ANNUAL REVIEW 2022/23 FURTHER FASTER TOGETHER



INTRODUCTION

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Welcome to the 2022/23 annual review for Cancer Research Horizons, the innovation arm of Cancer Research UK. Cancer Research Horizons comprises extensive commercialisation and drug discovery expertise and platforms to translate Cancer Research UK's research outputs into patient and public benefit.

A statement from lain Foulkes

lain Foulkes Chief Executive Officer, Cancer Research Horizons

Cancer Research Horizons marks year one

Cancer Research Horizons was built to operate at the interface between world-class research labs and industry partners – it is an engine that will accelerate the translation of cutting edgescience into innovations available to patients around the world.

A year ago, we drove a significant amount of change to form Cancer Research Horizons. We brought together six research units into one drug discovery organisation under one leadership team and provided more funding to advance novel, much-needed therapeutic approaches. We created the Ventures team, with access to a seed fund, which is helping to create exciting new startups; we created an in-licence team that can advance cutting edge early clinical programmes in partnership with an extraordinary network of early-stage clinical experts; and we strengthened our programmes to help support a talented generation of new entrepreneurs.



"A year ago, we drove a significant amount of change to form Cancer Research Horizons"

Cancer Research Horizons represents a critical part of Cancer Research UK's translational infrastructure. As a result of our work, there are currently 11 drugs on the market that have resulted in over six million courses of treatment to patients worldwide; over £600m has been delivered back to Cancer Research UK and its partners to further advance cancer research; and our startup companies have raised over £3bn in external investment to date to support R&D.

Partnership is key to everything we do at Cancer Research Horizons. Be that with Cancer Research UK-funded academics in partner institutions, the venture community that helps us take the necessary risks to accelerate the advance of new products, or the biopharma industry that helps us develop the treatments of tomorrow.

More specific to 2022, we saw progress in an alternative treatment option for breast cancer in patients who become resistant to existing therapies with the positive Phase 3 results of capiversatib – a new form of protein kinase B inhibitors. This drug is the result of a partnership that spans the Institute of Cancer Research, Cancer Research Horizons, Astex Pharmaceuticals and AstraZeneca.

This year, Cancer Research Horizons has continued to take on the tough challenges. Rare cancers present such a challenge and globally make up 22% of total cancer diagnosis each year. Despite their prevalence, the patients who suffer from these cancers have few if any treatment options. In 2022, our Centre for Drug Development (CDD), with the help of Cancer Research Horizons, launched DETERMINE, the first UK-wide national precision medicine trial in rare cancers, testing a range of therapies specifically targeting key genetic changes in cancer cells. This open platform trial, managed by the CDD and University of Manchester, provides an opportunity for different pharmaceutical companies to investigate whether an existing licensed drug could also benefit patients with rare cancers. Two major pharmaceutical companies are currently collaborating with the platform trial.

Sustaining strong bridges between academic researchers and industry is integral to our ability to keep the ground-breaking ideas and discoveries flowing to patient benefit. This year we were therefore pleased to see Astex extend its 15-year alliance with Newcastle University and Cancer Research Horizons, for five more years.

The Cancer Research Horizons Innovation & Entrepreneurship Awards 2022 marked our inaugural event for recognising the UK's most innovative and enterprising efforts to translate discoveries into benefit for cancer patients. The evening succeeded in highlighting the accomplishments of the UK's biopharmaceutical entrepreneurs, but I was especially pleased to hear the buzz of conversation that permeated the event as early career entrepreneurs engaged with serial entrepreneurs and seasoned CEOs. You can catch a glimpse of the evening and learn more about the winners in this review.

With 18.1 million new cases of cancer diagnosed worldwide in 2020, and data suggesting that number will increase to 28 million by 2040, our dedication to advancing outstanding science to unlock new innovations to treat unmet clinical need is unwavering. I hope you find this review inspiring and a demonstrable commitment to working in partnership to deliver benefits on behalf of patients everywhere.

Executive leadership team



Tony Hickson Chief Business Officer, Cancer Research Horizons

This year Cancer Research Horizons marked the first anniversary since fully integrating the Commercial Partnerships division with Therapeutic Innovation's drug discovery capabilities, as well as a season of sustainability and growth for the Commercial Partnerships team and our portfolio.

Against the industry background of the IPO window remaining largely closed, and venture investors tightening their belts, our Search & Evaluation function helped the organisation rise to new levels of engagement with principal investigators and, in meeting with unique companies, the commercial teams demonstrated a similar uptick. In 2022/23, the number of patent filings and active licencing agreements we concluded continued to climb. During the same period, we took equity interests in seven startup companies, bringing the total in the portfolio to 68, which together have raised over £3bn of investment to date.

This season also included Cancer Research Horizons raising its profile socially and politically. The inaugural Cancer Research Horizons Innovation & Entrepreneurship Awards was held this year. This black-tie event succeeded in highlighting some of the rising stars of the UK biopharmaceutical industry, with the constant hum of conversations and exchanges between burgeoning and seasoned entrepreneurs rivalling the compelling award announcements and speeches. Similarly, when the UK government proposed cutting R&D tax credits for innovative companies to combat tax fraud, Cancer Research Horizons worked closely with Cancer Research UK's policy team to highlight the impact this would have on our ability to grow companies and translate breakthrough ideas that deliver benefits for cancer patients. In the meantime, our CancerTools.org business established a new way to engage with academic partners in a unique collaboration with the Fred Hutchinson Cancer Center, and we have continued to fund the gap between discovery research and industrial development via our Therapeutic Catalyst and Data Innovation Awards to build a healthy portfolio of propositions for the future.

Looking to the horizon, our teams and networks remain poised to translate innovations, both great and small, and act as a trusted partner for industry, investors and academia. We look forward to working with you in the future.

Hamish Ryder

Chief Executive Officer, Therapeutic Innovation Cancer Research Horizons

The past year has been one of bedding-in and full integration of the Therapeutic Innovation team, following our formal launch in April 2022. A key goal for our first year of operation was to define a five-year strategic plan, centred on the Cancer Research Horizons mission and our ambition to double the number of potential breakthrough therapies originating in Therapeutic Innovation that advance to clinical trials.

In March 2023, the Cancer Research Horizons Board approved the plan which is founded on three pillars:

- Accessing world class science to drive portfolio build
- Enhancing selected capabilities in early drug discovery to accelerate a larger, more novel portfolio
- Partnership to underpin all aspects of operation, but particularly later stage drug discovery to ensure we can move a significant portfolio forward at pace



Portfolio generation has been a key focus for the new organisation, with engagement and collaboration with the Cancer Research UK-funded science network, including Cancer Grand Challenges, as a top priority. We have also increased our academic reach through establishing five-year agreements with the Oncode Institute (Netherlands), the Karolinska Institute (Sweden) and the Experimental Drug Discovery Centre (A-STAR Singapore), which have begun very positively.

Two of our in-house initiatives are demonstrating great value in eliciting novel ideas and approaches. The Functional Genomics Centre goes from strength to strength, developing ever more sophisticated capabilities in pooled CRISPR screening, and applying them in target identification strategies, and our Therapeutic Catalyst response-mode funding scheme has now evaluated over 50 proposals and funded nine exciting and novel projects.

Our commercial partnership portfolio landscape is also shifting, with the completion of the terms of our alliance with Bristol Myers Squibb on mRNA translation. Several new partnership discussions are advancing, and we anticipate announcing several in the coming year.

In terms of the portfolio of drugs in development that we have contributed to we were pleased to see several clinical advances over the course of the year, including the achievement of FDA Orphan Drug status and an MHRA Innovation Passport for roginolisib (iOnctura) in metastatic uveal melanoma, the initiation of a Phase 1b trial in pancreatic cancer with our autotaxin inhibitor (IOA-289, iOnctura), and the initiation of Phase 2 of the Pol0 inhibitor ART4215 in combination with a PARP inhibitor in BRCA deficient breast cancer (Artios).

The progress of these clinical programmes serves to maintain our desire and drive to translate the best science towards better outcomes for patients, and continued sourcing and progression of novel approaches will remain our focus in the coming year.

EXECUTIVE SUMMARY

Read about the events and achievements that have defined Cancer Research Horizons' 2022/23 financial year.



FURTHER FASTER TOGETHER: We are beating cancer

A year of growth and expansion characterise Cancer Research Horizons' 2022/23 financial year, as our organisation marked its first year since uniting the strengths of our established drug discovery engines with our network of world-class biology, cutting-edge technology platforms and clinical expertise. Cancer Research Horizons exists to beat cancer, by taking cutting edge innovations from the lab bench to the bedside, translating them into effective treatments and diagnostics for cancer patients. Changing our approach to drug discovery and commercialisation enhanced coordination across the organisation, the performance of existing programmes and teams and augmented the launch of new initiatives, all dedicated to the common goal of translating discoveries into clinical benefits for patients and society.

During the last financial year, the total income generated from royalty, Therapeutic Innvovation, and other income streams and activities reached £79m. Cancer Research Horizons reinvested £22m in Cancer Research UK after sharing with partner institutes and deducting operational costs, including the cost of employing almost 250 people. The organisation supports drug discovery research facilities nationally, with sites based in London, Cambridge, Newcastle and Glasgow, as well as occupying offices in London.

Notably, the Cancer Research Horizons Ventures team launched a new Seed Fund and took equity interests in seven startup companies. These equity interests grow the total number of startups in our portfolio to 68 companies. Additionally, the inaugural Cancer Research Horizons Innovation & Entrepreneurship Awards, an event that celebrated the UK's most innovative and enterprising efforts in oncology, took place in November 2022.

The Cancer Research Horizons Search & Evaluation teams met with over 470 principal investigators, leading to 118 invention disclosures and 45 patents filed. The Commercial Partnerships team signed 106 commercial deals established to advance novel assets and platforms with the potential to deliver clinical benefits to cancer patients.

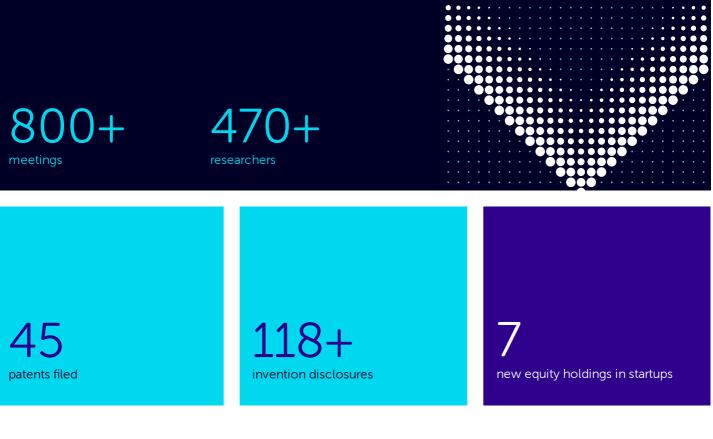
During 2022/23, the total number of active licensing agreements and agreements with unique partner companies reached 448 and 505, respectively. These numbers include the activities of two divisions: Commercial Partnerships and CancerTools.org. In this review, you will find numerous examples of innovative research and development collaborations along the entire diagnostic and drug discovery and development continuum. At the heart of each of them is a principal investigator or team of researchers championing discoveries and innovations that promise to change the cancer landscape.



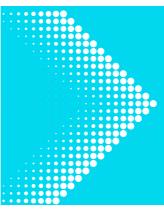
OUR IMPACT

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





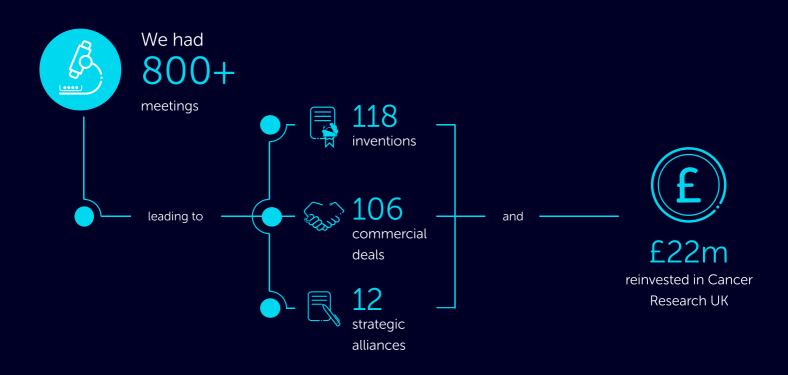


£79m total gross income





1 in 10 treatments or the equivalent of over six million courses* of treatment enabled worldwide through Cancer Research UKfunded research



*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. The patent on abiraterone expired in October 2022.

Therapeutic Innovation

5 S Projects arising from in-house drug	Therapeutic Innovation teams worked on: 35 Drug discovery and development projects			
discovery are currently advancing through clinical trials with partner organisations	Including: 24 Drug discovery projects 11 Drug development projects			

News: taking breast cancer treatment one step further

In October 2022, AstraZeneca reported positive results from CAPItello-291 Phase 3 clinical trial for the cancer drug capivasertib, a first-in-class therapeutic derived from a collaborative drug discovery programme between AstraZeneca, Astex Pharmaceuticals, the Institute of Cancer Research, and Cancer Research Horizons. The clinical trial success moves a much-needed new therapeutic option one step closer to reaching breast cancer patients who suffer a recurrence or disease progression following endocrine therapy.

Capivasterib targets protein kinase B (PKB), also known as AKT, an enzyme associated with the hallmark characteristics of a cancer cell including the promotion of survival and growth, cell proliferation and migration, and even angiogenesis. Hormone receptor status directly influences the number of treatment options available to breast cancer patients. Trial participants demonstrated hormone receptor positive and human epidermal receptor 2 (HER2) negative, a genetic disposition associated with 70% of the breast cancer population. Broadening the therapeutics options for these patients, capivasterib is the first clinical asset to reach Phase 3 from a dedicated discovery platform for developing and commercialising novel small molecule inhibitors of PKB to use as anticancer agents.

Trial participants received either capivasterib in combination with Faslodex (fulvestrant), a standard treatment for metastatic breast cancer or Faslodex and placebo. The trial demonstrated a statistically significant improvement in progression-free survival in the group of patients treated with capivasterib, in comparison to the placebo group.

CULTIVATING TRANSLATIONAL DISCOVERIES

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Cancer Research Horizons cultivates translational discoveries and business concepts in three ways: meeting with researchers, offering grants, and giving awards designed to catalyse innovative research and highlight entrepreneurial achievements.

Search & Evaluation

Over the past year, we've continued to provide a transparent and customer-centric service to our researchers. Our Search & Evaluation team has resumed in-person interactions and worked hard to support researchers in their translational endeavours.

We have had a very positive year and continue to see an increase in invention disclosures compared to the previous year.

We met with hundreds of principal investigators, both virtually and in person, in places where researchers shared their discoveries and discussed how to translate them into patient benefit.

In 2022/23, the average time from disclosure to formal decision was 60 days; 92% of disclosures received a decision within our committed timeframe of three calendar months (up from 86% in the previous year).

In total, we engaged more than 470 principal investigators, established 118 invention disclosures and filed 45 patents.



12 projects granted translational funding support

In 2022/23, we granted Translational Funding Awards to 12 projects across 11 institutions, ranging from in-vivo proof-ofconcept studies to key reagent or product generation. These awards support our researchers to move their ideas towards patient benefit.

"This funding provided us with critical resources to translate our preliminary findings on cytokine modifications to preclinical models in the hope of designing more efficacious therapies for haematological malignancies."

Ian Hitchcock, University of York



"This award will enable us to commence a multicentre UK study that intends to validate the use of tear fluid as a proximal liquid biopsy for early detection of brain cancer." **Petra Hamerlik** University of Manchester

Spotlight on tear biomarker profiling for early detection of brain cancer

Non-specific early symptoms of brain tumours can contribute to diagnostic delays and possible disease progression. General practitioners (GPs) seeing patients with non-specific symptoms should be able to identify patients who warrant further investigation without an increase in unnecessary brain imaging, which may expose incidental abnormalities. Consequently, there is a high unmet need for an affordable and accessible screening/triage tool in primary care. The University of Manchester's Professor Petra Hamerlik has a tool that aims to meet that need.

Tear samples are increasingly being used for the diagnosis of various ocular surface disease states such as diabetic retinopathy, allergy and dry eye. Unlike the collection of blood or cerebrospinal fluid, tear collection is non-invasive. Despite its proximity, it hasn't been explored for brain cancer diagnosis. Hamerlik's pilot study interrogated the utility of tear-bound proteome to differentiate brain cancer patients from healthy volunteers. Her team developed a tear-protein-based classifier that can differentiate brain cancer patient protein-based classifier that can differentiate brain cancer yatient protein the utility of the utility of

Dr Qiang Wang University of Edinburgh

Spotlight on early detection of lung cancer

Lung cancer is the leading cause of cancer death worldwide. Most lung cancer patients are diagnosed at a late stage, leading to poor survival rates; approximately 13% of patients survive five years. Early detection, and fast and reliable characterisation of lung cancer will enable the treatment of more patients and potentially improve their chances of survival.

Currently, there is no routine screening for lung cancer. Chest X-rays do not provide a definitive diagnosis because the images do not distinctly distinguish cancer and other conditions. To address this unmet need, Dr Qiang Wang from the University of Edinburgh is working to improve diagnosis by characterising lung cancer, applying artificial intelligence to ensure the disease is recognisable during an endoscopic procedure.

"We secured additional funding from Cancer Research Horizons," said Dr Qiang. "Their support was invaluable for enabling the efficient use of valuable patient samples and expanding the capabilities of our technology. It is reassuring to know that Cancer Research Horizons will keep supporting us in developing our technology."



To improve lung cancer diagnosis, the team captures images of lung tissue using a special microscopy technique. They then process these microscopy images using artificial intelligence to diagnose lung cancer and characterise its subtypes.

Dr Qiang Wang started this promising research with support from Cancer Research UK's Early Detection and Diagnosis Primer Award.



"We're very grateful for the exceptional help we've received from Cancer Research Horizons." **Roland Arnold** Birmingham University

Spotlight on the Bladder Cancer Prognosis Programme

Bladder cancer is the 10th most common cancer worldwide, with over 500,000 new cases of bladder cancer diagnosed each year. Even with effective surgery, chemotherapy and radiation, advanced bladder cancers are difficult to treat.

At Birmingham University, Professor Richard Bryan, Dr Benjamin Tura and Dr Roland Arnold are developing a searchable and user-friendly 'data warehouse' by optimising the linkage of existing and future Bladder Cancer Prognosis Programme (BCPP) clinical and laboratory-based (omics and digital pathology) datasets.

BCPP is a complex and comprehensive compilation of datasets derived from analysing bladder cancer samples collected over a 10-year span. The compilation follows programme grant funding by Cancer Research UK for compiling genomic, transcriptomic and proteomic data sets. The BCPP biospecimen collection is linked to longterm clinical outcomes and existing genomic, transcriptomic and proteomic datasets, and represents one of the most significant bladder cancer research resources in the world for both academia and industry.

With support from Cancer Research Horizons, the BCPP were given one of the first Winton CRUK Data Innovation Awards for the creation of a searchable and user-friendly BCPP data warehouse, allowing more streamlined commercial exploitation of the datasets. "We're very grateful for the exceptional help we've received from Cancer Research Horizons," said Dr Roland Arnold. "They introduced the BCPP team to the opportunity of the Winton CRUK Data Innovation Award and were very supportive throughout the application process. The Data and AI team have been instrumental in our company interactions. The award will allow us to make our data available in a structured way, to make it AI-ready and hence will multiply the value of our data for research and patient benefit."

Since its start in October 2022, the award has proven to be extremely beneficial to the research team, and the BCPP database has already resulted in enquiries from both academic and company partners.

Winton CRUK Data Innovation Awards

The Winton CRUK Data Innovation Awards are grants that aim to support, through the provision of funding and advice, researchers in increasing the accessibility and utility of data generated from their research. In addition to providing £75,000 that researchers can use to curate, clean or annotate their data, the Cancer Research Horizons Business Development team works closely with the research groups to develop a long-term data sharing strategy to maximise the impact of the data.

Building on the successful launch of the scheme in mid-2021, in 2022/23 we awarded a further two projects: one in mesothelioma led by Professor Kevin Blythe and the other in oesophageal cancer led by Professor Rebecca Fitzgerald. Both awards complement existing and significant Cancer Research UK funding investments with the aim of bringing together disparate datasets into a linked and curated database to simplify cohort building and analysis. The ultimate aim is to develop the data to the stage where it can be the centre piece of collaborations that derive more insights from the data. This is particularly important in mesothelioma where the rarity of the disease means finding high quality data for analysis can be difficult. The Winton CRUK Data Innovation Award given to Professor Blythe's group enables his team to work across NHS and university siloes to link datasets from a variety of different studies and create what will be one of the world's richest collections of mesothelioma data.



Translational focus: Early Detection and Diagnosis Awards

Cancer Research UK's Early Detection and Diagnosis Awards foster the translation of promising approaches to early detection and diagnosis by providing up to £500,000 (for up to four years) to researchers zeroing in on consequential precancerous cells and refining methods to detect them. These funding schemes, which include Primer, Project and Programme awards, support a wide variety of approaches across disciplines and cancer types. Each year, the committee selects over 20 projects that span from early discovery to the clinically advanced.

Nanotech and accessible ovarian cancer diagnosis

Paula Mendes and her team at the School of Engineering, University of Birmingham, are engineering a collection of nanoparticles to develop an affordable test to detect ovarian cancer in the primary care setting. These nanoparticles are superselective for picking up on the presence of glycans (or cell surface sugars) associated with ovarian cancer.

The funding from the project award will help the team to expand the number of superselective nanoparticles for detecting the different glycans associated with ovarian cancer, as well as optimise and validate a few additional glycoproteins for the assay. To select which combination of glycans to use in the final diagnostic test, the team will test the assay using serum samples taken from patients and a control group (Phase 1). During Phase 2, the most diagnostically useful combination of glycans will undergo further clinical validation needed to introduce a diagnostic test into primary care programmes. With about 70% of ovarian cancer cases in Europe diagnosed in the advanced stages of disease, the need for a simple and rapid test is clear.

Biomarkers to detect the emergence of stomach cancer

Gwen Murphy, Senior Research Fellow in the Cancer Screening and Prevention Department of Imperial College London, focuses on understanding the molecular epidemiology of gastrointestinal cancer. To enhance cancer screening and prevention of stomach cancer, Murphy will build on some promising findings to develop a panel of biomarkers for the early detection of stomach cancer using a blood or serum sample. The panel will also potentially elucidate risk stratification for the disease and monitor stomach cancer progression.

With the funding, Murphy will work out whether four biomarkers (ghrelin, vitamin B12, gastrin, pepsinogen 1 and 2), disclosed in her research, may be clinically meaningful precursors to the emergence of stomach cancer. If they are, translating the biomarkers into a routine lab test will require further development and investment. A simpler test is needed to improve early diagnosis and prevention because the current gold standard requires a high degree of technical specialisation (radioimmunoassay).

Therapeutic Catalyst Awards

"The Therapeutic Catalyst Award has been a vital bridge, connecting novel immuno-oncology insights from our academic work, to industrial scale development capabilities within Cancer Research Horizons and its network of partners. This enables accelerated progression of promising targets from bench to clinic, without the usual disconnect and dichotomous nature of purely basic and then purely commercial funding streams."

Dr Kevin Litchfield, University College London

Our Therapeutic Catalyst Awards were launched in late 2021 and have been a great success. The scheme operates as a collaborative venture between research scientists and drug discoverers within Cancer Research Horizons to accelerate the translation of novel ideas for therapeutic discovery. Awards can be up to £250,000 to support a 12–18month proposal.

To date, we have received over 50 expressions of interest (the initial stage of the process), leading to the approval of nine full awards by a panel with external experts. The awards aim to address a wide spectrum of activities, including target identification, target validation, and the development of early chemical assets. Successful awards have been made across the UK, with one also being linked to the USA. Current awards encompass research relevant to the development of therapeutic small molecules, antibodies, and DNA vaccines. Once approved, drug discoverers from Cancer Research Horizons are aligned to each proposal to assist in their development and complement the expertise of the principal investigator, giving the awards a more collaborative feel than traditional funding schemes.

Exciting results are already emerging from the first batch of awards, and we are exploring ways to take these forwards into the next stage of drug discovery. We continue to seek novel proposals from researchers within the UK and beyond who are keen to work collaboratively to accelerate the translation of research into novel therapies for patient benefit.

"Applying for the Therapeutic Catalyst Award was easy. I discussed ideas with the Cancer Research Horizons team. They directed me as to which parts were fundable and how best to position the plan. The proposal was short and the interview was interesting. Within a few months of first discussing the project we were starting the project."

Professor Victoria Cowling, Beatson Institute

Stimulating entrepreneurship

We're building a community of entrepreneurially minded researchers. Through our training, hands-on initiatives 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.

We have 12 active partners and have engaged over 470 researchers in 2022/23.

The Cancer Research Horizons entrepreneurial programmes



Innovation competitions

Innovation competitions providing bespoke oncology-specific entrepreneurial training and the opportunity to pitch to, and receive feedback from, expert judges for cash prizes.



Innovation events

Annual Cancer Research Horizons Innovation & Entrepreneurship Awards ceremony and annual Innovation Summits to inform researchers on how to engage in entrepreneurship and network with the local entrepreneurial ecosystem.



Business accelerators

Established partnerships with leading accelerators, ODP2, OncoStars, KQ Labs and Oncology Medtech. Each partnership operates a different model, allowing researchers to opt for the approach that will best serve them.



Training and customer discovery

Training-focused programmes provide the skills needed to develop ideas to meet a clear market need. We have partnerships with NxNW, ICURe Light and the Eureka Institute's translational school.



Mentorship programme

We aspire to create a nationwide mentorship network, providing researcher with one-to-one guidance from business experts to enable them to translate their research into patient benefit.

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Our first Innovation & Entrepreneurship Awards

The Cancer Research Horizons' Innovation & Entrepreneurship awards recognise the efforts and mindset of cancer researchers in innovation and entrepreneurship relative to the translation of discoveries into impactful applications for the benefit of patients. The first event of celebration and networking, a gala black-tie dinner and awards ceremony, was held on 6 December 2022, at the Royal Society.

INNOVATION AND ENTREPRENEURSHIP

We celebrated winners across different categories covering a broad range of entrepreneurial efforts.

2022

AWARDS



Early-career Entrepreneur of the Year

This award celebrates early-career cancer researchers who have shown entrepreneurial initiative and attitude through participation in bespoke training. Susanti Susanti founded PathGen Diagnostik Teknologi to provide affordable molecular diagnostic tools for detecting cancer in developing countries.

Anjui Wu founded Cansor after developing a procedure to identify the ctDNA methylation signature for solid tumours.

Winners: Susanti Susanti, PathGen Diagnostik Teknologi, and Anjui Wu, Cansor Ltd.



Woman Entrepreneur of the Year

This award celebrates the outstanding achievements of women entrepreneurs, at any stage of their career, by establishing businesses or setting up transformative partnerships to benefit cancer patients. Claire Lewis, Professor of Molecular and Cellular Pathology at the University of Sheffield, won for her long-standing commitment to cancer research innovation and entrepreneurship, including running a spin-out company, outlicensing multiple novel cancer therapeutics, and successfully collaborating with numerous commercial partners to develop new cancer drug candidates.

Winner: Claire Lewis, University of Sheffield.



New Startup of the Year

This award celebrates new UK-based companies who have laid the foundations for their new business and raised their first funding round in the last two years. The judges looked for evidence demonstrating a company's potential, including its groundbreaking technology and the possibility to deliver growth and impact in the cancer sector. Adendra is using new insights into dendritic cell biology to create nextgeneration immunotherapies for cancer patients.

Winner: Adendra Therapeutics Ltd.



Startup Achievement of the Year

This award celebrates startup companies that have achieved substantial milestones during the previous two years, such as pipeline developments, closure of financing rounds, and entering strategic partnerships or a significant exit. Achilles is a clinical-stage immuno-oncology biopharmaceutical company developing precision T-cell therapies to treat multiple types of solid tumours. It closed an initial public offering on NASDAQ to raise \$175.5m.

Winner: Achilles Therapeutics UK.

Further, Faster, Together (Industry–Academia Collaboration)



This award celebrates innovation in oncology achieved through industry–academia collaborations, including partnerships, licenses, and knowledge exchange. The iDx Lung Collaboration works alongside the University of Leeds, the NHS Lung Health Checks, and several commercial partners to trial innovative diagnostic tests for the early detection of lung cancer.

Winner: iDx Lung Collaboration.



Two special categories

In addition to the above categories, which undergo the nomination, shortlisting and judging panel processes, we have two special categories to recognise outstanding contributions to the academic cancer entrepreneurial field with the support of Cancer Research Horizons.



Cancer Research Horizons Entrepreneurship Medal

This award recognises an established academic entrepreneur who has created a viable business, demonstrating entrepreneurship and innovation; a person that has made significant, innovative and cumulatively outstanding contributions to enhancing the oncology field. Sir Steve Jackson's research into DNA damage response is crucial to our understanding of cancer and has already led to the development of the drug olaparib, which is used worldwide to treat certain ovarian cancers.

Winner: Sir Steve Jackson.



Cancer Research Horizons IMPACT Medal

This award recognises individuals or teams who have made impactful contributions in the field of oncology by progressing the application of their discoveries. The prize celebrates an inspiring team or an individual whose determination has driven forward the translation and commercialisation of their discovery to achieve patient benefit. Rebecca Fitzgerald and her team developed the Cytosponge, which allows non-invasive sampling of oesophageal cells to test for Barrett's oesophagus, a known risk factor for oesophageal cancer.

Winner: Rebecca Fitzgerald.



The winners at the Innovation & Entrepreneurship awards ceremony.

Case studies

Case study: OncoStars

Launched in 2019, OncoStars is an 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 2022/23, OncoStars received more than 400 applications, with 25 oncology companies shortlisted to join the programme. According to participant feedback, satisfaction increased for the Develop Phase of the programme to +72 (Net Promotor Score), up from +57 the previous year. As it currently stands, 44% of Panacea's founders are women. 92.5% of the participants rated mentorship as very good or excellent and 75% of Develop companies were invited to pitch in front of investors and partners, demonstrating the quality of the selected companies and value added via the programme. Overall the programme content was rated as good or excellent by over 90% of participants.

"The Panacea Stars experience has been invaluable. It has pushed our company to question previous assumptions and to form better strategies through exposure to the gamut of topics involved in starting a biotech/medtech company in intense bootcamps led by experts. Importantly, the networking opportunities are amazing and we have met mentors and fellow biotech entrepreneurs who we will keep in touch with throughout the startup journey."

Tiffany Ma

OncoStars participant and cofounder of GambitBio



Case study: Cancer Tech Accelerator

Our Cancer Tech Accelerator (CTA), in partnership with Capital Enterprise and UKRI-MRC, is now midway through its second programme, CTA2.0, with the impact of CTA1.0 now coming to the fore.

The CTA is a unique accelerator programme that offers researchers and early-stage companies training and extensive mentorship, as well as the opportunity to compete for £70,000 of funding, as they embark on their entrepreneurial journeys to develop innovative oncology medtech and data-driven solutions.

2022/23 saw our CTA1.0 cohort come together for an impressive demo day at the Royal Society of Chemistry where companies pitched to an audience of investors and researchers, and the launch of our second programme, CTA2.0, which received applications from almost 100 teams around the UK and around the globe.

Together, CTA1.0 and CTA2.0 have now provided entrepreneurial training for over 200 individuals and has released £920,000 of non-dilutive funding to selected teams. Importantly, teams from the CTA have cumulatively gone on to raise £15m of follow-on funding, demonstrating the outstanding calibre of the teams, technologies and training within this programme.

"The team delivering the CTA are all both highly experienced and hugely responsive, meaning we always felt like we had access to the right expert at the right time. This allowed us to focus our strategy around a tangible, high-impact business model which we are now executing against."

Peter Bannister Cofounder, Migration BioTherapeutics



The Migration Biotherapeutics team. Left to right: Peter Bannister, Kristin Polman, Davide Danovi.



CTA1.0 demo day, September 2022, Royal Society of Chemistry.



CTA2.0 pitch day, February 2023, IDEALondon.

Case study: Venture Builder Incubator

In 2022/23 we continued our partnership with the University of Edinburgh and the Bayes Centre Data-Driven Entrepreneurship Innovation to sponsor places for cancer researchers at the university's Venture Builder Incubator (VBI). This programme is designed to help PhD students and early-career researchers turn their research into business opportunities, build their skills and secure funding.

Seven teams were selected for the 14-week tailored programme, two of which received additional funding. Overall, the programme was well received by the participants and all the founders stated that they would recommend it to peers.



"Extremely useful programme to begin the journey as a startup. Equips you with crucial tools and info. Would feel lost without all the advice."

Greg Verghese founder of Morph.ai – King's College London

"VBI helped us translate our research into a business and grow our network, and has given us confidence in talking about our company with new collaborations."

Faith Howard and Natalie Winder Cofounders of NANOncolytics – University of Sheffield







VBI participants at the University of Edinburgh.

CREATING AND FUNDING NEW VENTURES

Cancer Research Horizons has a long-standing track record of establishing and growing startup companies. We've played a role in the creation of 68 startups, with our portfolio of existing companies raising in excess of £3bn in total capital. The dedicated Cancer Research Horizons Ventures team is tasked with identifying innovative oncology-focused venture propositions, the exceptional entrepreneurs behind them and accelerating the formation and financing of early-stage startups.



Our new Seed Fund

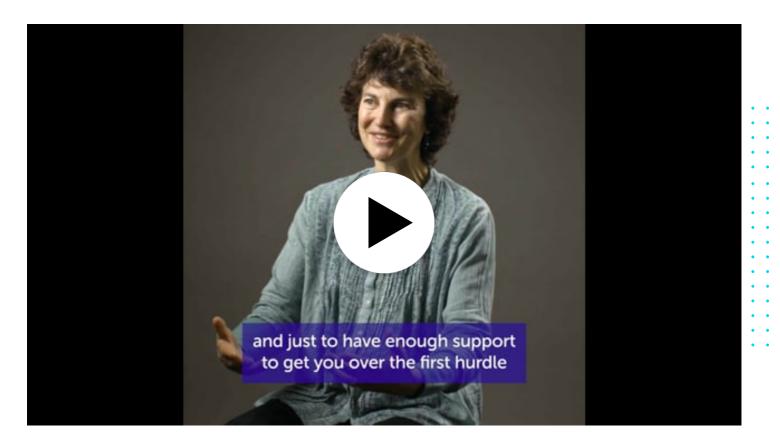
In June 2022, we launched the Cancer Research Horizons Seed Fund with the primary purpose of bridging one of the most challenging stages: attracting early-stage risk capital. The new Fund will build on our startup success and accelerate and expand new company creation and early growth.

Managed by the Cancer Research Horizons Ventures team, our Seed Fund is an impact-driven and evergreen philanthropy fund that invests in promising, early-stage propositions from within and beyond the Cancer Research UK network. The fund was launched with a rolling £15m/5-year investment commitment from Cancer Research UK. Complementing this, Cancer Research Horizons set a fundraising target of an additional £15m to match the Cancer Research UK investment and extend the fund's leverage, scale, and longevity.

The fund invests up to £1m at various early stages, ranging from technology validation for startup propositions through to making equity investments in high-potential, early-stage companies in the cancer space. Our investment remit is broad and includes new therapeutics, preventative measures, diagnostics, medical devices, and AI and data-driven solutions.

We are science-led, actively pursuing the truly novel ideas with the potential to induce a step change in the field of oncology. Investment decisions are made based on the prospect of increasing the chances a lifesaving cancer treatment or diagnostic will reach the market. For example, the funding would ideally assist an early-stage company to attract the follow-on funding necessary for it to grow.

In the event any financial returns are generated, they will be returned to the fund and into cancer research.



Sergio Quezada, Rebecca Fitzgerald and Andrew Turnbull discuss how our Seed Fund helps translate research.

Seed Fund year in review

Over 2022/23, we identified approximately 60 potential investment opportunities from across both academic researchers (from our research community and beyond) and existing startup companies seeking early-stage capital. Of these, approximately 35 opportunities were evaluated in greater depth by our internal triage group, and eight full Seed Fund proposals were submitted to our Seed Fund Investment Committee.

Over 2022/23, we committed £2m of Cancer Research Horizons' Seed Fund, with deployment subject to investment conditions being met (e.g. securing co-investment). This included two committed investments in new companies in the process of being formed based on discoveries arising from Cancer Research UKfunded research. On formation, the companies will operate in stealth mode to ensure they retain a competitive advantage over potential competitors.

New startup portfolio companies

Over the course of 2022/23, Cancer Research Horizons took new equity interests in seven startup companies, including the three companies highlighted below.

Alethiomics: taking on myeloproliferative neoplasms

Alethiomics is a drug discovery company focused on developing targeted therapies to treat a family of blood cancers called myeloproliferative neoplasms (MPN). A spinout from the University of Oxford, the Company is based on world-leading discoveries in clinical haematology and single-cell multi-omics by its founders, Professor Adam Mead and Professor Beth Psaila.

Alethiomics

Infinitopes: curtailing cancer metastasis

Infinitopes is a pioneer in precision immunomics medicines. A Cancer Research UK-led biotech spinout from Oxford University, the company aims to empower the immune system to fight cancer metastases with unique, de novo antigen discovery technologies, innovative high-efficiency vectors and intelligent clinical trial design.



Oxomics: Al-powered next-generation diagnosis

Oxomics is developing a minimally invasive, single-shot platform technology for disease diagnosis and prognosis. The technology combines analysis of metabolites in blood samples with machine learning to identify patterns of change that indicate disease. Oxomics will first demonstrate detection of lung cancer and melanoma metastasis in patients before expanding to diagnosis of many different cancers across broad populations, including those with non-specific symptoms.

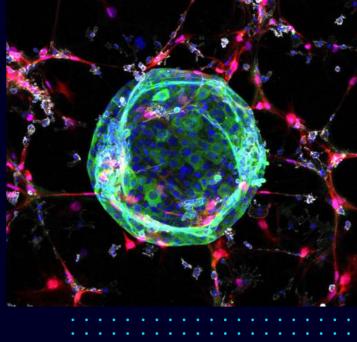


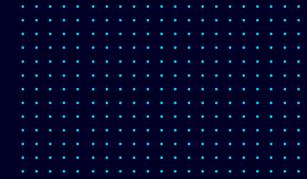
Portfolio update

We have built an incredible assembly line for startup companies to bring early-stage technologies out of the research lab and translate them into patient benefit. Our startup portfolio secures funding from investors around the world who believe in our world-class science and the power of partnership.

In 2022/23, five companies in our portfolio initiated new clinical studies (see below), and a number of our other portfolio companies reported significant preclinical and clinical milestones. Collectively, our portfolio of companies raised over £100m in investment, despite the challenging financial climate.

The year also saw the acquisition of three companies in our portfolio: Oxford-based GENinCode acquired Abcodia, and the global biopharmaceutical company Takeda finalised its acquisitions of GammaDelta Therapeutics and Adaptate Biotherapeutics after exercising its options to acquire in 2021/22. In other news, Fierce Biotech named STORM Therapeutics one of its 2022 "Fierce 15" (designating it as one of the most exciting biotechnology companies in the industry). Cyted reached the milestone of providing 10,000 oesophageal cancer detection tests for NHS patients. Furthermore, ADC Therapeutics (an exited portfolio company) and Sobi received European Commission approval of ZYNLONTA for the treatment of relapsed or refractory diffuse large B-cell lymphoma.





Clinical updates from our startup portfolio



Artios initiated a Phase 2 study of Pol θ inhibitor ART4215 in combination with PARP inhibitor talazoparib in **BRCA** deficient breast cancer, and a Phase 2 study of ATR inhibitor ART0380 plus gemcitabine in platinum-resistant ovarian cancer.



Amplia announced dosing the first patient in its Phase 1b/2a ACCENT study of the FAK inhibitor AMP945.



Monte Rosa Therapeutics announced dosing the first patient in its Phase 1/2 study of MRT-23569, a GSTP1directed molecular glue degrader, for the treatment of MYCdriven tumours.

onctura

iOnctura initiated a Phase 1b pancreatic cancer study of its next-generation autotaxin inhibitor IOA-289.



STORM Therapeutics announced dosing the first patient with oral METTL3 inhibitor STC-15 in a solid tumour Phase 1 study.

BIOCAPTIVA

Spotlight on BioCaptiva

Cancer Research Horizons made a follow-on investment into BioCaptiva as part of the company's £2.2m seed extension round in June 2022. BioCaptiva has developed a novel DNA capture device (BioCaptis) aimed at addressing a key market challenge for liquid biopsy technologies — low input levels of cell-free DNA (cfDNA).

By combining apheresis with the BioCaptis technology, its liquid-biopsy system captures cfDNA directly from small volumes of plasma that are impractical to process using existing methods. Employing apheresis to improve early cancer detection delivers quantities of cfDNA comparable to over 100 individual blood draws from one patient, providing greater quantities of input DNA. The approach championed by BIOCAPTIVA also promises to open new avenues for more comprehensive genome analysis, and lead to more precise and enhanced clinical decisions.

BioCaptiva plans to use the investment from the additional seed funding round to fund the first-in-human trials with BioCaptis and prepare for initiating regulatory trials in early 2024.



Leveraging Cancer Research Horizons investment

To leverage our investments, our Ventures team routinely seeks to co-invest with like-minded earlystage investors. Alongside steps taken to strengthen our investor network during the financial year, in January 2023 we were successful in our application to become one of Innovate UK's investor partners in their Future Economy Investor Partnerships programme. Innovate UK is part of the UK government's Research and Innovation funding agency for investing in research and science. This programme brings together Innovate UK's use of grant funding, and investor partners' aligned funding and expertise. The initiative's aim is to stimulate research and development in micro-, small- and medium-sized enterprises, while accelerating equity investment into those companies so that they can grow more rapidly through innovation.

Becoming an investor partner means our Ventures team will work with Innovate UK and other investor partners to consider innovative businesses that apply for grant funding alongside its investment. The other investor partners include venture capital funds, corporate investors, business angel groups and social impact investors, coming from across the UK, Europe and the US.



FACILITATING ACCESS TO RESEARCH TOOLS

CancerTools.org is a centralised resource that simultaneously permits scientists to either deposit or acquire tangible research materials that would help to advance their research. Over the past year, the organisation continued to rapidly expand its offering and global community of researchers, and initiated an array of unique collaborations with academic institutes and some of the finest global cancer centres.



The CancerTools.org team at the 2023 Annual Meeting of the American Association for Cancer Research in Orlando, Florida.

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What's new with CancerTools.org

CancerTools.org is the first of its kind: a non-profit, cancer-focused biorepository where researchers can deposit research tools developed in their labs, including antibodies, cell lines, organoids, small molecules, mouse models, cell culture media and other state-of-the-art technologies. With our in-house production and global coverage, we can produce, store and supply these tools to fellow scientists to use in their research and deepen our understanding of cancer and drive innovation.

Since launching in April 2022, we have successfully enhanced the number of partnerships with academic institutes to democratise research tools globally, which is central to the mission at CancerTools.org.

This year CancerTools.org partnered with one of the leading and most technologically advanced cancer hubs in North America: Fred Hutchinson Cancer Center. Through our collaboration with its Business Development & Strategy group we brought in a host of monoclonal antibodies generated by Fred Hutch researchers to offer to the wider cancer research community. From antibodies against CD34 and CD44 to multiple integrin proteins, these are the fundamental disease biomarkers that further our understanding of the nuances associated with cancer biology and its development.

With a shared mission of driving innovation and accelerating the development of new inventions, this is a significant partnership for CancerTools.org to enhance the reach of the scientific advances from Fred Hutch researchers.

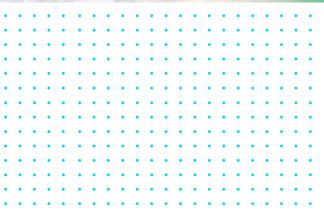
To further support cancer research across the globe and advance scientific knowledge, another important partnership this year was with Oregon Health & Science University (OHSU). Their researchers from the Department of Cell, Developmental and Cancer Biology deposited novel antibodies that can be used to evaluate active- and slow-cycling cell populations, particularly bidirectional plasticity with Lgr5-expressing stem cells.

Growing and nurturing such partnerships demonstrates our commitment to new resources and capabilities in providing cancer-specific research tools to academic and commercial researchers.

PROGRESSING INNOVATIVE THERAPEUTICS

Cancer Research Horizons operates along the entire continuum of drug development, augmenting cuttingedge technology platforms, research alliances, collaborations, and providing access to a network of 200 drug discovery researchers as well as clinical trial networks that span the UK. Three new international alliances, and a clinical trial milestone are among this year's highlights.





The Therapeutic Innovation Strategy in brief

Cancer Research Horizons' mission is to bring together the brightest minds, boldest ideas and best partners to fast-track scientific breakthroughs into cancer patient benefit.

Our Therapeutic Innovation division, a new translational engine comprising 200 drug discovery scientists across six sites, was created to deliver a stepchange in patient impact. We plan to achieve this through reconfiguring our organisation and how we work to fully capitalise on our unique bridging position between academia and the commercial world.

We plan to engage earlier and more broadly with breakthrough science, seeking to apply our translational insight to bring more high-quality projects into our portfolio. We will focus on selected priority areas of scientific focus that will form the basis for the bulk of our portfolio build, but are also open to evaluate and support all ideas that may be translated to significant patient benefit. We will refocus our resource and technology development to emphasise cuttingedge target validation and feasibility, and selected capabilities in early drug discovery to enable scaling and agile progression of a highly novel portfolio.

This combination of network engagement, selective focus, and drug discovery capabilities, which other organisations cannot replicate, will drive the identification of novel targets and the efficient generation of early hit matter. Our differentiated drug discovery proposition will foster partnerships and investment from industry, and attract venture capital, philanthropy and the interest from other charities necessary for advancing our portfolio through midand late-stage drug discovery at pace. We have set the bold and aspirational ambition of doubling the patient benefit output of our predecessor organisations, measured by the surrogate of new therapies entering clinical trials.

International partnerships

Cancer is a global problem, which needs to be tackled by a worldwide community. Recognising the importance of this within the discovery and development of new therapeutics, we have initiated three new international partnerships within the past 18 months, with translationally focused cancer centres. These comprise the Oncode Institute (Netherlands), the Karolinska Institutet (Sweden) and the Experimental Drug Discovery Centre (Singapore).

Each partnership brings unique and synergistic insights and expertise to complement the capabilities of our drug discovery scientists and help to accelerate therapeutic discovery. We are excited to be partnering with these world-leading research and translational networks who share our vision to go further, faster, together, to beat cancer.



Oncode Institute



Through our five-year strategic alliance with the Oncode Institute, we are collectively able to expand our network of researchers to look for new opportunities to connect teams, and engage with them to discover novel therapeutics. Our joint strategy includes exploration of a range of activities including themed alliances, access to capabilities, and joint events and training.

We have already established a drug discovery partnership with Jos Jonkers (NKI) in DNA repair. This capitalises on the world-class expertise of Jos' laboratory coupled with Cancer Research Horizons and Cancer Research UK's long track-record in translating DNA damage response research into the clinic.

We are exploring other opportunities for collaborative therapeutic discovery including new approaches to target the tumour microenvironment and examining differential approaches to identify novel cancer targets. As we build our relationships with the Oncode research network, we will also explore a range of models to bring in additional investment including cocreation of new companies and partnerships with biopharma.

"For me, it's exciting to learn what's needed for a good drug target. I very much enjoy discussions about potential opportunities, figuring out the questions we want to see addressed to decide whether a target has what it takes. It's exciting for us to be on this journey where we challenge ourselves to take a wholly different perspective from what we do as fundamental researchers."

Professor Jos Jonkers

Netherlands Cancer Institute (NKI)/Oncode Institute

Karolinska Institutet



Our new five-year strategic alliance with the Karolinska Institutet, a world-leading medical university based in Sweden, is dedicated to accelerating the translation of academic cancer research into improved treatments for patients. Working together, both partners will drive forward a shared long-term strategy of promoting and supporting industry collaborations, and aiding in the generation of new scientific discoveries that can be rapidly translated into the clinic.

This includes the extensive research funded within the Karolinska that spans many aspects of cancer, including cell therapies and immune cell modulation.

Under the new partnership we will explore joint activities including research collaborations, theme-based alliances and mutual access to facilities, expertise and tools.

Experimental Drug Development Centre



We have recently signed a five-year partnership with the Experimental Drug Development Centre (EDDC), Singapore's national platform for drug discovery and development hosted by the Agency for Science, Technology and Research (A*STAR). EDDC are a like-minded organisation that shares our vision for collaborative drug discovery, and aims to accelerate the translation of cancer research in Singapore into improved treatments for cancer patients.

This strategic alliance will focus on leveraging the complementary capabilities, platforms and technologies from both partners, to develop oncology pipeline assets across a range of development stages and therapeutic modalities. We will seek to identify novel areas of cancer biology and convene joint efforts around target identification and validation, and drug discovery and development.

Deep Science Ventures

During the past year we began a new partnership with Deep Science Ventures to explore cocreation of innovative startup companies incubated within Cancer Research Horizons' Therapeutic Innovation Laboratories. This partnership builds on an existing collaboration with Deep Science Ventures, which led to the formation of three new cancer therapeutic companies.

The approach starts by examining some of the biggest problems within cancer treatment and designing focused solutions from an early stage using scientific knowledge from across the Cancer Research Horizons and Deep Science Ventures networks. Once we have identified a discrete area for venture building, we recruit founders-in-residence with an entrepreneurial character and relevant expertise around the area of interest to develop a new therapeutic concept, and work with Deep Science Ventures and Cancer Research Horizons' drug discovery team towards establishing a company and proof-of-concept data.

Within the new alliance, Deep Science Ventures and Cancer Research Horizons have already identified their first joint venture. We are developing a multi-pronged therapy to reprogramme the phenotype of problematic cells in the tumour microenvironment, in vivo. Our technology will not only revert the immuno-suppressive phenotype, but will also create the environment for immunemediated tumour elimination. The expert team at Cancer Research Horizons will support the future venture with lab space and in-kind wet lab resource. Deep Science Ventures has recruited two founder analysts, Elisa Arthofer and Loïc Roux, to lead the development of this opportunity. These founders will benefit from the expertise within Cancer Research Horizons and the wider Cancer Research UK network to help accelerate the opportunity.









The Cancer Research Horizons–AstraZeneca Functional Genomics Centre

The Functional Genomics Centre (FGC) was established in 2019 as a collaboration between AstraZeneca and Cancer Research Horizons to build a centre focused on developing and applying genetic screening in oncology. The FGC is developing novel CRISPR technologies to better understand cancer biology, creating biological models that may be more reflective of human disease and advancing computational approaches to improve analysis of big datasets. A main aim of the FGC is to enable access to these technologies for scientists and clinicians funded by Cancer Research UK. The FGC has nation-wide impact with a portfolio of 35 completed or active projects from 16 different institutes across the UK.

In 2022, the FGC created a joint three-year strategy to strengthen the partnership and give clarity to its future direction. Central to its strategy is the implementation of functional genomics capabilities that enable screening in more complex disease relevant models and better understanding of target biology and drug mode of action.

The FGC is currently focused on developing single-cell CRISPR (scRNA CRISPR) to derive more complex phenotypes, CRISPR activation to understand activating mutations and amplifications, combinational libraries to identify new synthetic lethal interactions, and mutation screening to better understand targets and drug mode of action.



The FGC team.

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"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 collaborating 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."



Our Antibody Alliance Laboratory team with their Longstanding Alliance award.





Ian Hitchcock from the Antibody Alliance Laboratory talks about oncogenic driver mutations in myeloproliferative neoplasms.



Antibody Alliance Laboratory receives ASAP Excellence Award

The Antibody Alliance Laboratory, a joint facility between Cancer Research Horizons and AstraZeneca, combines our cancer biology expertise with the worldclass antibody engineering technology of AstraZeneca.

The alliance gives us access to AstraZeneca's internationally recognized antibody phage display libraries and connects Cancer Research UK's large academic network with AstraZeneca's biological expertise.

The Antibody Alliance Laboratory won the Longstanding Alliance award at the 2023 Alliance Excellence Awards, run by the Association of Strategic Alliance Partnerships. The award recognises partnerships that have sustained excellence over at least five years, usually having overcome challenges by adapting to evolving conditions.

Researchers can join our team of 20 drug discovery and antibody engineering scientists by working in this award-winning laboratory, whether they are funded by Cancer Research UK or not. Alongside our experts in antibody phage display and the expression of highquality proteins, researchers can steer a project, coauthor publications and patents, and bring new skills back to their labs.

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ADVANCING CLINICAL DRUG DEVELOPMENT

As the world's only charity-funded drug development facility, Cancer Research UK's Centre for Drug Development is unique in its focus on ushering first-inclass and best-in-class therapeutics through early stage clinical development. In 2022/23, the Centre for Drug Development teams continued to de-risk these high-risk programmes and engage industry in creative ways to bring new clinical benefits to cancer patients.

The DETERMINE trial: shifting the clinical trial paradigm to advance the treatment of rare cancers

Cancers that are diagnosed in fewer than 6 in 100,000 people each year are defined as rare, but together they make up 22% of all cancers diagnosed worldwide, more than any single type of cancer. As such, people with rare cancers make up a large cohort that is consistently underserved by treatment options.

DETERMINE* aims to address that. Open to adults, teenagers and children, the trial evaluates whether drugs targeting identifiable genetic alterations that are approved for use in some cancers can be used to treat patients with other cancers, including rare cancers, who have the same genetic alteration.

The Centre for Drug Development sponsors and manages the trial, with the University of Manchester as the lead centre. When the trial opened in November 2022, Roche provided seven of their targeted drugs for evaluation across five treatment arms. In December 2022, Novartis joined to provide access to their drug(s) as well. The Cancer Research Horizons business development team are in active conversation with multiple potential partners to add new treatment arms and appropriate technologies to DETERMINE. We hope more pharmaceutical and biotechnology companies will continue to contribute to this breakthrough trial.

Its unique design means that any treatment that appears to be working for patients on the trial will be submitted for review by the Cancer Drugs Fund (CDF). The intention is that the CDF team, working with NHS England Clinical Policy team, will then decide whether a period of data collection in the CDF is appropriate to assess if the drug could be used as a routine treatment option on the NHS for patients with this cancer type.

The team dosed their first patient in March 2023, with the first trial site opening at the Christie Hospital in Manchester. There are now trial sites in Oxford, Cambridge and Newcastle, with additional sites due to open across the adult and paediatric Experimental Cancer Medicine Centres network. In recognition of the quality of work behind the DETERMINE trial, it garnered two awards this year: the Centre for Drug Development won the Team Excellence in the Management of Clinical Data Award from the Association of Clinical Data Management, and the trial itself won the 2023 Bionow Healthcare Project of the Year Award for its innovative design and ability to help this large group of underserved people with rare cancers.



"With technological advances in genetic testing we've learned that some rare tumours contain genetic abnormalities which may benefit from targeted treatment currently only available for more common cancer types."

Matthew Krebs

Chief Investigator for the DETERMINE trial.



*DETERMINE: Determining Extended Therapeutic indications for Existing drugs in Rare Molecularlydefined Indications using a National Evaluation platform trial.

Spotlight

UCB and two antibody therapies

In March 2023 we began a multi-project collaboration with global pharmaceutical company UCB, uniting their renowned antibody discovery expertise with the clinical development capabilities of Cancer Research UK's Centre for Drug Development.

In our first partnership pursuing more than one agent with one company, we will take two of UCB's investigational antibody candidates, UCB6114 and UCB4594, through clinical trials. If successful, they have the potential to offer cancer patients access to new targeted treatment options.

UCB6114 is a potential first-in-class antibody targeting gremlin-1, a glycoprotein secreted by the tumour stroma. UCB4594 is an antibody targeting the immune checkpoint, human leukocyte antigen G (HLA-G).

While the Centre for Drug Development is leading the design and delivery of Phase 1/2 clinical trials, UCB will continue to manufacture both candidates, complete the ongoing UCB6114 clinical study (ONC001) and provide support. UCB will retain exclusive rights to further develop and commercialise both assets and will receive a licence to the results of the clinical trials from Cancer Research Horizons in return for success-based milestone and royalty payments.



Hummingbird Bioscience goes all in

In March 2023, Hummingbird Bioscience, a clinical-stage biotechnology company, exercised its option to license the clinical trial results of its HER3-targeting antibody, HMBD-001, from Cancer Research Horizons.

The Centre for Drug Development is sponsoring and managing the first-in-human Phase 1/2a clinical trial on HMBD-001, which aims to establish the recommended Phase 2 dose for patients with HER3-expressing solid tumours who are resistant to approved therapies. Based on the existing dose escalation data, Hummingbird Bioscience will initiate additional biomarker-stratified clinical trials with HMBD-001, which will run in parallel with the Centre for Drug Development's trial.

"Our Cancer Research UK collaboration has been pivotal for the development of HMBD-001 and brings us one step closer to providing a precision therapy for patients with HER3-expressing cancers."

Piers Ingram

Chief Executive Officer of Hummingbird Bioscience

Hummingbird's decision to exercise its licensing option early in the clinical development process highlights its enthusiasm for the promising data emerging from the trial and is a testament to Centre for Drug Development's quality of work.





EMBRACING NEW TECHNOLOGY

Scientific discovery evolves constantly so Cancer Research Horizons consistently embraces and supports emerging areas, from new diagnostic technology platforms to artificial intelligence, which is currently making waves in cancer research. We are working with startup companies to help bring the potential benefits gleaned from these technologies to cancer patients.



Early detection news

During 2022/23, several of the licensable diagnostic technology platforms in the Cancer Research Horizons biomarker and diagnostic portfolio progressed towards becoming products. They represent a combination of new approaches that stem from a greater understanding of cancer cell evolution and tools to interrogate the complexities of cancers cells and the environment that surrounds them. Here is a summary of some of these technology platforms and the recent progress they made. Click the links in the description to find the full details and licensing opportunities.

Platform

ORACLE

Description

The <u>Outcome Risk Associated Clonal Lung Expression (ORACLE)</u> diagnostic approach/genetic test combines machine learning with an understanding of cancer cell evolution to distinguish between high- and low-risk tumours. The test will help to guide early clinical decision making for lung cancer patients.

Business and development status

Patent application filed

Proof of concept: The investigators analysed multi-region, multiomic data from patients with non-small cell lung cancer (NSCLC) recruited within the <u>TRACERx study</u>. to address the diagnostic challenges associated with genomic intra-tumour heterogeneity (ITH) and chromosome instability (CIN). This challenge is a common features across cancer types. This new approach robustly predicted which early-stage lung cancer patients were at a high risk of mortality, including those missed by existing clinical criteria.

ECLIPSE

Description

ECLIPSE is a novel, highly sensitive informatic method developed to track tumour evolution over time using low circulating tumour DNA (ctDNA) fraction samples (>0.1%) of liquid biopsies by leveraging genomic information for each mutation from a matched tumour tissue sample. The approach has the potential to make the detection power for ctDNA much higher than standard liquid biopsy methods.

Business and development status

International patent application filed

Proof of concept: In a cohort of ctDNA-positive samples within the TRACERx study, ECLIPSE detected clonal ctDNA in 61% of patients, while standard liquid biopsy methods detected clonal ctDNA in only 16% of patients.

T Cell ExTRECT

Description

<u>T Cell ExTRECT</u> is an informatic method of DNA sequencing analysis that enables the estimation of T cell fraction present in tumours. Measuring the fraction would potentially provide an efficient method for assessing immune microenvironment influences on tumour evolution that have prognostic and predictive insights into a patient's response to immunotherapy.

Business and development milestones

International patent application filed

Validation and proof of concept: Using five different tests, the accuracy of the T Cell ExTRECT in comparison to RNA sequencing methods. Additionally, a low T Cell ExTRECT score correlated with a worse prognosis in a cohort of lung adenocarcinoma patients. T Cell ExTRECT was predictive of checkpoint inhibitor therapy response across eight main cancer types.

PCF-SELECT

Description

Designed to detect genomic aberrations informative for therapeutic selection, <u>PCF-SELECT</u> is a circulating tumour DNA (ctDNA)-targeted, next-generation sequencing panel for use before a change of treatment for metastatic castration-resistant prostate cancer (mCRPC). Key benefits of this technology include detection of a breadth of genomic alterations at high sensitivity, a computational approach to minimise false positives, and a need for only low amounts of plasma DNA.

Although currently optimised for prostate cancer, the approach could be applied to other cancer types.

Business and development status

Proof of concept: The verification of PCF-SELECT and its associated computational method's performance under conditions including the ability to detect lesions at low ctDNA level and within complex copy number states, was repeatedly achieved using synthetic simulations, serial mCRPC patient samples and comparisons with independent standard assays.

Al partnerships

With the rapid growth in the application of artificial intelligence (AI) and machine learning (ML) to drug discovery, Cancer Research Horizons has been partnering with AI-enabled biotechs to help address key questions in drug development. In particular we have been excited by the possibility of using AI to help inform development of some of our late-stage preclinical assets and in particular the insights that AI can provide in disease positioning. Through partnerships with Turbine and Predictive Oncology, we are building hypotheses for our CDC7 and glutaminase inhibitors that will allow us to identify the most suitable patient population and map a potential path to the clinic.



Turbine

Cancer Research Horizons partnered with tech-enabled biotech Turbine to develop novel disease positioning and patient stratification strategies for Cancer Research Horizons' late-preclinical CDC7 inhibitor programme. CDC7 overexpression is correlated with poor survival in a broad range of cancers, but a clear picture is lacking on which patients could be effectively and safely treated by CDC7 inhibition. The collaboration is accelerated by Turbine's Simulated Cells platform. Simulated Cells leverages AI/ML in addition to large datasets to mimic the molecular behaviours of a cancer cell and its response to genetic or chemical perturbations. Cancer Research Horizons and Turbine will then validate the Simulated Cellsdriven hypotheses in vitro and in vivo, to increase the probability of clinical success of the CDC7 inhibitors.

Predictive Oncology

We recently initiated a collaboration with Predictive Oncology that aims to help determine the cancer types and specific patient populations that our potent small molecule inhibitors of glutaminase could most effectively treat. The collaboration will utilise Predictive Oncology's PEDAL[™] platform, which is an AI/ML platform supported by experimentation from an extensive patient-derived tumour sample bank. PEDAL[™] makes high-confidence drug response predictions, enabling a more informed selection of drug–tumour type combinations for clinical development, increasing the probability of clinical success by efficiently addressing tumour heterogeneity during preclinical stages.



FINANCIAL SUMMARY

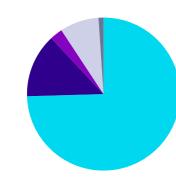
Cancer Research Horizons has a range of income streams and spending commitments. Here we breakdown our financial activity from 2022/23.

Cancer Research Horizons financial activity

£79m

Total gross income

£26m Distributions to partners £34m Other operating costs £22m Reinvested in Cancer Research UK after tax adjustment



Income

	Key royalty streams	£59m
	Therapeutic Innovation	£11m
	Other licensing activities	£2m
	Reagents business	£7m
	Other income	£0.8m
Tota	al income	£79m

Expenditure

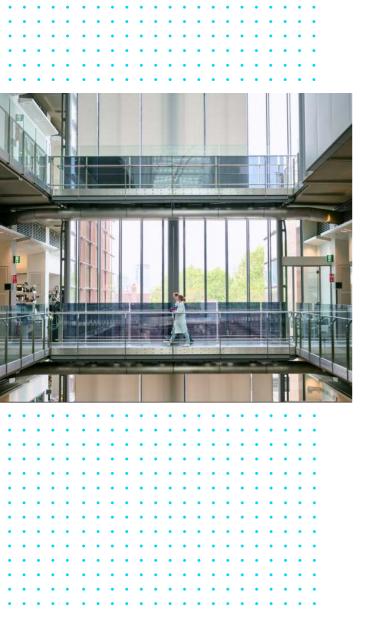
Tot	Total expenditure								
	Other operating costs	£17m							
	Investment in entrepreneurship	£0.5m							
	Patent expenditure	£1m							
	Staff costs	£16m							
	Distributions to partners	£26m							

LOOKING TO THE HORIZON

LINES HE IMPRESSION

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Cancer Research Horizons continues to look forward and think strategically about where oncology research is going and to target areas of unmet need for cancer patients.



Our two major strategic priorities for the year to come are:

- 1. The testing and treatment of cancers in children and young people (CYP)
- 2. The early detection and diagnosis of cancer Consequently, efforts are underway to strengthen the foundations and establish roadmaps designed to bridge the gaps in research, clinical development and attract investment associated with these challenging areas.

Despite an improvement in the overall number of children surviving cancer over the last four decades, cancer remains the leading cause of death in children and the most common cause of death by disease in teenagers and young adults. Cancer in children and young people is different to that in adults. The reduced occurrence of cancer in CYP in comparison to cancer in adults provides a pressing opportunity for Cancer Research Horizons to work closely with Cancer Research UK to address the unmet clinical needs for this age group. Cancer Research UK is the largest charitable funder of research into cancer in CYP in the UK, and the organisation's track record has already helped to transform survival in this area by funding some of the most successful paediatric oncology clinical trials.

However, we need to do more. As the innovation arm of the charity, Cancer Research Horizons can help to de-risk and progress novel technologies further down the development path. This helps to mitigate the risk of investing in this niche area and stimulates the development of novel diagnostics and treatments tailored to the metabolism of young people or targets difficult to treat cancers, such as sarcoma. Consequently, Cancer Research Horizons is taking a more active role in serving as the conduit in translating the research currently funded by the charity, and a dedicated team has been assembled to bring together experts and attract global partners to tackle the unique challenges facing children and young people with cancer.

Cancer Research Horizons also plans to do more in the early detection space. Although diagnosis and prevention are optimal approaches for curtailing the cancer disease burden, their value to public health is not reflected in the level of investment these technologies attract. Several Cancer Research UK funding schemes, most notably the Early Detection and Diagnosis Awards, lead to the identification and development of novel biomarkers and diagnostics with the potential for translation for patient benefit. Alongside the launch of a Cancer Research UK National Biomarker Centre, Cancer Research Horizons expects biomarkers to be an area of strategic focus going forward.

PARTNER WITH US

Tell us about your exciting projects and we can help you develop the next generation of cancer treatments. Help us bring forward the day when all cancers are conquered.

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