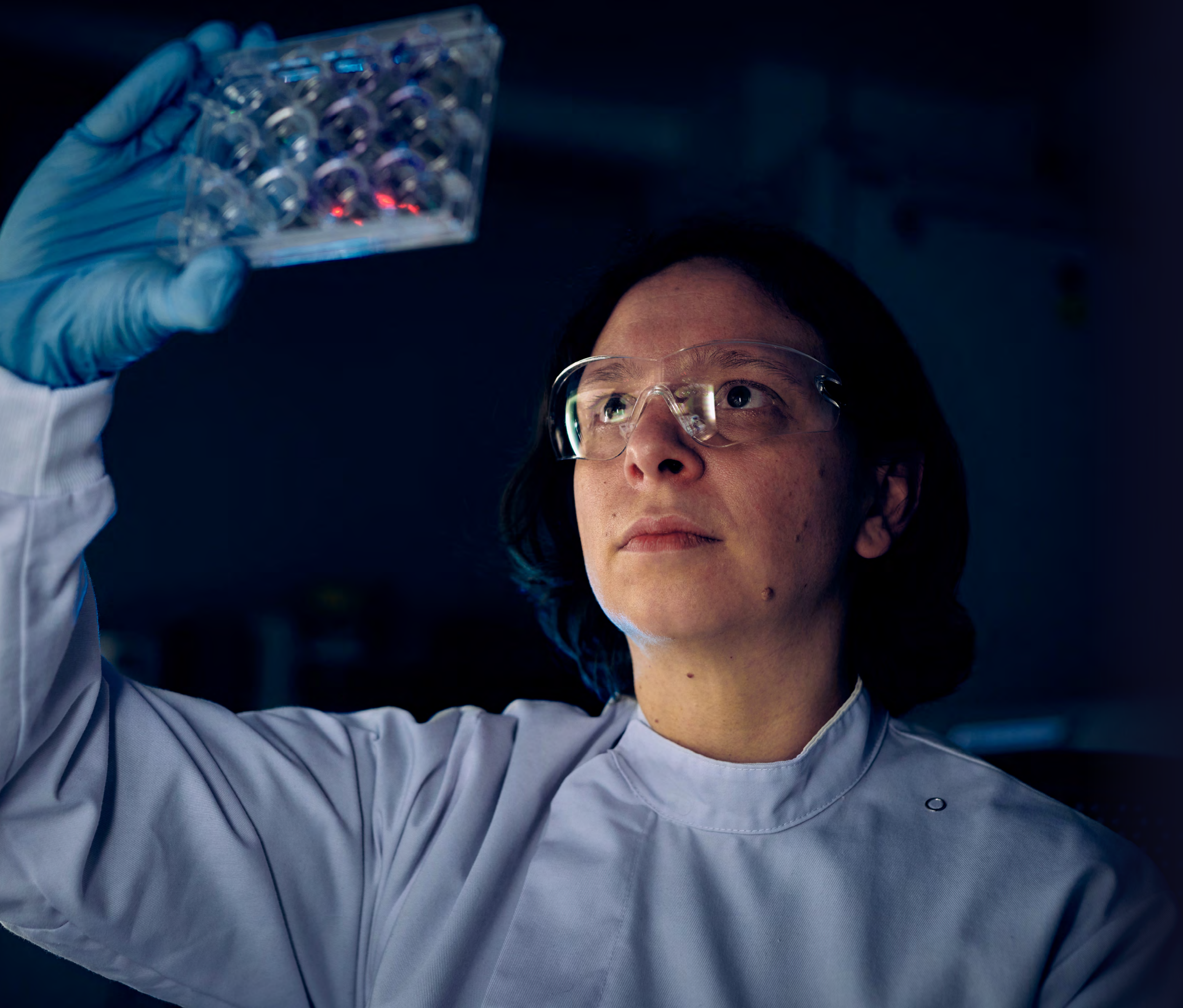


CANCER RESEARCH HORIZONS ANNUAL REVIEW 2021/22

FURTHER FASTER
TOGETHER
WE WILL BEAT CANCER



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INTRODUCTION

Welcome to the first annual review for Cancer Research Horizons, the innovation engine from Cancer Research UK. Our new organisation combines our drug discovery and commercialisation functions under one clear brand and with a single focus: to translate Cancer Research UK's research outputs into patient benefit.



THE NEW INNOVATION ENGINE FROM CANCER RESEARCH UK

Cancer Research UK exists to beat cancer. For the past 120 years, we've been making discoveries that have saved countless lives, and which benefit millions of people around the world each year.

But we know that not enough of our world-leading research is progressing at pace from the lab bench to the bedside. So, in April 2022, we launched Cancer Research UK's new innovation

engine, Cancer Research Horizons, to translate more cutting-edge innovations into effective treatments and diagnostics for people with cancer now.

By uniting our commercial partnerships and therapeutic innovation expertise, we offer the full spectrum of drug discovery and clinical capabilities, and we're uniquely placed to support translational funding, licensing, collaboration and spin-out creation.

We bring together world-leading minds, bold ideas and the right partners to bridge the gap between academic research and the market. And we focus on the tougher, more profound ideas that can lead to true innovation.

Our business is breakthroughs. We want to bring forward the day when all cancers are conquered.

And we believe that day is on the horizon.



WE'RE A POWERFUL PARTNER IN THE FIGHT TO CONQUER CANCER

4,000
exceptional researchers
in our network

60+
spin-out companies
already formed
with our support

£300m+
of annual research spend

11
cancer drugs
already brought
to market with
our help



INTRODUCING CANCER RESEARCH HORIZONS, THE INNOVATION ENGINE FROM CANCER RESEARCH UK

Iain Foulkes

In the past year, we've made some big changes to the way we work that we believe will set us up for greater success in the years to come. Firstly, we rebranded to become Cancer Research Horizons. This is not just a name change – we are changing how we work so we can go further, faster, together.

Cancer Research Horizons is an innovation engine built to complement Cancer Research UK's network of exceptional researchers. Through a complete re-organisation of our drug discovery capabilities, we have brought together five scientific units and more than 200 scientists to share expertise, capabilities and technologies. Together, we take cutting-edge innovations from the lab bench to the bedside, translating them into effective treatments and diagnostics for cancer patients.

In this report, you'll read about the extraordinary progress we've made in the past year. But this is just the beginning of what we want to do. In 2020/21, £1.8bn of investment in cancer research from government, charity and industry sources generated £5.1bn of economic impact for the UK – that's £2.80 for every £1 spent. So, as well as improving survival and boosting the

quality of life for cancer patients – which will always be our primary motivation – the work we're doing is adding significant value to the UK economy. Cancer Research UK alone generated £973m in economic benefits in 2020/21, including 9,010 jobs, while 10 of our largest spin-out companies together spent £421m on cancer R&D in the UK, which generated 10,850 jobs and £824m of gross value added for the private sector.

But as cancer cases are set to grow by 40% over the next 20 years, we need to maintain this level of growth and maximise the impact of cancer research for patients. This is exactly what Cancer Research Horizons is for. The space we occupy in the industry of research commercialisation, drug discovery and development is unique. We want to use it to drive a step change in the translational output of the science

we fund. We will work hand in hand with our research community and the life science sector around the world to build radical new ideas to deliver benefits on behalf of patients everywhere.



Iain Foulkes
Chief Executive Officer, Cancer Research Horizons



OUR NEW THERAPEUTIC INNOVATION DIVISION

Hamish Ryder

Following an in-depth review and evaluation of future options for Cancer Research UK's drug discovery model, we have created the Therapeutic Innovation division of Cancer Research Horizons.

This represents a radical shift in the approach we take to drug discovery – from the former model of independently funded and assessed drug discovery units to a single organisation under a highly experienced leadership team, with one shared portfolio and budget.

The leadership team makes decisions on funding, resourcing and the formation of new alliances and collaborations, and sets the tone for the culture in our labs and sites across the UK. They're also responsible for administering response-mode funding via the Therapeutic Catalyst scheme, as part of the 'single portfolio' ethos.

The division brings together more than 200 drug discovery-focused scientists across six laboratory locations: the Beatson Institute in Glasgow, Newcastle University, the

Francis Crick Institute in London, and the Babraham Research Campus, Cambridge Biomedical Campus (Functional Genomics Centre) and Granta Park (Antibody Alliance Lab) in Cambridge. Together, we will build on our track record of forming new strategic alliances and companies and entering new therapies into clinical trials in recent years.

Our ambition is to bring about a step-change in our impact on patient outcomes. We'll go further in our engagement with groundbreaking science, accessing deep insight to take calculated risks and starting the translation process sooner. We'll move the best ideas forward faster by leveraging our critical mass, internal capabilities and expert partners. And most importantly, we'll bring together the best minds and capabilities in academia and the commercial sector because we

believe that team science is at the root of deep understanding, the right portfolio decisions and, ultimately, better patient outcomes.



Hamish Ryder
Chief Executive Officer, Therapeutic Innovation,
Cancer Research Horizons



COMMERCIAL PARTNERSHIPS OVERVIEW

Tony Hickson

This year has represented one of transition for Cancer Research UK's Commercial Partnerships team. The formation of Cancer Research Horizons has brought the commercial support functions of the team together with the charity's drug discovery capabilities to form a fully integrated biotechnology and techbio commercialisation company.

The creation of this new innovation engine coincided with the winding down of the COVID-19 lockdowns, allowing us to re-engage face-to-face with many of our researchers. However, headwinds remain, with a number of our partnered drugs and devices held up by delays in clinical trials as the UK emerges from the pandemic-linked pause. We also saw the end of a vibrant streak of funding for healthcare companies and the IPO window largely close by the end of the year.

Importantly, these external forces have not blunted our ambition. During the year, we created a search and evaluation function and a new ventures unit, which are working closely with more than 4,000 Cancer Research UK-funded researchers around the world to advance their ideas. Our partnerships and spin-outs

resulted in seven new first-in-human clinical trials being initiated. And we reframed our Cancer Tools business, so that it will work with academic partners globally to ensure research tools can be exchanged more quickly and efficiently.

Going forward, there is much to look forward to. Our new cancer seed fund will attract interest from aspiring new start-ups and, following their launch this year, we'll continue to fund more Therapeutic Catalyst and Data Innovation Awards to build a healthy pipeline for Cancer Research Horizons.

All of this is designed to help us take Cancer Research UK-funded research ideas **further** and move **faster** by partnering **together** with industry and our academic

partners. We look forward to working with you in the future.



Tony Hickson
Chief Business Officer, Cancer Research Horizons



HIGHLIGHTS AND IMPACT 2021/22

Cancer Research Horizons exists to ensure that new discoveries and insights from research ultimately end up helping people with cancer. In this section, we provide some examples of recent developments.



OUR YEAR IN NUMBERS



We spoke to
>600
researchers,
including

>334
Principal Investigators



>95
invention disclosures



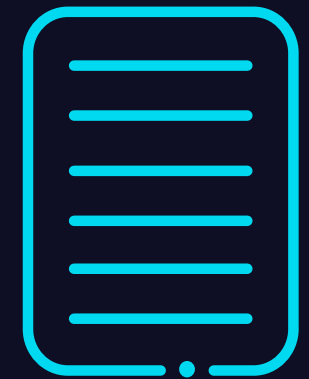
29
patents filed
(17 priorities and 12 Patent
Cooperation Treaties)



>£440m
investment raised
by portfolio



£37.5m
reinvested in
cancer research



>600
Entrepreneurial
Programme partners

26

drug discovery
projects

18

partnered

9

biological

9

small molecule

8

non-partnered



3

Spin-out companies
created



7

new therapies advanced
to patients by Cancer
Research Horizons, our
partners and our
spin-out companies



2

new candidate drugs
selected for clinical
formal approval by
Cancer Research
Horizons



108

commercial deals signed

10

drug
development
candidates
(partnered)

5

in preclinical development

5

in clinical development



NEW DRUG REACHES THE MARKET FOR B-CELL LYMPHOMA

Nothing is more important to us than seeing new, tangible patient benefits arising from our funded science. In 2021/22, we were pleased and proud to see the launch of the 11th drug from our portfolio, Zynlonta®. This is the first Antibody Drug Conjugate (ADC) to use a pyrrolobenzodiazepine (PBD) dimer, which cross-links DNA to prevent cell division.

The drug's history can be traced back to the formation of a Cancer Research Horizons spin-out company, Spirogen, in 2001. In the mid-2000s, we began the first preclinical and early clinical testing of PBD dimers as standalone systemic agents through the cancer research unit at the University of Bradford and a Phase 1 clinical trial in the UK, both supported by Cancer Research UK.

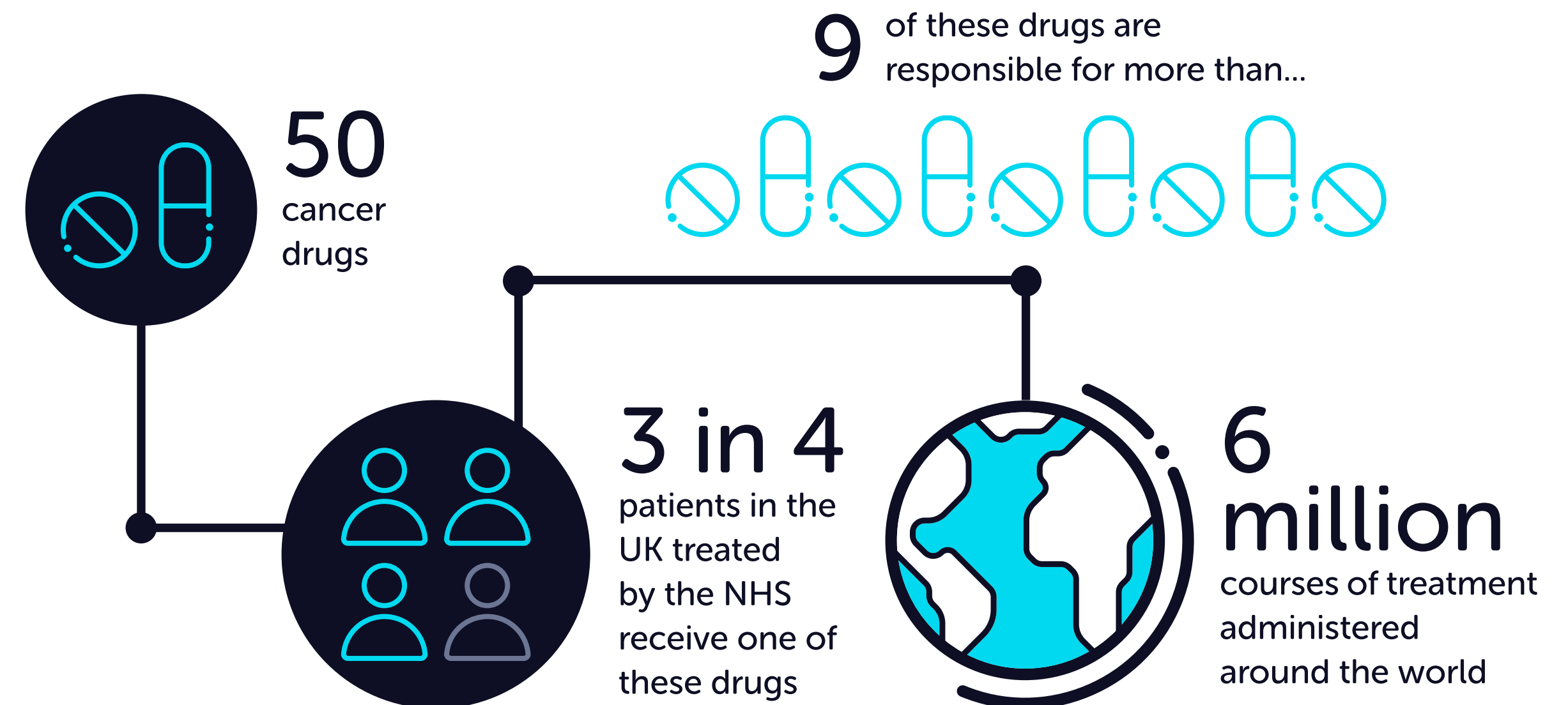
In 2012, a second spin-out second company was formed, ADC Therapeutics, to progress Zynlonta®. The first dose was administered in March 2016 and proceeded smoothly through Phase 1 clinical trials. In June 2020, ADC Therapeutics announced the results of their Phase 2 trial, which showed that 48% of patients responded to Zynlonta®, with 24% entering complete remission.

"Cancer Research Horizons' initial investment has resulted in chemistry that has attracted over \$1bn from capital markets, all of which has been invested in bringing new therapies to cancer patients."

Ameet Mallik,
CEO of ADC Therapeutics

6 MILLION COURSES OF TREATMENT ADMINISTERED WORLDWIDE

In total, research funded by Cancer Research UK has helped develop more than...



This global figure was calculated using commercially available drug-prescription datasets provided by IQVIA, as well as published drug dosing studies, for nine drugs Cancer Research Horizons has had a direct hand in helping to bring to market: dexrazoxane, vismodegib, abiraterone, temozolomide, rucaparib, olaparib, erdafitinib, etoposide and pemetrexed.



7 FIRST-IN-HUMAN DRUG STUDIES INITIATED THIS YEAR

In 2021/22, seven new studies were initiated by Cancer Research Horizons partners or spin-out companies, demonstrating our commitment to progressing novel cancer drugs towards patient benefit at pace.



Cancer Research Horizons and Teon Therapeutics announced that the first patient had been successfully dosed in their Phase 1/2 trial of Teon's first-in-class oral, once-daily dosed adenosine receptor antagonist, TT-702, for the treatment of people with a range of difficult-to-treat cancers.

Cancer Research Horizons, Vaccitech plc and the Ludwig Institute for Cancer Research announced the first patient had been dosed in the Phase 1/2a MAGE trial for a lung cancer immunotherapy vaccine.

Cancer Research Horizons and Hummingbird Bioscience announced the first patient had been dosed in their Phase 1 trial of Hummingbird's anti-HER3 antibody, HMBD-001, for the treatment of people with a range of hard-to-treat HER3-driven cancers.

iOnctura announced the first patient had been dosed in a healthy volunteer study of the next generation autotaxin inhibitor IOA-289, the first autotaxin inhibitor for cancer to progress to clinic.

Artios announced the first patient had been dosed in the Phase 1/2a study of the POLθ inhibitor ART4215.

Nuvectis Pharma initiated a Phase 1 trial of NXP800 for people with advanced ovarian cancer. NXP800 targets the HSF1 pathway.

GammaDelta Therapeutics initiated a Phase 1 trial of GDX012, an allogeneic, non-engineered, variable delta 1 gamma-delta T-cell therapy for people with acute myeloid leukaemia.



NEW INITIATIVE LAUNCHED TO FIND TREATMENTS FOR RARE AND CHILDHOOD CANCERS

In 2021/22, we launched a multi-drug, adaptive precision medicine clinical initiative that aims to find out whether drugs already licensed for certain types of cancer can treat other rare adult and paediatric cancers. The DETERMINE trial will be one of the largest platform trials targeting rare cancers in the world. We're sponsoring and managing the five-year trial, which is being led by the University of Manchester together with the Royal Marsden NHS Foundation Trust, the University of Birmingham and the Christie NHS Foundation Trust. It will begin recruiting nationwide this year.

In the first phase, Roche is providing seven of their targeted therapies to be evaluated, with more pharmaceutical partners expected to join and contribute drugs as the trial progresses. People who are interested in

taking part will undergo genetic testing for identifiable mutations and will be enrolled on the study if their genomic profile suggests a match to a treatment that is likely to benefit them. If any drug is shown to benefit a group of patients, data can be submitted to the NHS Cancer Drug Fund, which may decide to permit expansion of use of that drug for patients with this cancer type following further data collection.

DETERMINE 





RESEARCHER SUPPORT AND ENGAGEMENT

Funding good cancer research will only get us so far. To accelerate new ideas and fresh findings from the lab into the clinic, we equip our funded researchers with the support and expert advice they need to successfully translate and commercialise their work.



UPDATES

STARTING THE POST-COVID RECOVERY

Over the past year, we've continued to provide a transparent and customer-centric service to our researchers and adhered to the pledges we made in our Customer Service Commitment, launched in 2020-21.

Despite the difficult operating conditions still imposed by COVID-19, our team remained on hand to support researchers in their translational endeavours and has been focussing on getting back to in-person interactions.

Although we are still suffering from the operating challenges posed by COVID-19 to wet lab research, we have seen a sign of recovery with an increase in invention disclosures compared to the previous year.

We met with more than 330 principal investigators, often in a virtual setting, where researchers shared their discoveries and discussed how to translate them into patient benefit.

In 2021/22, the average time from disclosure to formal decision was

51 days

(down from 55 days in the previous year)

86%

of disclosures received a decision within our committed timeframe of three calendar months (up from 65% in the previous year)



In total:

330+

principal investigators engaged

29

patents filed

97

invention disclosures





AWARDS

14 PROJECTS GRANTED TRANSLATIONAL FUNDING AWARDS

In 2021/22, we granted Translational Funding Awards to 14 projects across 11 institutions, ranging from *in-vivo* proof-of-concept studies to key reagent or product generation. These awards support our researchers to move their research ideas towards patient benefit.



"The award is vital for our plan to translate our T-cell ExTRECT method into a clinically useful tool that will provide actionable medical insights for cancer patients at greater cost effectiveness."

Dr Robert Bentham, Senior Research Fellow in Nicholas McGranahan's group at University College London



"Our award will enable us to perform a valuable validation study for our bioinformatic tool, called ECLIPSE, which is designed for clonal reconstruction of tumours using DNA circulating in plasma."

Dr Alexander Frankell, Senior Research Fellow at University College London and the Francis Crick Institute



SPOTLIGHT ON BETTER PREDICTING PATIENT RESPONSE TO NEW CANCER DRUGS

Around 85% of cancer drugs that enter clinical trials fail, mostly at the more expensive Phase 2/3 stages. This is because, for various reasons, preclinical cell line-based models for cancer are currently too poor to reliably predict patient response. One issue is that the models don't represent the true genetic diversity seen in people's cancers.

At Newcastle University, Dr Ed Law and Dr Helen Blair are leading a team who are developing the HiDRA platform, an AI-enhanced co-culture platform that seeks to address this issue in blood cancers. The technology is based on work by Professor Olaf Heidenreich's lab, funded by Cancer Research UK, and allows users to keep patient material viable for at least a week. Drugs are rapidly applied to this material and analysed using high-content microscopy and image analysis to quickly obtain information about their efficacy. The team specialises in applying complex combinations of up to four drugs, as blood cancers are mostly treated with combined therapies.

With support from Cancer Research Horizons, the HiDRA team performed extremely well in accelerator competitions, including the Cancer Tech Accelerator and Oncostars in 2021. "We're immensely grateful for the exceptional help we've received from Cancer Research Horizons," says Dr Ed Law. "They engaged with us very early on, sowing the seeds of commercialisation exploration and, more recently, making us aware of accelerator programmes. We were lucky enough to progress on to the second phase of the Cancer Tech Accelerator, giving us access to high-level mentorship that has refined our understanding of the market and the all-important narrative behind our platform."

When it became clear that the team needed a better understanding of the market and IP landscape in this space, Project Development funding was rapidly released to commission a report by IP Pragmatics on the AI-enabled assay market. This will be invaluable in guiding the next steps for the team and the technology.



"We're immensely grateful for the exceptional help we've received from Cancer Research Horizons."

Dr Ed Law, Newcastle University



SPOTLIGHT ON USING DATA TO IMPROVE IMMUNOTHERAPY OUTCOMES

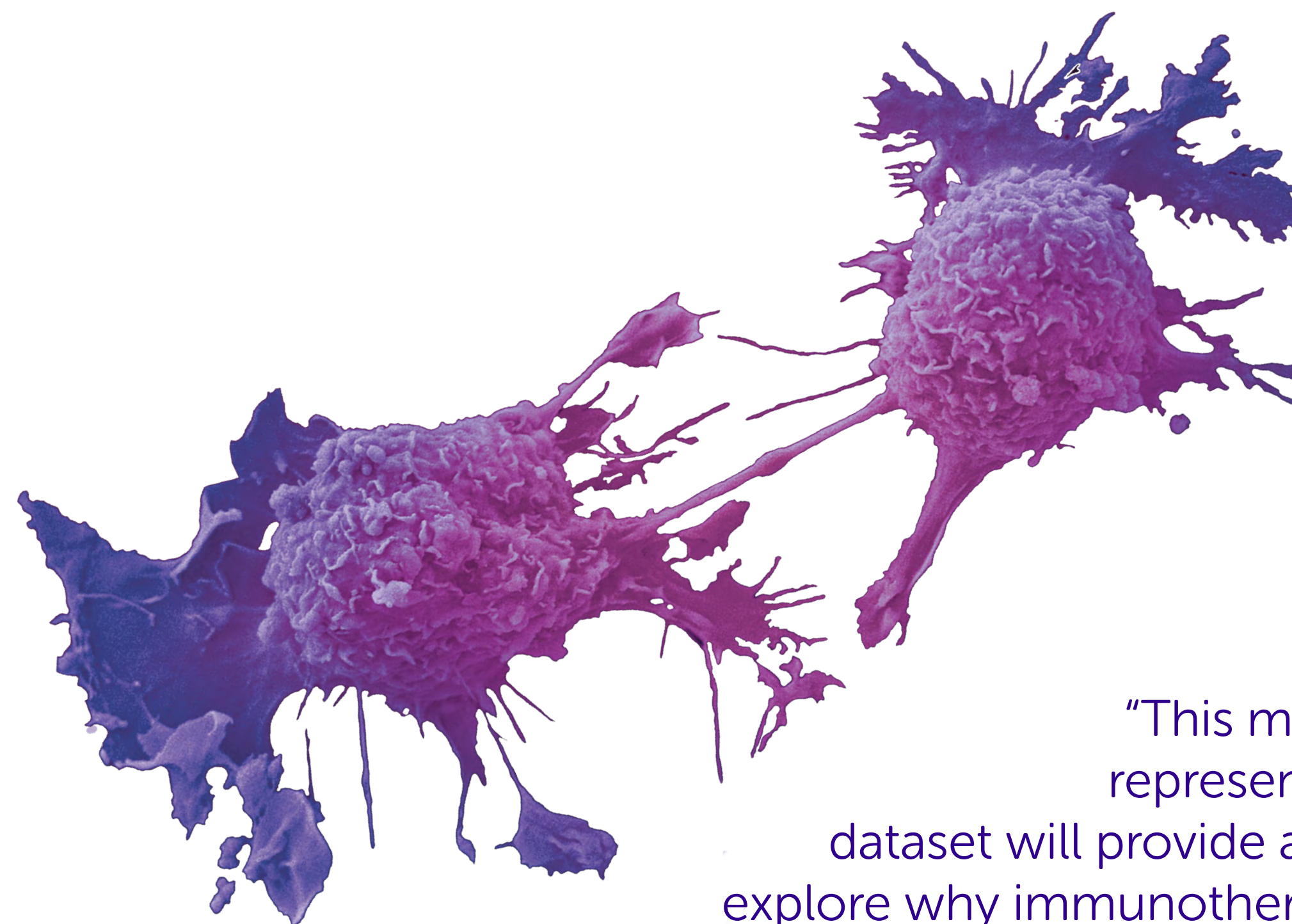


It's well-known that certain groups of people are under-represented in clinical trials, including people from socioeconomically deprived areas or who have other underlying diseases or conditions. However, the information collected about patients as part of their normal care in hospitals' electronic health records, known as real-world data (RWD), offers the opportunity to generate evidence where clinical trial data doesn't exist.

In 2021/22, the Cancer Research UK Manchester Radnet programme collected data from more than 400 people with advanced stage non-small cell lung cancer who have been considered for immunotherapy treatment since 2017. This data includes complete biomarker analyses, longitudinal blood scoring and imaging analysis, long-term outcomes and anecdotal information about their quality of life.

With funding from the Winton Foundation Cancer Research UK Data Innovation Awards (a Cancer Research Horizons initiative), Dr Fabio Gomes and his team are now curating an anonymised, high-quality real-world dataset that's comparable to clinical trial datasets.

The dataset could be used to support machine learning analyses that identify interactions between people with underlying diseases or conditions and their outcomes in the context of immunotherapy efficacy and safety, or to underpin AI approaches for imaging biomarkers that could predict a patient's response to the treatment. While in the clinic, it could be used to personalise and optimise treatment care plans and pathways.



Lung cancer cell splitting

"This more inclusive and representative real-world dataset will provide an opportunity to explore why immunotherapy works better for some patients than for others and how it can be better personalised for people with advanced lung cancer."

Dr Fabio Gomes, The Christie NHS Foundation Trust



AWARDS

THERAPEUTIC CATALYST LAUNCHED

In 2021/22, we launched our Therapeutic Catalyst to accelerate the translation of laboratory discoveries into new treatments for cancer patients.

"The awards are very different to previous funding schemes in that we want to form much closer collaborations with academics at the early stages of drug discovery to validate and de-risk targets and technologies," explains Steve Wedge, Chief Scientific Officer of Cancer Research Horizons. After a simple expression of interest, projects are selected for development into a full proposal and the investigators are each assigned a Cancer Research Horizons drug discovery expert to provide advice on their plans. They can apply for up to £250,000 to support a 12–18 month proposal, which is reviewed by a panel that includes external experts.

The successful projects are then run collaboratively, with the funding used to support resources in the labs of either or both partner(s). "Therapeutic discovery is a multi-disciplinary team effort and we want academic researchers to feel that they are an integral team member," says Steve. "Together, we can rapidly assist the translation of their ideas towards new therapeutic options for people with cancer."

One of the first recipients of a Therapeutic Catalyst was a team headed by Professor Chris Schofield at the University of Oxford, with Professor Akane Kawamura at Newcastle University and Professor Johann De Bono and Dr Alec Paschalis from the Institute of Cancer Research, London. "Cancer Research Horizons gave us extremely helpful translational insights that helped us to develop a full proposal," says Chris. "We've held highly productive interactive project meetings with Cancer Research Horizons scientists and it feels like a collaborative endeavour."

Johann added: "We welcome this new funding scheme, which shares our aspiration to advance research towards the discovery of new cancer medicines."



Find out more about
Therapeutic Catalyst



"It feels like a collaborative endeavour."

Professor Chris Schofield,
University of Oxford





AWARDS

WINTON FOUNDATION CANCER RESEARCH UK DATA INNOVATION AWARDS LAUNCHED

In 2021/22, we launched the Winton Foundation Cancer Research UK Data Innovation Awards, with support from the Winton Foundation. These awards offer researchers funding of up to £75,000 to curate, clean and annotate interesting datasets generated from their research.

We also offer them support from expert business managers to work through the contractual and ethical issues regularly seen when handling complex patient derived datasets. And at the end of the award, we'll help them maximise the impact of their dataset by establishing a range of data sharing commercial partnerships.

Since we launched the initiative, we have reviewed seven projects and approved three, with two more approvals pending. One of the successful projects is the Bladder Cancer Prognosis Programme at the University of Birmingham, led by Professor Rik Bryan. With their award, the team will unite a number of disparate datasets generated by their analysis of bladder cancer samples to create a unified and more easily searchable database. This will not only help the team make the most of their own data, but also enable it to be used in a range of commercial collaborations, from digital pathology analysis to target identification.

With data becoming an increasingly important tool in the fight against cancer, we're actively looking to build our portfolio of Data Innovation Awards with the capacity to support up to five projects per year.



Find out more about Winton Foundation Cancer Research UK Data Innovation Awards





UPDATE

INCREASING ACCESS TO CRISPR

The Functional Genomics Centre (FGC) provides cancer researchers with access to cutting-edge CRISPR technologies to help with their research.

In 2021/22, the team benchmarked the performance of existing libraries and leveraged the data to design optimised, minimal genome-wide CRISPR libraries. These improve FGC screening efficiency by reducing the per-screen cost by around 40%, while preserving assay sensitivity and specificity, and enabling researchers to probe complex models where reagents are precious and limited. They will also allow researchers to significantly reduce the experimental scale of genome-wide screens, increase throughput and improve levels of environmental sustainability.

"Working with the FGC has given us access to CRISPR screening capabilities that we would not have been able to replicate independently," explains Dr Ivan Ahel, a Senior Wellcome Trust Research Fellow at the University of Oxford. "The team worked super efficiently

and in a very collaborative way, and we had detailed and enjoyable scientific and technical discussions during the process."

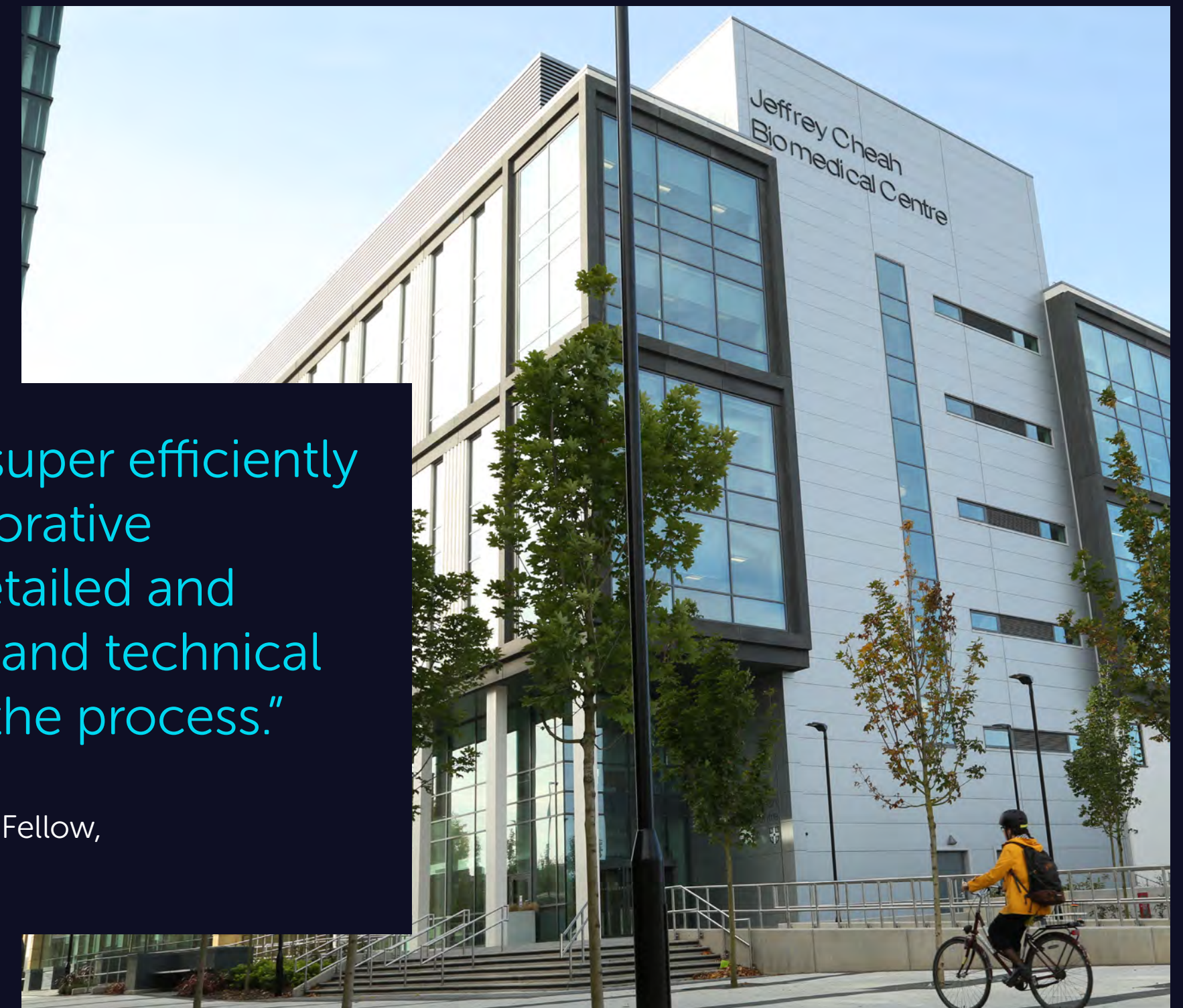
The FGC launched in 2019 to develop novel CRISPR technologies that will deepen our understanding of the biology of cancer. Based at the Milner Therapeutics Institute in Cambridge, the centre has a portfolio of 40 active projects.

"The team worked super efficiently and in a very collaborative way, and we had detailed and enjoyable scientific and technical discussions during the process."

Dr Ivan Ahel,
Senior Wellcome Trust Research Fellow,
University of Oxford



FUNCTIONAL
GENOMICS
CENTRE





STIMULATING ENTREPRENEURSHIP

We're building a community of entrepreneurially minded researchers. Through our training and mentorship opportunities, and strong partnerships with lead programme providers, we equip our scientists with the skills, insights and confidence they need to accelerate their ideas into cancer-beating treatments.



ONCOSTARS

Launched in 2019, OncoStars is our flagship entrepreneurship and venturing programme in partnership with Panacea Innovation.

With a focus on oncology, OncoStars delivers bespoke training and mentorship in two phases: the Action Phase covers the fundamental entrepreneurial skills needed for the formation of new ventures, while the Develop Phase focuses on enabling aspiring companies to de-risk their project and build for the future.

In 2021/22, OncoStars received more than 300 applications, with 22 oncology companies shortlisted to join the programme. According to participant feedback, satisfaction increased for the Develop Phase of the programme to +57 (Net Promotor Score), up from +38 the previous year. In total, around 60 mentors offered more than 450 hours of mentorship to the participating companies and received a satisfaction score of 90%, while the programme content was rated as good or excellent by over 80% of participants.



"My experience with OncoStars has been absolutely fantastic. The ongoing engagement and support has helped our firm as we've traversed the uncanny valley between ideation and enterprise. I'd highly recommend it to other entrepreneurs who are looking to take the next step."

John McCarthy,
OncoStars participant and Co-founder and CEO of Pramanta Sciences



THE VENTURE BUILDER INCUBATOR

In 2021/22, we partnered with the University of Edinburgh and the Bayes Centre DDE (Data-Driven Entrepreneurship) Innovation to sponsor places for cancer researchers at the university's Venture Builder Incubator. This programme is designed to help PhD students and early career researchers turn their research into business opportunities, build their skills and secure funding.

In the first year of this new partnership, eight teams were selected for the 14-week tailored programme, of which two saw their company grow and two received additional funding. Overall, the programme was well received by the participants and all the founders stated that they would recommend it to peers.

"Being introduced to a network of Venture Builder cohorts past and present was invaluable," said one of the participants, Dr Estefania Esposito, Co-founder of Therapevo. "They all had different backgrounds, and even when they had similar backgrounds, they all added something: an experience, an idea or an opinion."

Another participant also felt the value of the peer support: "When applying for the Venture Builder Incubator, 10zyme didn't exist beyond a dream in the back of my mind. The programme has given me the confidence to believe in my ideas and invention. I've felt part of an inspiring community, where everyone supports one another, and participants and providers genuinely care about each other's successes."



"Being introduced to a network of Venture Builder cohorts past and present was invaluable."

Dr Estefania Esposito,
Co-founder of Therapevo



CANCER TECH ACCELERATOR



In 2021/22, we joined forces with Capital Enterprise, Roche UK and the Medical Research Council to launch the Cancer Tech Accelerator programme (CTA).

The programme offers researchers the opportunity to compete for funding of £70,000, develop their game-changing idea or innovative technology and build the next big health-tech start-up.

In the first phase of CTA, 127 researchers from 30 different institutes working across 50 projects were supported through the programme. Of these, 34 projects applied for the second phase of funding and seven were successful, each receiving £70,000.

On average, the participants rated the bootcamp and team building exercise of the programme highly (4.2 out of 5).



"CTA has allowed us to develop our artificial organ model repertoire and expand our network of surgeons through Cancer Research UK. We now hope to run a pilot study with oncology surgeons who will be able to use our models for surgical training."

Dr Zhengchu Tan, CEO, OrganA



EUREKA INSTITUTE FOR TRANSLATIONAL MEDICINE

In 2021/22, we partnered with the Eureka Institute for Translational Medicine (Eureka) to deliver their first oncology-focused virtual school.

Eureka aims to build an interdisciplinary community of translational professionals who can inspire, catalyse and sustain translational medicine for the benefit of patients and society as a whole. The oncology focused virtual school is open to early career researchers working in cancer research regardless of their source of funding. In 2021, 36 participants from across the UK took part in the three-day school covering topics that are key to a good translational approach. One of the participants, Dr Laura Wisniewski, noted: "It was the most useful training I have ever been to – I think it will change more than just my career path."

We also selected four Cancer Research UK fellows to attend the Eureka International Certificate Programme in Translational Medicine held in March 2022 in Syracuse, Italy. This course covers the key aspects of translational medicine and other important topics such as leadership skills, team working and creativity in science. Dr Shishir Shetty, a Cancer Research UK Advanced Clinician Scientist and principal investigator at the

Centre for Liver and Gastrointestinal Research at the University of Birmingham, explains: "The course emphasises that translational medicine should be an aspect of our day-to-day work and that we can put the patient at the centre of everything we do from the most basic discovery science right through to drug discovery and clinical trials."



"It was the most useful training I have ever been to. I think it will change more than just my career path."

Dr Laura Wisniewski,
participant



SPOTLIGHT ON MAGDA MEISSNER

Having lost her sister to sarcoma at the age of 41, Dr Magda Meissner knows that the translation of research into patient benefit is often too slow. During her Clinical Trial Fellowship at the University of Cardiff, she took part in the Activate Challenge and the Eureka Institute's International Certificate Course to build her understanding of translation. "Cancer Research Horizons' Entrepreneurial Programme has given me a constant supply of opportunities to discover new things, particularly around how to work with industry and the NHS to help patients," she says.

Now a consultant at Velindre Cancer Centre in Cardiff, Magda divides her time between the genomics lab, the clinical trials unit and the sarcoma clinic. She is also pursuing translation opportunities, for example, spotting tumour DNA in blood samples to speed up cancer diagnosis and guide treatment decisions.



"Cancer Research Horizons' Entrepreneurial Programme has allowed me to discover new things."

Dr Magda Meissner



We would like to say a special thank you to Alison Howe for her generosity and support of our entrepreneurship programmes.



ACCESS TO RESEARCH TOOLS

In 2021/22, we launched CancerTools.org, a non-profit, global community of cancer researchers from more than 175 institutes across six continents. The members contribute research tools and share knowledge to deepen our understanding of cancer, drive innovation in cancer research and accelerate discoveries.



A NEW GLOBAL COLLABORATIVE FOR RESEARCH TOOLS



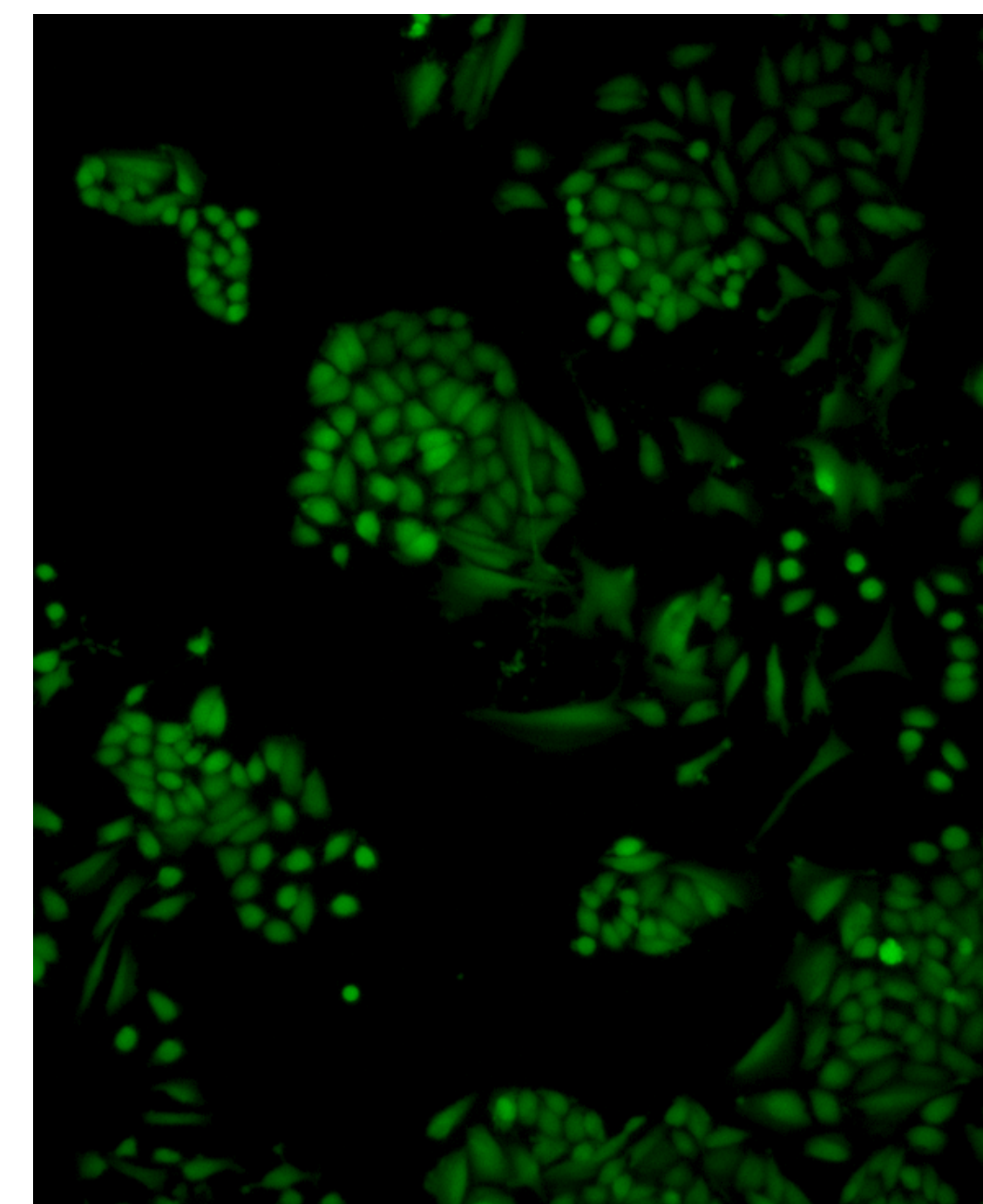
CancerTools.org is a single, accessible web resource that houses a comprehensive portfolio of more than 5,000 unique and innovative research tools contributed by scientists. These tools include antibodies, cell lines, experimental models, organoids and other state-of-the-art technologies, which have been curated and made available to cancer investigators to support their research.

Just before the launch in April 2022, the European Association for Cancer Research (EACR) joined the CancerTools.org community, bringing more than 10,000 members from more than 100 countries who are working across the full spectrum of the field, from basic through to translational and clinical research. This is the first professional organisation to join the collaborative.

“By partnering with CancerTools.org, we will create new opportunities for our members by promoting the concept of contributing research tools to advance cancer research,” said Jane Smith, Chief Executive of the EACR. “This is an exciting opportunity to combine the forces of CancerTools.org and the EACR to expand the portfolio of research tools and make them quickly and easily accessible to cancer scientists worldwide.”

“This is an exciting
opportunity to expand
the portfolio of research
tools and make them
quickly and easily
accessible to cancer
scientists worldwide.”

Jane Smith, Chief Executive, EACR



LN18 Glioma cell lines cultures in a physiologically relevant cell culture media - Plasmax™

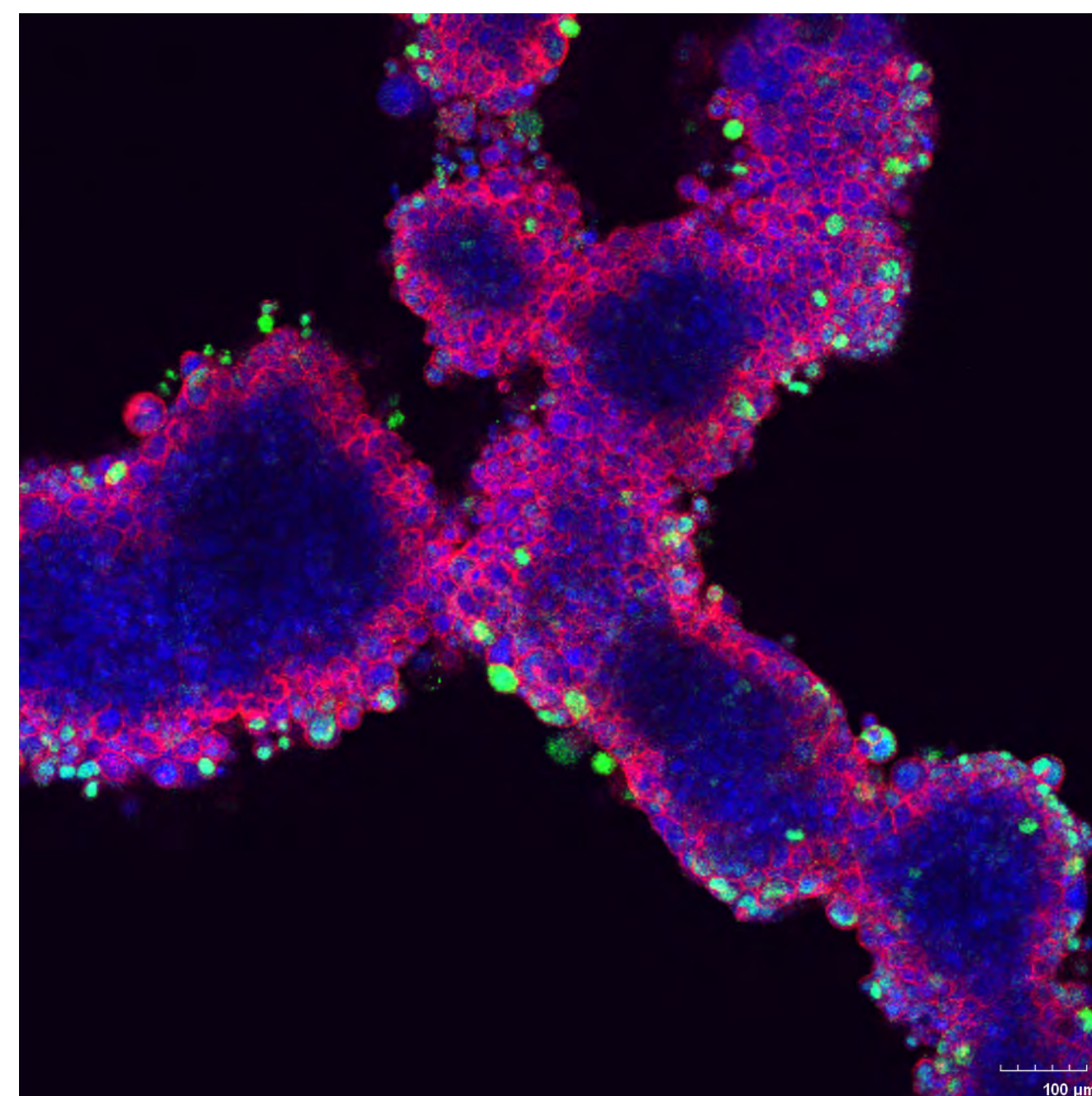


SPOTLIGHT ON MINI ORGANS FROM FUKUSHIMA MEDICAL UNIVERSITY

CancerTools.org has joined forces with Fukushima Medical University in Japan and their technology transfer partner, Summit Pharmaceuticals International, which provides cutting-edge technology and products from all over the world to the domestic pharmaceutical industry in Japan. Together, they will produce patient-derived organoids and distribute them worldwide through CancerTools.org to accelerate the pace of cancer research. This is the first time that primary tumour tissue-derived organoids will be included in the portfolio.

The organoids, called F-PDOs, are well-characterised experimental models derived from people with 15 different types of cancer. They are essentially 'mini-organs' with a similar genetic profile, morphology and physiological nature to the source tumour tissue, which provides a more accurate and patient-specific model to assess the safety and efficacy of drugs in comparison to traditional systems.

"Our collaboration with CancerTools.org will allow us to achieve our goal of making these incredible technologies accessible to other researchers," said Motoki Takagi from Fukushima Medical University. "It's an exciting opportunity for us to demonstrate to our scientists how their research efforts can expand beyond the confines of their own lab and help to accelerate cancer research and the associated discoveries worldwide."



Lung cancer organoid. Red - EGFR positive cells fluorescently labelled with an anti-cetuximab antibody. Green - Ki67 positive cells fluorescently labelled with an anti-Ki67 antibody. Blue - DNA stained with DAPI.



"CancerTools.org will allow us to make these incredible technologies accessible to other researchers."

Motoki Takagi,
Fukushima Medical University



COLLABORATIONS, PARTNERSHIPS AND ALLIANCES

We work closely with our partners to accelerate more discoveries into effective tools, treatments and diagnostics for people with cancer through intellectual property licensing, collaborations, clinical partnerships and longer-term alliances.



UPDATES FROM OUR EXISTING ALLIANCES



Biopharmaceutical company iOnctura is now progressing two novel therapies through the clinic. In late 2021, iOnctura completed a Phase 1a healthy volunteer study for an oral small molecule autotaxin inhibitor discovered by Cancer Research Horizons, called IOA-289. This showed that IOA-289 was well tolerated with no dose-limiting toxicity. The compound will progress to a Phase 1b clinical trial for people with pancreatic cancer, which is planned for later this year.

The company's other lead compound, IOA-244 (PI3 kinase inhibitor), has successfully completed the first part of a Phase 1 trial and is now being tested in people with different solid tumours and blood cancers.

iOnctura was founded in 2017 as a spin out from Cancer Research UK and Merck Healthcare KGaA, with molecules licensed from Merck KGaA and Cancer Research Horizons. They're developing next-generation molecules for pioneering new cancer therapies, focusing on hard-to-treat cancers. In April 2021, iOnctura was awarded the ASAP Alliance Excellence Award in the Individual Alliance Excellence category.



Formed by Cancer Research UK and SV Health Investors in 2016, Artios Pharma Ltd is developing cancer treatments that target DNA Damage Response pathways. One of the projects in-licensed from Cancer Research Horizons was POI θ a DNA polymerase. POI θ is a tumour-specific DDR target involved in microhomology-mediated end joining that is overexpressed in many tumours and found in low levels in healthy tissue. A subsequent drug discovery campaign resulted in the identification of the POI θ inhibitor ART4215, which entered the clinic in September 2021. Interim Phase 1 data supports a well-tolerated safety profile for ART4215 and in August 2022, Artios Pharma Ltd announced a Phase 2 study for ART4215 in combination with the PARP inhibitor talazoparib in BRCA-deficient breast cancer.

In 2021/22, Artios Pharma Ltd also independently in-licensed a small-molecule ATR inhibitor from the University of Texas MD Anderson Cancer Center that has recently progressed into Phase 1b clinical trials. ATR inhibitors are a promising class of new drugs that target the ATR (ataxia telangiectasia mutated and Rad3-related) kinase, which is involved in DNA damage repair.



The successful multi-project drug discovery alliance between Cancer Research Horizons, Newcastle University and Astex Pharmaceuticals has been extended for up to five more years. The alliance, which has already been active for a decade, harnesses the powerful expertise of the partners to identify and develop novel small molecule cancer drugs. Their current portfolio includes projects in target validation, hit identification and the later stages of drug discovery, with an MDM2-p53 inhibitor (ASTX295) currently being evaluated in clinical trials.

"This has been a productive and highly enjoyable collaboration and we are delighted to further extend the alliance term," said David Rees, Chief Scientific Officer at Astex. "Working with the Newcastle University team has brought valuable insights into cancer target biology and complementary technical approaches to those of Astex. We look forward to progressing our partnership further, with the additional backing of the new Cancer Research Horizons."



In 2021/22, our alliance with Merck KGaA, which focuses on the Hippo pathway, filed patents and successfully identified a lead candidate to progress into the clinic. The Hippo pathway controls the size of organs by regulating cell proliferation and apoptosis, and its deregulation has been linked to cancer growth and metastasis. It's a challenging area of biology and this important milestone is testament to patience, tenacity and excellent collaboration and knowledge-sharing of the team since we launched the alliance back in 2015.



SPOTLIGHT ON COLLABORATIONS AND LICENCES

TARGETING BIOMARKERS

In 2022, we launched an exciting five-year collaboration between Boehringer Ingelheim and the Cancer Research UK Manchester Institute's Cancer Biomarker Centre, a team of 95 researchers led by Professor Caroline Dive. The goal is biomarker discovery for a range of compounds from Boehringer Ingelheim's promising pipeline of potential new lung and bowel cancer treatments.

Biomarker-informed patient management is at the very heart of precision medicine, a drive to maximise patient benefit by matching treatments to patients based on the individual characteristics of their cancer. Caroline and her team bring a range of dedicated facilities and specialised skillsets to the collaboration, as well as access to innovative technology

platforms, sustainable biobanking, strict regulatory compliance and large patient cohorts through the Christie NHS Foundation Trust. The collaboration will undertake a broad range of activities, including target studies and efficacy testing, as well as identifying predictive biomarkers of therapy response.



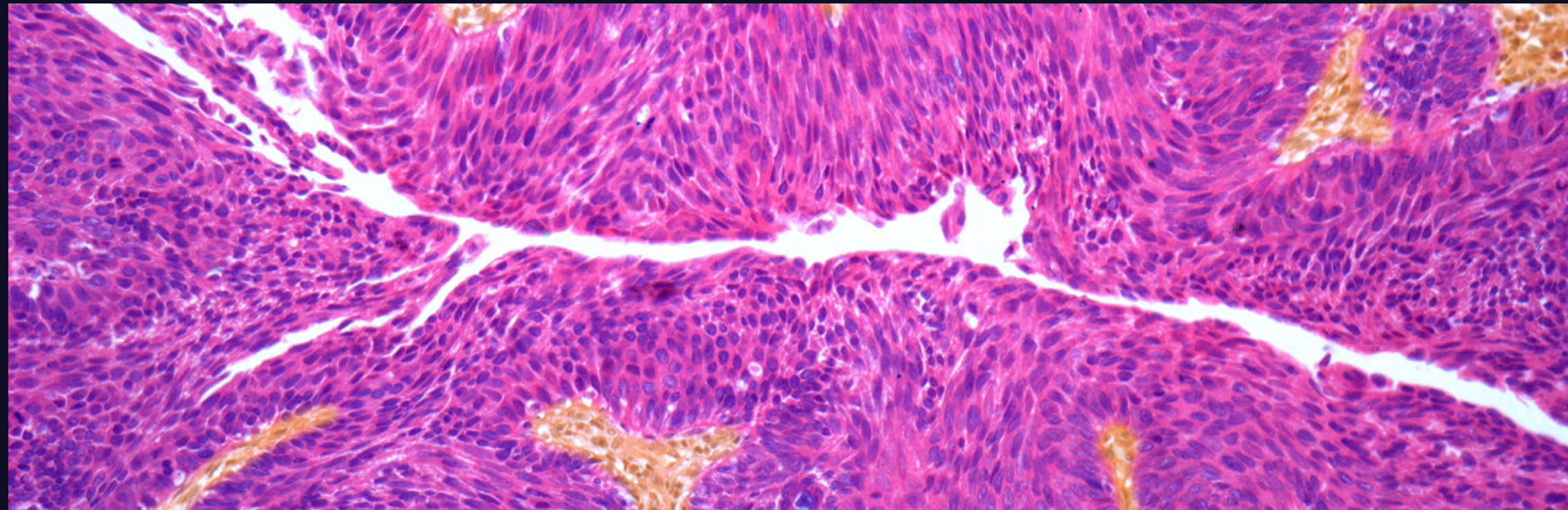
"We're really excited to start working with scientists in Boehringer Ingelheim to advance new therapies to the clinic, with clinic-ready biomarkers to select those most likely to respond."

Professor Caroline Dive,
Cancer Research UK Manchester Institute

A SUPERIOR RADIOTRACER

In 2021/22, we signed a worldwide licence with biotech company Radiopharm Theranostics for the radiotracer Pivalate 18F-Fluoro-Pivalic Acid (18F-FPIA). 18F-FPIA was invented by researchers at Imperial College London, under the guidance of Professor Eric Aboagye, and is based on a short-chain carbohydrate that's very stable and shows superior imaging performance in comparison to clinical standard PET imaging. It was exclusively licensed to Radiopharm Theranostics to be developed for both diagnostic and therapeutic applications.

Radiotracers are radioactive liquids that are injected into the bloodstream several hours before a scan. During this time, the radiotracer travels through the blood and collects particularly in areas where the bone is breaking down and repairing itself. These areas of activity look darker on the scan and can help with the diagnosis of disease.



Bladder cancer cells

A BETTER TEST FOR BLADDER CANCER

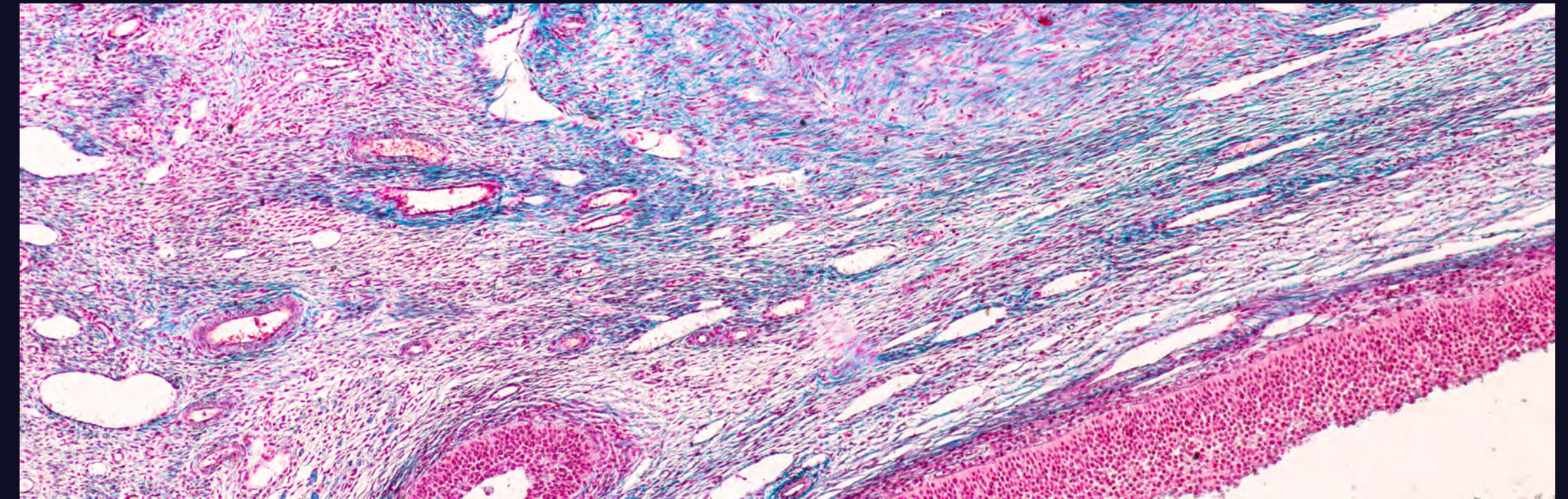
In 2021/22, we partnered with the University of Birmingham and Nonacus, a provider of genetic testing products for precision medicine and liquid biopsy, to develop a non-invasive test for bladder cancer. The test will use highly sensitive liquid biopsy technology developed by Nonacus and a panel of biomarkers, validated by the university's Dr Rik Bryan and Dr Douglas Ward, to diagnose the disease from urine samples.

While the liquid biopsy approach is attractive, identifying the low levels of tumour DNA in a background of DNA from normal tissues

requires highly sensitive analytical techniques to obtain accurate results. The researchers used deep sequencing of 23 genes from tumour samples collected from 956 newly diagnosed, treatment-naïve patients, which identified 451 unique mutations that were present in over 96% of tumours. They also demonstrated that these mutations were identifiable in urine samples collected at the same time as tumour sampling.

Coupling the mutation panel with the unique molecular identifiers and the proprietary target capture technology provided by the

Nonacus Cell3 Target™ will provide a much more sensitive test than the existing PCR-based approach. The researchers are already working on validating this combination in a further 600 cases (including non-cancer cases) and expect the test to be available later this year.



Ovarian cancer cells

ADVANCING INNOVATIVE DRUG TARGETING HSF1 PATHWAY INTO FIRST CLINICAL TRIAL

The past year saw an important milestone in the development of NXP800, a novel oral small-molecule heat shock factor 1 (HSF1) pathway inhibitor that was discovered by the Cancer Research UK Cancer Therapeutics Unit at the Institute of Cancer Research, London. The HSF1 pathway is implicated in cancer cell growth, metastasis, and survival across a variety of cancers.

In preclinical studies, NXP800 inhibited tumour growth in xenograft models of two kinds of ovarian cancer, which are both serious, hard-to-treat diseases. In 2021/22, our partner, the CRT Pioneer Fund

LP (raised and managed by Sixth Element Capital), sub-licensed the rights to develop and commercialise NXP800 to biopharma company Nuvectis Pharma, who have initiated a Phase 1 clinical trial in the UK for people with advanced cancers. We've also entered a collaboration with Nuvectis and the Institute of Cancer Research, London to support the NPX800 development programme.





GROWING THE USE OF IBIS SOFTWARE

In 2021/22, we've completed seven commercial licensing deals for IBIS software, bringing the total to more than 30 active licensees. IBIS software is a risk evaluator tool that incorporates the Tyrer-Cuzick breast cancer risk prediction model. This model, which is used internationally by clinicians, utilises questionnaire-based data, including breast density, family and personal history, and lifestyle and genetic factors, to determine the 10-year and lifetime likelihood of developing breast cancer.



SHARING OUR BREAST CANCER DATA

We continue to licence data from OPTIMAM, our ever-growing database of mammography images, to academic institutions across the world, enabling them to train their machine learning breast cancer diagnostic algorithms and develop systems that have the potential to transform diagnosis of the disease. In 2021/22, the OPTIMAM Steering Committee at Royal Surrey NHS Foundation Trust approved 31 new applications from institutions across 15 countries and four continents. By the end of the year, we completed eight licences to enable the transfer

of mammography data, with another eight in active negotiation.

OPTIMAM comprises processed and unprocessed mammography images from more than 170,000 women, which have been collected through the UK's national breast screening programme since 2008. A unique element of OPTIMAM is its pseudo-anonymisation system, which links images and clinical outcome data.



TARGETING IMMUNOMETABOLISM

In 2021, we announced an exclusive development and commercialisation licence to biotech company Sitryx, which is backed by a leading transatlantic investor syndicate that includes the company's founders, SV Health Investors. The licensed rights originated at Cancer Research UK's Beatson Institute in Glasgow and comprise small-molecule inhibitors of a promising new target. This target plays a critical role in immunometabolism, a fast-emerging area of investigation into the role of metabolic pathways in immune cell function. Changes to these

pathways have been shown to be pivotal in the development of several severe diseases, including a range of autoimmune conditions and cancers.

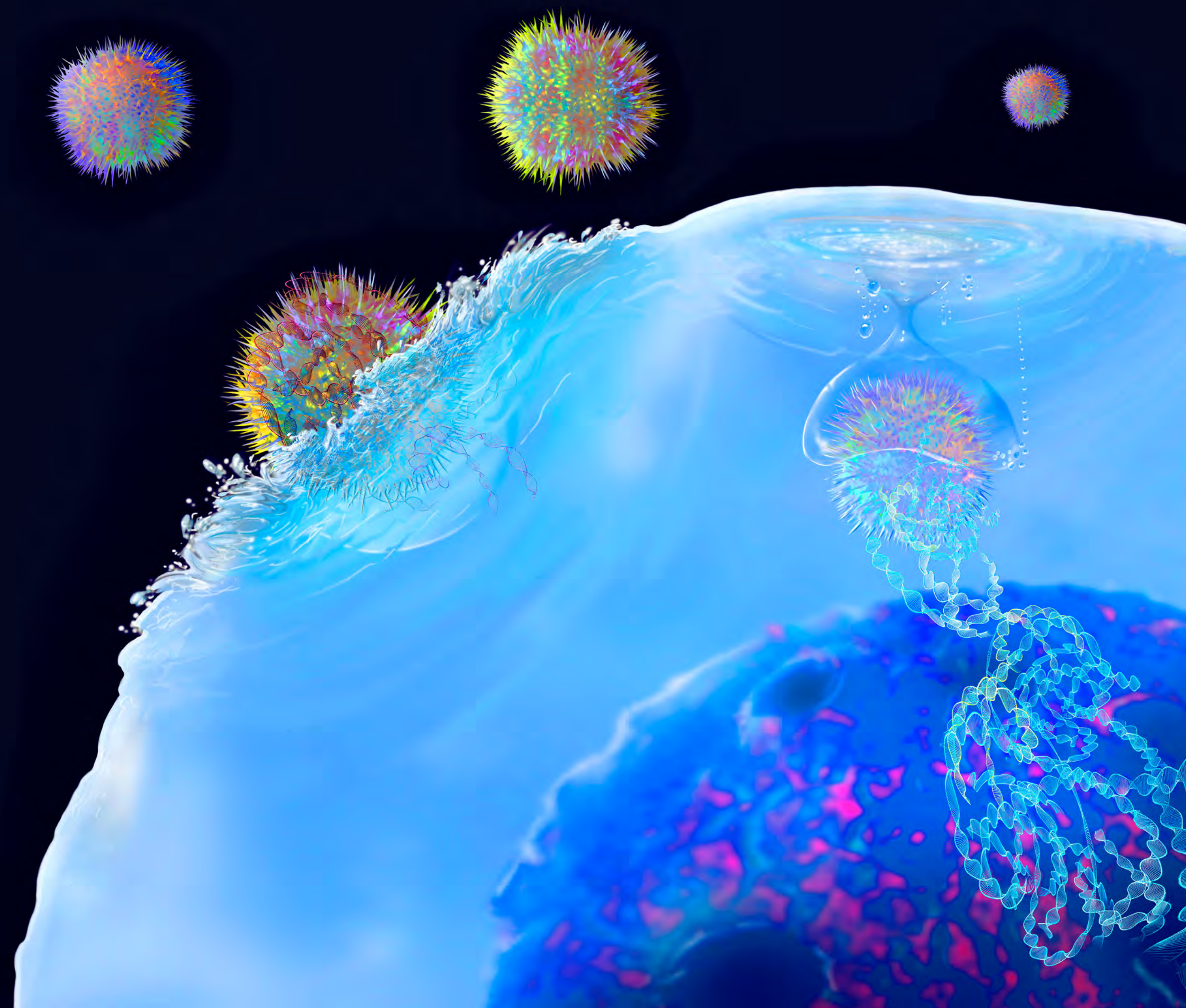
Under the terms of the agreement, Cancer Research Horizons is eligible to receive development, regulatory and commercial milestones and royalty payments on potential sales from immunometabolism targeted therapeutics developed by Sitryx.



BRINGING A NEW CAR T-CELL THERAPY TO PATIENTS

In 2021/22, we partnered with US biotech company Aleta Biotherapeutics to collaborate on the early clinical development of Aleta's CAR T-cell engager candidate, which has been developed to treat people with B-cell lymphoma and leukaemia whose disease has progressed after CD19 CAR T-cell therapy. As a bi-specific engager of the cellular receptors CD19 and CD20, the ALETA-001 drug aims to redirect residual CD19-targeted CAR T cells from a patients' original treatment to cancer cells that have lost the CD19 receptor from their surface but still retain CD20. This re-targeting may provide a cost-effective way to harness an existing treatment for certain patients, rather than giving them a further round of cell therapy.

Under the terms of the partnership, Cancer Research UK's Centre for Drug Development will fund, sponsor and conduct the Phase 1/2a clinical trials of the ALETA-001 drug together with the University Hospitals Birmingham NHS Foundation Trust in the UK. When the recommended dose of ALETA-001 for Phase 2 development has been determined, Aleta intends to launch a multi-centre, single-arm Phase 2 trial in the US focused on diffuse large B-cell lymphoma patients. Aleta will also retain the rights to further develop and commercialise ALETA-001 and will receive a license to the results of the clinical trials that Cancer Research Horizons run in return for milestone and royalty payments.





SPIN-OUTS AND INVESTMENTS

During the year, three new spin-out companies were launched in which we hold founding equity, while our portfolio of existing spin-outs raised over £440m, bringing the total capital raised by our portfolio to date to more than £2.8bn.



NEW SPIN-OUT COMPANIES



In 2021/22, we launched ManTRa DX, a diagnostics development company spun out of the University of Manchester. The company is looking at a way to assess low levels of oxygen in solid tumours, known as hypoxia, which is associated with resistance to treatment and a poor prognosis. Around half of solid tumours will be hypoxic, which reduces the efficacy of surgery, radiotherapy and many cancer drugs. However, there is currently no way to measure the level of hypoxia in tumours in routine clinical practice.

ManTRa DX has developed tumour-site-specific gene expression signatures to assess hypoxia, which could be used to direct therapy choices and therefore deliver major advances in personalised cancer medicine.



A new company spun out of the University of Edinburgh in 2021/22, BioCaptiva is developing BioCaptis – a revolutionary cell-free DNA (cfDNA) capture device that has the potential to transform liquid biopsy testing and enhance cancer detection. The company is solving the problem of insufficient cfDNA input by harnessing the capabilities of apheresis to separate the blood sample so that their new system, Biocaptis, can capture cfDNA directly from volumes of plasma that are impractical to process using existing methods. This delivers quantities of cfDNA equivalent to over 100 individual blood draws from one patient.

By providing higher quantities of cfDNA, this technology potentially allows the testing of a far greater number of cancer types and stages in a much wider range of patients, improving early diagnosis and monitoring of disease and enhancing clinical trial data.



A spin-out from Cancer Research UK-funded researchers at the University of Cambridge, Stroma Biosciences is developing novel and first-in-class cancer therapeutics by targeting survival signals in the tumour stroma, the structural components holding tumour tissues together. Using a validated disease-activated platform to screen primary tumour samples, their emerging pipeline includes several targets to treat both solid and blood cancers. Cancer Research Horizons has taken a shareholding in Stroma in connection with the IP licences the company has received from the University of Cambridge.





NEW ACQUISITIONS AND LISTINGS

For the first half of 2021/22, the biotechnology funding markets continued to be buoyant, then began to slow. Our portfolio of companies took full advantage of the market conditions raising £443m, with three acquisitions and two of our companies listing on global stock exchanges.



Takeda Pharmaceutical Company Limited announced the exercise of its option to acquire Cancer Research Horizons' spin-out company GammaDelta Therapeutics Limited for a pre-negotiated upfront amount and future potential milestone payments. Focused on exploiting the unique properties of gamma-delta T cells, GammaDelta's cell therapy platforms include technologies designed to generate both blood- and tissue-derived allogeneic immunotherapies for the treatment of solid and blood cancers.



Takeda Pharmaceutical Company Limited also exercised its option to acquire Adaptate Biotherapeutics, a spin-out from GammaDelta Therapeutics Limited with support from Cancer Research Horizons, Kings College London and the Francis Crick Institute. Adaptate is developing therapeutic antibodies designed to modulate the activity of a patient's own cytotoxic gamma-delta T cells in situ. Their approach offers the potential to safely and effectively address the challenges often encountered by current cancer immunotherapies.



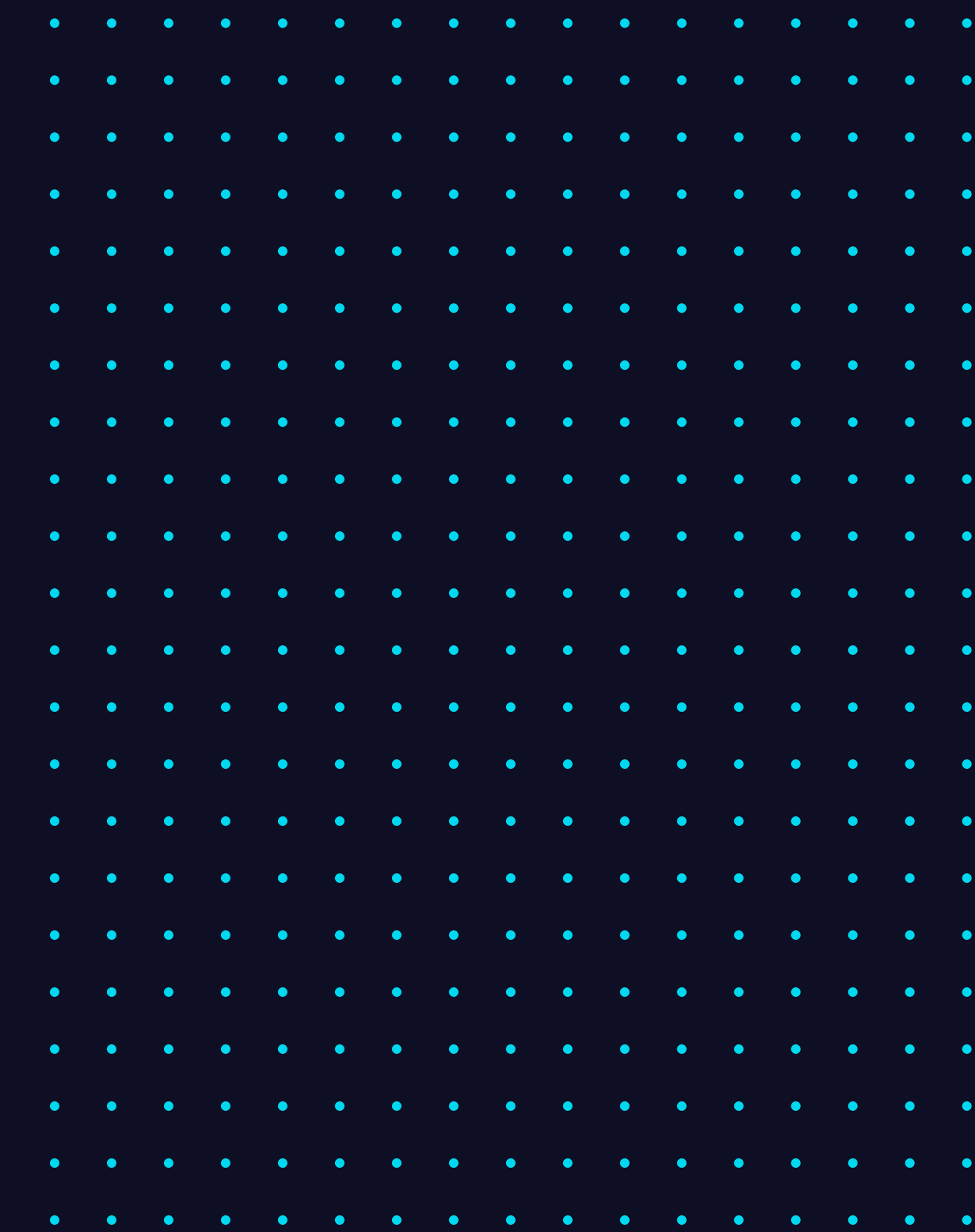
NeoGenomics Inc acquired Inivata Ltd, a clinical liquid biopsy company focused on harnessing the potential of circulating tumour DNA, for \$390m. Inivata's technology platform is based on pioneering research from Dr Nitzan Rosenfeld at the Cancer Research UK Cambridge Institute.



Molecular glue-based precision medicine developer Monte Rosa Therapeutics underwent an initial public offering on the NASDAQ market, raising \$255.6m. Formed in 2018 by Cancer Research UK, the Institute of Cancer Research, London and Versant Ventures, Monte Rosa is a biotech company that's developing a portfolio of novel small-molecule precision medicines that employ the body's natural mechanisms to selectively degrade therapeutically relevant proteins.



Achilles Therapeutics plc closed an initial public offering on NASDAQ, raising proceeds of \$175.5m. Achilles is a clinical-stage immuno-oncology biopharmaceutical company developing precision T-cell therapies to treat multiple types of solid tumours. The company was formed in 2016 by Cancer Research UK and Syncona Ltd, with the support of UCL Business and the Francis Crick Institute.



SUSTAINABILITY

We're driving award-winning sustainable practices in cancer drug discovery.





TWO NEW AWARDS TO RECOGNISE OUR SUSTAINABILITY PRACTICES



Developing new treatments involves significant time, effort and resources, including large amounts of energy and water as well as many single-use plastic items and solvents, which create large amounts of waste. To minimise our environmental impact, in 2021 our London and Cambridge-based Cancer Research Horizons labs joined two sustainability programmes: Green Impact and LEAF (Laboratory Efficiency Assessment Framework).

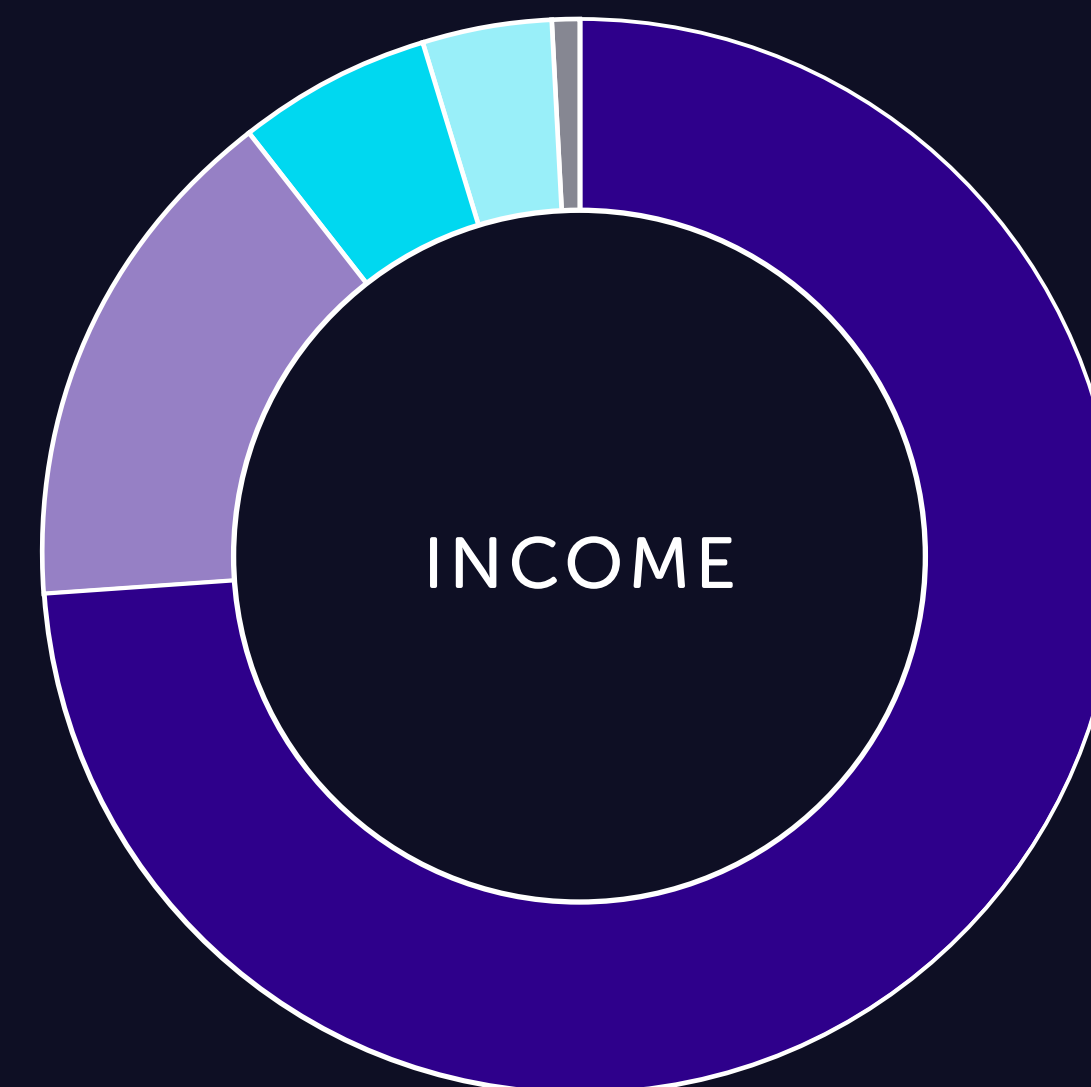
With representatives across all the departments, we were able to tackle different issues and brainstorm solutions that ultimately led to a reduction in resource use and waste. We're now proud to hold the LEAF Silver Award 2022 for our labs at the Babraham Research Campus in Cambridge and the Francis Crick Institute in London, and the Green Impact Silver Award 2021 for our labs at the Crick and the Cancer Research Horizons-AstraZeneca Functional Genomics Centre in Cambridge.

We also have a number of passionate sustainability ambassadors, who drive the transition to more sustainable research practices and promote Cancer Research UK's mission to become a sustainable organisation.

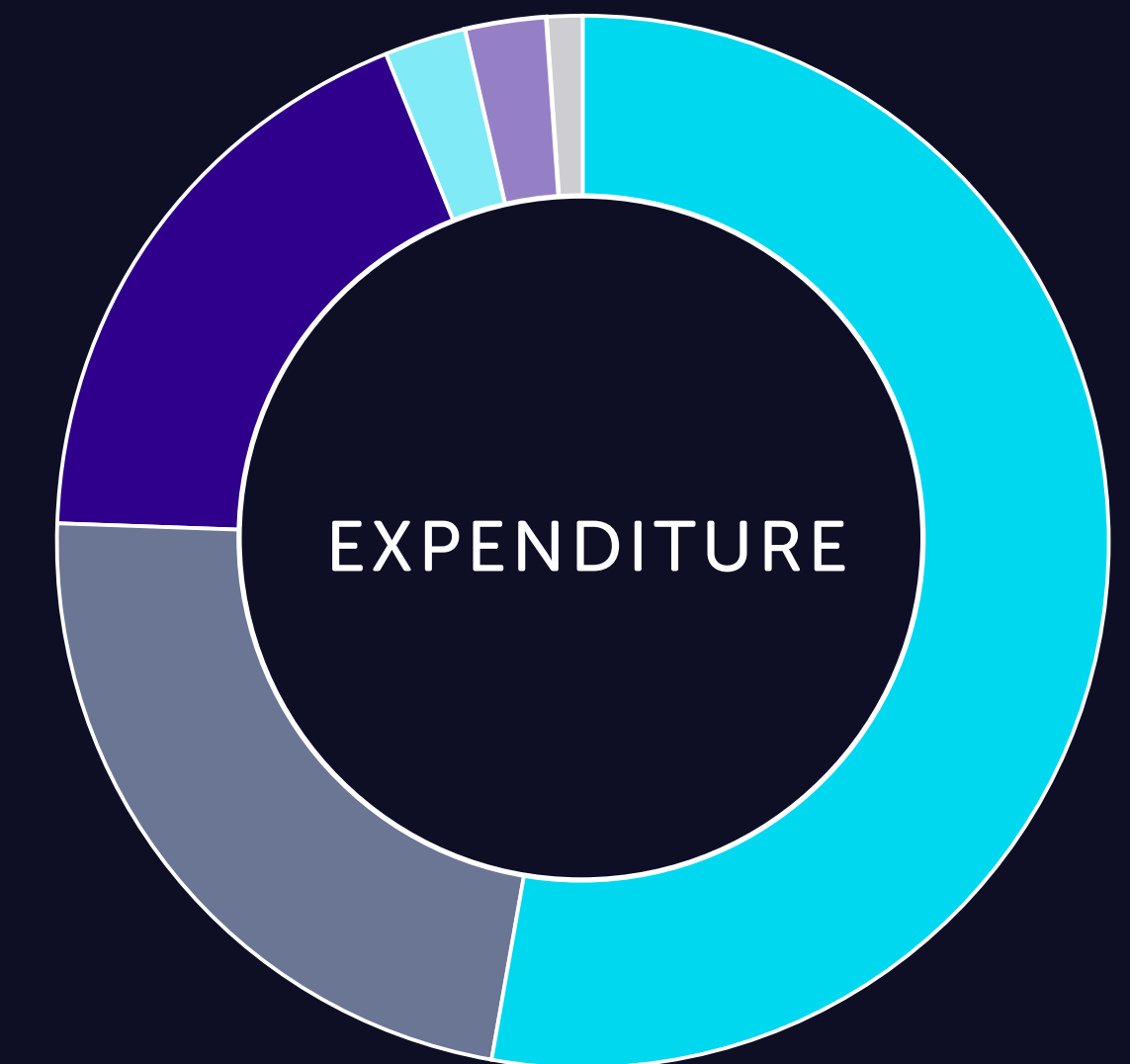




CANCER RESEARCH HORIZONS FINANCIAL ACTIVITY



INCOME		£'000s
Key Royalty Streams		69,273
Therapeutic Innovations Streams		14,638
CancerTools Reagents Business		5,477
Other Licensing Activities		3,698
Other income		593
Total Income		93,678



EXPENDITURE		£'000s
Distributions to Partners		32,121
Other Operating Costs		13,796
Staff Costs		11,146
Drug Discovery Project Funding		1,534
Patent Expenditure		1,417
Investment in Entrepreneurship		608
Total Expenditure		60,623



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Company Secretary



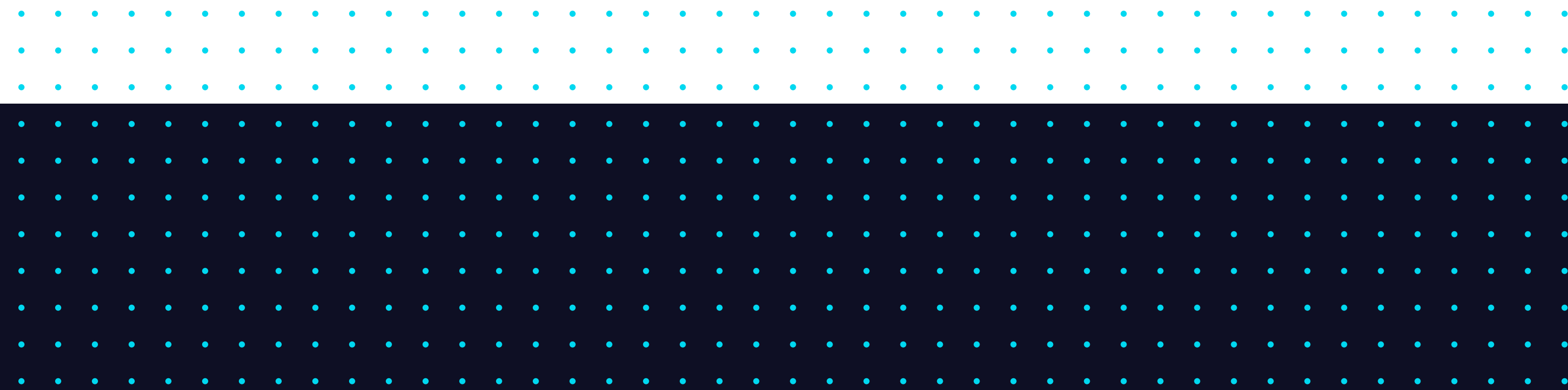
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Chief Business Officer



MICHELLE MITCHELL
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(observer)



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Chief Operating Officer,
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(observer)





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TONY HICKSON
Chief Business Officer



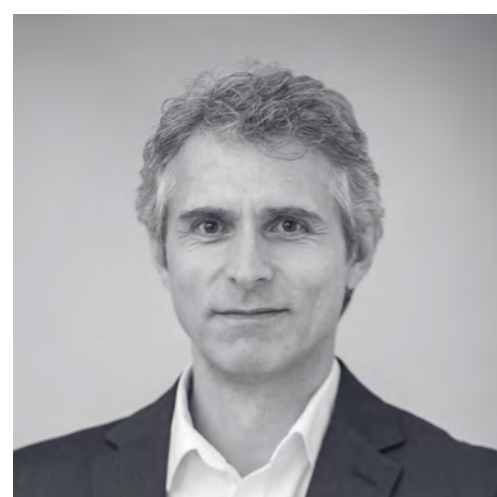
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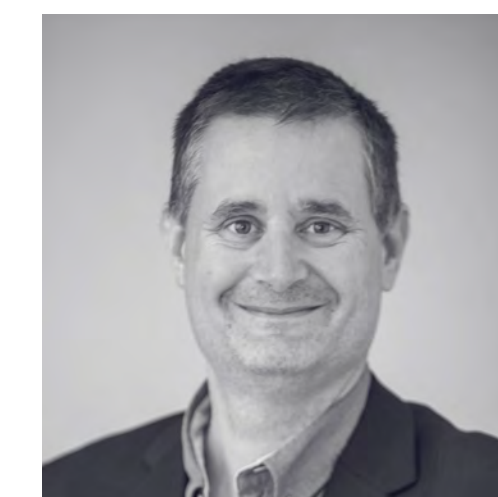
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Strategic Alliances



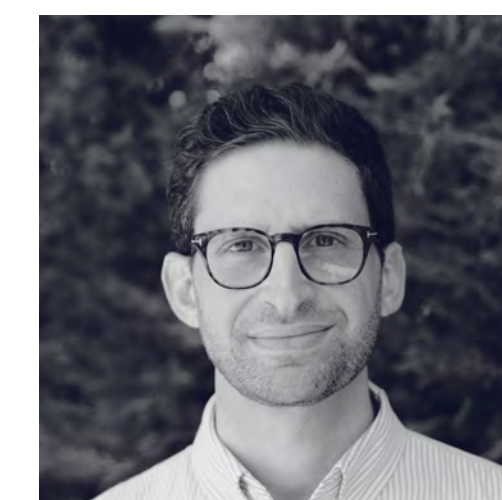
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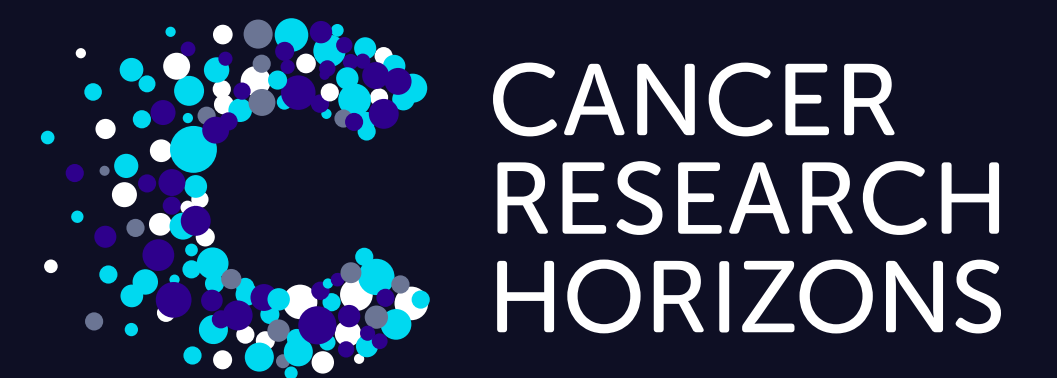
GEORGE TZIRCOTIS
Partnerships Lead

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can help you develop new products.

Help us bring forward the day when
all cancers are conquered.

horizons@cancer.org.uk



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