



Commercial Partnerships

Annual Review 19/20

Together we will beat cancer

Our missions & values

CRUK's vision is to bring forward the day when all cancers are cured. Over the last 40 years, cancer survival rates in the UK have doubled. In the 1970s just a quarter of people survived. Today that figure is half. In order to improve on this, we need to work with industry partners to progress the best ideas to market. This is where the Commercial Partnerships team can help.



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See our financial review on page 35

Our achievements 2019/20



>600

Researchers we interacted with



Invention disclosures



Patents filed (25 priorities & 13 PCTs)





2 Spin-outs created



>£400m

Investment raised by portfolio in year



43 Portfolio spin-outs created to date





Total raised by spin-outs to date



\$265m

Impact Medicine Fund raised with SV Health Investors

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£43m

Reinvested in cancer research



£96m

IP-related gross revenue



Business accelerator partners added



Cancer Research UK (CRUK) is committed to supporting research on improving the diagnosis, treatment and prevention of cancer.

One way we enable this is to work with industry.

We join forces with our partners in industry to gather together all the expertise and resources needed to translate promising research into new therapeutics, diagnostics and other innovations that benefit cancer patients. Without these essential partnerships, research with significant potential may never reach those who need it.

Our Commercial Partnerships team act as the meeting point between our charity-funded research and industry. We help to accelerate the translation of research into products for patient benefit through the development and commercialisation of exciting new discoveries. In addition, any revenue received by us through our commercial partnerships is reinvested back into developing lifesaving research.

This annual review aims to demonstrate our commitment over the last year to the researchers whom we support with achieving their translational ambitions, the companies with whom we partner and the cancer patients to whom our efforts are ultimately dedicated.

Tony Hickson, Chief Business Officer, Cancer Research UK



Highlights from the 19/20 financial year

Balversa® (erdafitinib) – Was approved for bladder cancer during the year.



Autolus, developing more persistent T Cell therapies –raised

\$180m of new finance in the year.

Achilles Therapeutics, developing personalised T Cell therapies – raised

£100m of new finance in the year.

We have now supported

10 drugs to market

helping patients.

137 new ideas for new drugs, tests and devices were disclosed to CRUK by funded researchers during the year.

Our **spin-out portfolio** has now raised over

£1.5bn

in total, with more than £400m raised in the last year.



Partnerships with **3 new accelerators** were struck over the course of the year, with over **30 new oncology focused businesses benefitting** from the help provided.

Over £500m

in **cumulative royalties** to date have been generated and reinvested back into research by CRUK and our academic partners.





Zytiga® (abiraterone acetate) has now been dosed in over 330,000 prostate cancer patients, generating over

£230m in royalties to date.

This year our immuno-oncology alliance with **Ono Pharmaceutical** and **LifeArc** was awarded the Best Partnership Alliance at the prestigious Scrip Awards, which recognises major achievements in the industry.

What we do and why

We're dedicated to advancing discoveries to beat cancer



Cancer Research UK's Commercial Partnerships team, a part of the Research and Innovation division of CRUK, develops promising ideas into successful cancer therapeutics, vaccines, diagnostics and enabling technologies. Our deep understanding of both academia and industry enables us to translate research into commercial propositions to deliver patient benefit and commercial value that will support further cancer research. 66

We help bridge the gap between research discoveries and industry engagement. Ultimately however, it's about patient benefit.

> DR IAIN FOULKES Exec Director, Research & Innovation



Where we do it

The commercialisation of technology is a global business. Our role is to find the best partner for CRUK discoveries wherever they may reside. Such partners are the ones that will maximise the chances of a product or service reaching the market and benefitting cancer patients. We have over 280 partners now present on 6 continents across the world and staff based across the UK and in the USA. Despite this global approach, we still partner extensively with UK based companies (e.g. we have several partnerships with AstraZeneca) and always request clauses in our agreements around ensuring affordable pricing policies in the UK.



Our principles for doing business

Our commitment to being professional in what we do

Our deep understanding of the perspectives of both academia and industry enables us to translate promising research into commercial propositions for the greatest patient benefit and maximum financial return. As such, we strive to act in accordance with the principles and commitments set out below:



COMMERCIAL PARTNERSHIPS

Our priorities reflect our vision of 'Advancing Discoveries to Beat Cancer'. Our primary driver is patient benefit.



EFFECTIVE PARTNERSHIPS

We identify and cultivate productive relationships with companies that share our values and care about improving the lives of cancer patients.



IP DEVELOPMENT

We want to see CRUK discoveries progressed to market as fast as possible. As such, we seek our partners' commitment to the diligent development of the intellectual property we provide them access to.

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FAIR FINANCIALS

We seek a fair financial return to CRUK and our partners commensurate with the development stage and value proposition.

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RESERVED RESEARCH RIGHTS

We reserve the right for our researchers to continue to use any IP we license for research purposes and for publication.



RISK MANAGEMENT

Bearing in mind acceptable business practice, we mitigate CRUK's exposure to commercialisation risks associated with the development and sale of licensed IP.

Our commitment to CRUK funded researchers

We never stop publication of your research nor delay your CRUK funded publication. Our role is to work with you to ensure you can achieve your academic goals whilst also being translational/entrepreneurial. We firmly believe they are not mutually exclusive. With this is mind we have developed a customer charter, key highlights for which are provided



SUPPORTING YOU WITH YOUR NEW IDEA OR INVENTION

• We will contact all grant recipients within **3 months** of award and introduce ourselves and our support services.

• We will follow-up on any ideas you disclose to us within **7 days**. We will never take longer than **3 months** to assess a new idea (and can move much more quickly if publication requires us to).

• If we agree with you to file a patent, we will introduce you to a patent attorney and aim to file within **1-3 months** (again, faster if needed). We cover all the costs of this and only recover them from commercial proceeds if the idea is commercialised.

MARKETING YOUR TECHNOLOGY TO THE OUTSIDE WORLD

• We will keep you informed of our marketing activity every quarter. Sometimes we may need to call on you to support this activity (e.g. meet with an industrial company to explain the technology to them).

• If, despite everyone's diligent efforts, we determine the technology cannot be commercialised as planned, for scientific or commercial reasons, we will let you know within **1 month** and discuss whether your host institute might be interested in taking on responsibility for commercialisation.



WHEN YOUR TECHNOLOGY HAS BEEN PARTNERED (E.G. LICENCE OR COLLABORATION)

• If you are involved with ongoing research activity under the licence, we will be in contact regularly (at least every **6 months**) to ensure project progression and keep you informed of activity by the licensee.

• Where you are not involved in the ongoing activity, we will keep you informed annually of progress with the project, including achievement of project milestones (and associated payments) and provide annual reports (where available).



Our commercial objectives

Whilst our track record to date has been good, we can never stand still in a rapidly changing world and research environment. At the start of the financial year we therefore set ourselves 6 main objectives to ensure we continuously strive to improve.

| 1 | SUPPORT OUR RESEARCHERS WITH TRANSLATIONAL ACTIVITY | | We will provide more extensive, local and visible support to researchers to translate their ideas. |
|---|--|---|---|
| 2 | ENCOURAGE ENTREPRENEURIAL CULTURE & SKILLS IN OUR RESEARCH COMMUNITY | (Î) | We will build an innovation ecosystem and foster an innovation culture within our research community. We will drive higher levels of engagement with the UK scientific network and increase the volume of opportunities available for translation. |
| 3 | DEVELOP INDUSTRY PARTNERSHIPS IN THERAPEUTICS | A B B B B B B B B B B B B B B B B B B B | We will cement and build upon our existing relationships and seek new partnerships in CRUK's strategic priority areas. |
| 4 | DIVERSIFY AND MAXIMISE OPPORTUNITIES BEYOND THERAPEUTICS | (KA) | We will adapt to the convergence of disciplines by partnering with diagnostics, device, digital and AI companies. |
| 5 | INVEST IN OUR PEOPLE AND PROCESSES, PROMOTE DIVERSITY | | We will ensure our staff have the diversity, skills and opportunities they need to achieve our vision. We will encourage our staff to take ownership of how their careers can develop and provide them with opportunities to do so. |
| 6 | LEVERAGE AND RETURN CAPITAL | | Through our commercial activities we will leverage investment from industry to amplify CRUK's funding power and maximise the value of the charity's intellectual assets, generating a net contribution to reinvest in CRUK's core purpose. |

Objective 1: Supporting researchers with translational activity

Providing researchers with close proximity support and responsiveness

Over the course of this year we have endeavoured to get closer to our researchers and to provide translational support to them, wherever they may be.

This year signalled a significant advance in the UK-wide coverage provided by our Translational Support Team. We have team members now located across the entirety of the UK, providing a single point of contact with Commercial Partnerships and helping researchers to identify and develop projects with the potential to benefit cancer patients. Our service includes intellectual property advice and protection, project development, advice on different translational funding mechanisms and initiatives, facilitating collaboration across the CRUK network and with industrial partners, amongst others.



Forging relationships with host institutions to provide better support for researchers:

Opportunity Sourcing and Translation Team members are embedded within institutions, allowing them to develop a deep understanding of the science and local ecosystem, as well as forging relationships with researchers. Embedded team members are highly visible and available for researchers to interact with, making it easier to get advice and support for projects. Additionally, embedded team members are often jointly funded by, and work closely with, the host institution technology transfer organisation. This ensures alignment between the host institution and CRUK and provides a clear and consistent service to researchers.

A better customer experience for our researchers:

We are committed to providing researchers with a highly transparent and best practice service. This year we performed a customer journey mapping exercise to better understand the needs and expectations of researchers when they work with us and used this to create a customer charter which spells out our commitments to researchers (see earlier section on our commitment).

To ensure that we are delivering a high-quality service we will also perform an annual customer satisfaction survey to gauge our performance and constantly identify areas for improvement.



We have listened to what our researchers were telling us. Now we are acting on it.

> DR STEPHEN SHAW Associate Director Opportunity Sourcing and Translation



Case study

Dr Harriet Story

After completing a PhD developing theragnostic liposomes to treat and image tumours via chemical exchange saturation transfer (CEST) at UCL, Harriet spent a year at Imperial Innovations before joining the Opportunity Sourcing and Translation Team as a Translation Manager. Harriet is jointly funded by UCL Business and CRUK; consequently, Harriet is deeply embedded within the UCL Business Team and spends half of her time supporting CRUK-funded researchers at UCL and the rest of her time providing IP and commercial support to staff at University College London Hospitals (UCLH) NHS Foundation Trust.

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Performing this joint role provides me with exposure to an extraordinary range of translational activities and the unrivalled opportunity to draw on the previous experiences and capabilities of two of the UK's most successful technology transfer organisations; CRUK's Commercial Partnerships and UCL Business. From the perspective of my CRUK role, being fully embedded within UCLB is an essential part of being able to rapidly respond and build relationships with UCL-based researchers.



Providing access to key resources

CRUK strives to ensure our researchers have access to appropriate resources to provide them with the best chance of progressing their new ideas towards market, whether it be a therapeutic drug, a new test for cancer, a surgical device or new software code. Below are just two of examples of this years' activity with regard to the many core services CRUK provides and Commercial Partnerships helps to promote and support:

Accessing antibody capabilities

The CRUK-AstraZeneca Antibody Alliance Laboratory (AAL) is a strategic partnership to support academics in accelerating the translation of their novel biology into potentially first-in-class antibody-based cancer medicines. The standalone lab, located in Cambridge, combines the complementary expertise of academic insight and industrial drug development capability. AstraZeneca provides access to its world-class human antibody phage display libraries and established antibody-engineering technologies to deliver lead candidates ready to enter clinical development.

AAL case study:

Treating rare childhood cancers: Professor Richard Gilbertson, Director CRUK Cambridge Centre.

Working with AAL, Professor Gilbertson isolated the first antibody that detects, in human tissue, a fusion protein resulting from a complex chromosomal rearrangement in patients with supratentorial ependymoma. This is a rare paediatric tumour of the brain and spinal cord with less than 50 cases/year in the UK. The ability to detect the protein could support development of a therapeutic and will potentially transform patient care by informing the most appropriate treatment regime for individuals.



Professor Richard Gilbertson, Director CRUK Cambridge Centre

Accessing gene-editing/functional genomic capabilities

In 2019, AstraZeneca and Cancer Research UK established the Joint AstraZeneca-CRUK Functional Genomics Centre (FGC). The overarching mission of the FGC, with the expert guidance of Professor Greg Hannon, Director of CRUK Cambridge Institute, is to be a centre of expertise in genetic screens, cancer models, CRISPR vector design and computational approaches to big data. This centre, established in the heart of the Cambridge Biomedical Campus, will support CRUK funded researchers by providing access to cutting edge CRISPR technology. Since opening its doors in September last year, the FGC has started collaborating on projects brought forward by our research community. In addition, we are actively collaborating with AstraZeneca to develop new and improved CRISPR tools that we can then also make available to CRUK funded researchers and the wider research community.



Professor Greg Hannon, Director of CRUK Cambridge Institute

14 Our achievements

OBJECTIVE 1 CONTINUED

This year has been an impressive year for Commercial Partnerships in terms of engaging with researchers and building our portfolio as demonstrated by a marked increase in invention disclosures, patent applications and technologies under management.



Top 10 institutes by invention disclosures

OBJECTIVE 1 CONTINUED Patent applications filed

| NAME | FIRST UK FILING (PRIORITIES) | FIRST INTERNATIONAL FILING (PCT) | TOTAL |
|---|---------------------------------|--|-------|
| Cancer Research UK Cambridge Research Institute | 5 | 3 | 8 |
| University of Cambridge | 4 | 1 | 5 |
| University College London | 4 | 1 | 5 |
| University of Oxford | 7 | | 7 |
| Beatson Institute for Cancer Research | 3 | | 3 |
| Newcastle University | | 3 | 3 |
| The Institute of Cancer Research | 1 | 2 | 3 |
| University of Birmingham | 3 | 1 | 4 |
| Cancer Research UK London Research Institute | | 1 | 1 |
| CRUK Manchester Institute | 1 | 1 | 2 |
| CTxONE PTY LTD | 1 | 1 | 1 |
| TOTAL | 25 | 13 | 38 |

NB: Patents with multiple originating institutions are represented against each institution, but the totals only sum up unique applications.

16 Our achievements

OBJECTIVE 1 CONTINUED

Technologies actively managed by Commercial Partnerships

- Biomarker and Diagnostics
- Small Molecule
- Technology and Materials
- Biological Therapeutics





Selected drugs progressing to market

| Agent | Company | Institute | Development stages | | | |
|-------------------------|------------------------|-----------------|--------------------|----------|-----------|--------|
| | | | Phase I | Phase II | Phase III | Market |
| Zytiga® (abiraterone) | Johnson & Johnson | ICR | | | | |
| Lynparza® (olaparib) | AstraZeneca | ICR, Sheffield | | | | |
| Rubraca® (rucaparib) | Clovis/Pfizer | Newcastle | | | | |
| Temodal® (temozolomide) | Merck | Aston | | | | |
| Erivedge® (vismodegib) | Genentech/Roche | CRUK, Harvard | | | | |
| Onpattro® (patisiran) | Alnylam | Cambridge | | | | |
| Balversa™ (erdafitinib) | Johnson & Johnson | Newcastle | | | | |
| Zinecard® (Dexrazoxane) | BTG/Pharmacia & Upjohn | CRUK | | | | |
| Capivasterib | AstraZeneca | ICR | | | | |
| ADCT-402 | ADC Therapeutics | UCL | | _ | | |
| SCIB1 | Scancell | Nottingham | | - | | |
| IOA-244 | iOnctura | CRUK-TDL | | | | |
| CT7001 | Carrick Therapeutics | Imperial, Emory | | | | |
| СТ900 | Carrick Therapeutics | ICR, (BTG) | | | | |
| RG7802 | Roche | CRUK | | | | |
| AUTO4, AUTO6 | Autolus | UCL | | | | |

The portfolio expressed above represents a small subset of a portfolio of over 90 assets in active development, all of which are receiving support from the Commercial Partnerships team.

We've been ranked second for the number of oncology licenses completed* (*Nature's Trends in Oncology Dealmaking 2018)

Objective 2: Encourage entrepreneurial culture and skills in our research community

- The Issue: Evidence indicates that our research base is not translating as much as we might wish them to. Between 2012 2017 only 5% of grant awardees reported IP or licensing outputs and only 2% reported spin-out creation.
- The Challenge: Promote a culture of entrepreneurship amongst CRUK funded researchers with a target of engaging 10-15% of our researchers in translational activity.

Activity this year

We set up our entrepreneurial programmes initiative (EPI)

The EPI is a range of initiatives aimed at promoting an academic culture where entrepreneurship is enabled and incentivised. Over the course of the year we implemented an array of different programmes, each providing researchers with the opportunity to learn new skills, access vital resources and expand their networks. These include:

• Innovation Events & Workshops

Business Accelerators

- Entrepreneurial Competitions
- Training & Mentorship

Our programmes have been set-up throughout the UK with applications welcome nationwide.

As changing the culture within academia is a long-term 10 year+ aspiration, the EPI is targeted at, although not exclusive to, *early career researchers* with the aim of seeding a new generation of researchers who view research and translation as equally important.

During our first year, the EPI has successfully run several events and set-up partnerships that bring together leading entrepreneurial and innovation organisations across the UK. This has enabled us to leverage existing infrastructure, allowing us to make an immediate impact.



Entrepreneurial Programmes Initiative (EPI) 2019

Only 1 in 10 of Cancer Research UK's discovery researchers engaged in commercialisation activity between 2012-2017. We aim to improve this significantly.

BENEDICT CONWAY, Entrepreneurial Programmes Manager

STIMULATING ENTREPRENEURSHIP

INNOVATION EVENTS & WORKSHOPS

We now run a series of annual innovation summits & regional workshops to educate researchers on how to engage in entrepreneurship. Building on the successful London Innovation summit, this year we ran a well attended Innovation Summit in Manchester and also ran a Translation workshop for CRUK junior fellows in London. Over 300 researchers have benefitted from our events to date. EXAMPLES OF ACTIVITY THIS YEAR

INNOVATION COMPETITIONS

This year we ran an Innovation Prize competition with a focus on training and developing ideas to provide the resources and skills required to translate research in early 2018 followed by the CRUK oncology "Activate Challenge" in Scotland later in the year.



TRAINING SCHEMES

Training-focused programmes provide the skills needed to develop ideas to meet a clear market need. During the course of the year we secured new partnerships with Innovate UK on the ICURe programme & Start Codon for interactive online training and networking.

BUSINESS ACCELERATOR PARTNERS

Over the course of the financial year we established new partnerships with 3 accelerators: Panacea Oncostars, Deep Science Ventures & a provider base in the north (not yet public). Each partnership operates a different model and are open to all UK based researchers in cancer, allowing researchers the flexibility to choose the model most suitable to their needs or proximity. Over 35 companies have been developed through our partnered programmes so far.

Deep Science Ventures



CONVERGE



Innovate UK

Objective 3: Develop industry partnerships in therapeutics

We can never stand still and we seek novel partnerships with industry every year. The next few pages provide a few cases studies of successful partnerships.

CRUK to develop novel Her3 antibody into the clinic

Originally developed by Singapore-based Hummingbird Biosciences, HMBD-001 targets the HER3 receptor, which when activated through binding to other cancerassociated proteins, turns on a strong signal that causes cancer cells to grow and divide. The Centre for Drug Development has entered into a collaborative partnership with Hummingbird to complete preclinical development and run a first-in-human clinical trial of this promising therapeutic.

First-in-human trial of lung cancer vaccine

CRUK's Centre for Drug Development entered into a partnership with Vaccitech Oncology Limited (VOLT) to deliver a phase I clinical trial of VOLT's novel immunotherapy vaccine candidate for patients with nonsmall cell lung cancer (NSCLC). The vaccine was developed through VOLT's proprietary technology platform, creating viral vectors engineered to express tumour-associated antigens MAGE-A3 and NY-ESO-1.

Immuno-oncology microbiome therapeutic and biomarker development

Several studies have shown that the gut microbiome plays a critical and causative role

in determining which patients respond to checkpoint inhibitor therapy. However thus far they have failed to identify a consistent gut bacterial signature associated with response. In May 2020, Microbiotica, Cancer Research UK and Cambridge University Hospitals NHS Foundation Trust ("CUH") entered into a collaboration to identify and develop microbiome co-therapeutics and biomarkers for cancer patients receiving immune checkpoint inhibitor therapy.

iOnctura raised EUR 15 million

iOnctura was founded in 2017 as a spin-out from Merck, with Merck and Cancer Research UK providing a best-in-class pipeline of molecules that harness both direct and immune-mediated anti-cancer activities in solid cancers and cancer fibrosis. The company closed a EUR 15 million Series A financing led by INKEF Capital and co-led by VI Partners with participation by new investor Schroder Adveq. iOnctura's founding investor, M Ventures, also participated in the fundraise.

Novartis signs collaboration with the CRUK Beatson Institute

The Cancer Research UK Beatson Institute has entered into a multi-year collaboration with Novartis to continue the development of KRAS inhibitors, first discovered by the Institute. In 2017, Cancer Research UK and the Cancer Research Technology Pioneer Fund (CPF), managed by Sixth Element Capital, committed £2.5 million in collaboration with the National Cancer Institute (NCI) in the US to develop gold standard tests to analyse these novel RAS inhibitors. The new collaboration between Novartis and the Drug Discovery Unit at the Cancer Research UK Beatson Institute builds on this. [See page 23]

Myricx Pharma was formed

This drug discovery spinout from Imperial College and the Francis Crick Institute is focused on the preclinical development of PTM pathway inhibitors in cancer. The company is based at the state-of-the-art £170M Molecular Sciences Research Hub at Imperial's new White City Campus.



Azeria Therapeutics announced a £32 million financing

Azeria was founded in 2017 by Sixth Element Capital, manager of the CRT Pioneer Fund, and Cancer Research UK's Commercial Partnerships team with the aim of building a world class pioneer factor 1 oncology company, developing breakthrough treatments for hormone resistant breast cancer patients. The company announced a £32 million Series B financing in which Syncona has committed £29.5 million alongside existing investor, the CRT Pioneer Fund.

Arxx Therapeutics Partnership – Tumour microenvironment

Disease upregulated extracellular S100A4 is responsible for eliciting excessive activation of the pro-fibrotic, pro-inflammatory and tumourpromoting microenvironment. Neutralization of extracellular S100A4 represents a compelling and novel approach to treat a range of human indications, spanning from autoimmune and fibrotic diseases to metastatic cancers. Under a license agreement with CRUK, Arxx Therapeutics will further develop the lead drug candidate, 6B12, towards the clinic. This programme originated through research at the Danish Cancer Society and was then assigned to CRUK to seek out commercial partnership opportunities for its development.



ArcherDX Cancer Monitoring Technology obtains breakthrough device status

As part of an on-going collaboration, TRACERx investigators, led by Professor Charles Swanton, Group Leader, UCL and the Francis Crick Institute, and Dr. Christopher Abbosh, Principal Clinical Fellow, UCL, are utilising ArcherDX's technology to detect low-volume molecular residual disease at high levels of sensitivity to help achieve TRACERx's goal of a more personalized approach to developing cancer treatments. The company received Breakthrough Device Designation from the U.S. Food and Drug Administration (FDA) for its Personalised Cancer Monitoring (PCMTM) technology. [Link here]

Autolus Therapeutics raised \$100.8 million

Days after announcing the first response rates from a Phase I/II trial of CAR T cell therapy AUTO1, Autolus, a company in which Cancer Research UK has an equity position, raised \$100.8 million in a follow-on offering, with an additional \$80m raised in a subsequent round. In the AUTO1 study, after one month, CD19-targeting AUTO1 led to molecular complete responses in eight of nine evaluable patients with relapsed or refractory B cell acute lymphoblastic leukemia (ALL). At five months, six of 10 were alive and in molecular remission. There were no cases of grade 3 or higher cytokine release syndrome.



Adaptate Biotherapeutics formed to develop antibody-based therapies that modulate gamma delta T-cells

T-cells are a distinct T-cell sub-type that respond to molecular patterns of distress and have been shown to have tremendous potential in treating cancer and other immunological disorders. Adaptate Biotherapeutics was formed to further develop several potential drug targets and antibodies that have potential to modulate the activity of T-cells in situ. The founding of Adaptate has been made possible by investment from Abingworth and Takeda Pharmaceutical Company Limited and has additionally benefited from the support of King's College London, the Francis Crick Institute and Cancer Research Technology.

Achilles Therapeutics raised £100 million

This Series B financing was led by RA Capital Management, founding investor Syncona and joined by important new investors including Forbion, Invus, Perceptive Advisors and Redmile Group. The funds will deliver two human proofof-concept studies using a unique personalised T cell therapy approach targeting clonal neoantigens in non-small cell lung cancer and melanoma. [See page 26]

Aptamer Therapeutics and CRUK partnership formed

Following the successful awarding of a CRUK Biotherapeutic Drug Discovery Project Award, Aptamer Therapeutics formed a new collaboration the University of Manchester and Cancer Research UK. The project will explore the potential of aptamers as therapeutic agents for the treatment of Chronic Myelomonocytic Leukaemia (CMML) and other myeloid malignancies.

AstraZeneca-CRUK Functional Genomics Lab launches

AstraZeneca and Cancer Research UK launched the Joint AstraZeneca-CRUK Functional Genomics Centre (FGC). The overarching mission of the FGC is to be a centre of expertise in genetic screens, cancer models, CRISPR vector design and computational approaches to big data. [See page 13]

Novartis partnership - Novel RAS Inhibitors

- During the year we signed a new partnership with Novartis to develop an innovative approach for hard-to-treat cancers being developed at the CRUK Beatson Institute.
- More than 30% of all human cancers, including 95% of pancreatic cancers and 45% of colorectal cancers, are driven by mutations of the RAS family of genes. However, over the past 30 years, it has not proved possible to find a direct pharmacological approach to target RAS that has yielded a drug. Scientists at the Cancer Research UK Beatson Institute. supported by Cancer Research UK, have been pursuing a highly structure-based design approach to discover small molecules that will directly disrupt RAS activity.
- In October 2019 Sixth Element Capital LLP (6EC), a UK-based fund manager established to manage investments for the £70 million CRT Pioneer Fund (CPF), and the Cancer Research UK Beatson Institute announce a multi-year agreement with Novartis to progress development of novel RAS inhibitors, discovered by the Institute's Drug Discovery Unit for hard to treat cancers. Novartis are collaborating with the Beatson team to further develop the RAS inhibitors and has the option to exclusively license compounds identified through the collaboration



Access to the substantial resources and technical expertise of Novartis will help accelerate this vital research into the clinic.

DR PHILIP MASTERSON Associate Director, Business Development

UNOVARTIS



Beatson Institute

CRUK/LifeArc/Ono Immunooncology Alliance

We launched our Cancer Immunotherapy Alliance with LifeArc and Ono Pharmaceutical in 2019. It represents a multimillionpound strategic partnership to progress new immuno-oncology drug targets and accelerate the development of treatments that address unmet needs in cancer.

Bringing together the research expertise of our academic network, with complementary drug discovery expertise of our Therapeutic Discovery Laboratories, LifeArc and Ono, this unique alliance is developing an exciting portfolio of small molecule and antibody drug discovery projects.

This year:

- The alliance was awarded Best Partnership Alliance at the prestigious Scrip Awards in late 2019 which recognises major achievements in the industry.
- We ran a launch event in May 2019 attended by more than 40 participants from all parties.
 - We saw wide engagement with PIs across the UK and beyond – more than 40 confidential disclosure agreements signed; 5 academic workshops held.

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The collaboration will identify targets for the development of both antibody and small molecule therapeutics.



DR LAURA FLETCHER Associate Director, Strategic Alliances



Bicycle Therapeutics partnership with CRUK's Centre for Drug Development

This year we entered into our second partnership with Bicycle Therapeutics to advance novel bicyclic peptide immuno-oncology drug (BT7401) candidate.

BT7401 is the latest immunooncology drug candidate developed by Bicycle Therapeutics based on its innovative bicyclic peptide technology. It designed to circumvent the limitations of the current generation of antibodies targeting CD137 and provide a safer treatment option for cancer patients, including for those who stop responding to checkpoint inhibitors. In partnership with Bicycle, our Centre for Drug Development will work with CRUK's network of scientific and clinical investigators to progress BT7401 through preclinical studies and sponsor a first-inhuman clinical trial of BT7401 to assess its safety and antitumour activity.

The collaboration with Bicycle is the 25th deal under the Clinical Development Partnerships initiative intended to advance the clinical development of promising oncology agents and increase the number of innovative medicines available to patients. Under our agreement, Bicycle retains the right to advance BT7401 and milestone and royalty payments would be made to Cancer Research UK.



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We are excited to extend our relationship with Cancer Research UK by collaborating with them on BT7401. Cancer Research UK is a partner of choice, with a broad network of collaborators and extensive expertise in cancer treatment.



DR KEVIN LEE CEO Bicycle Therapeutics



Achilles Tx raises £100m during the year

Achilles Therapeutics is developing personalised \dot{T} cell therapies targeting clonal neoantigens protein markers unique to the individual that are expressed on the surface of every cancer cell. The company is building on discoveries from our landmark TRACERx Non-Small Cell Lung Cancer study and research led by Achilles co-founders Professor Charles Swanton, CRUK's Chief Clinician (UCL, the Francis Crick Institute), Professor Sergio Quezada (UCL) and Professor Karl Peggs (UCL). Following the formation of Achilles Therapeutics in 2016, the company has moved from concept to clinic rapidly, recently raising £100m in finance and now has 2 programmes in the clinic for Non-Small Cell Lung Cancer and Melanoma.





Objective 4: Diversify beyond therapeutics

During the year we continued to increase the diversity of our portfolio with technology, medtech and software all representing a growing proportion of our pipeline.

Case study of a dataset

The OPTIMAM dataset is one of the largest and most well annotated dataset of breast mammograms worldwide. The unique element of the OPTIMAM database is the pseudoanonymisation system developed at the Royal Surrey NHS Foundation Trust, which links images and clinical outcome data. Patients can be tracked through their consecutive interactions with the screening programme, creating a longitudinal dataset that can be used to identify cancers that arise between the 3-yearly screening visits. Researchers can then review prior 'normal' screening results to try and identify characteristics that would allow the earlier detection of the cancer. In addition to the images and associated clinical data, the team have expertly annotated the dataset so that areas of interest are highlighted.





Portfolio Composition

Case study of a research tool

Ilaria Malanchi and Luigi Ombrato, Francis Crick Institute

The pcPPT-mPGK-attR-sLPmCherry-WPRE vector is a breakthrough in tumour research. It allows for spatial identification of the local metastatic cellular environment within tissue. Ilaria Malanchi and Luigi Ombrato, researchers at the Francis Crick Institute, developed this system to engineer tumour cells, giving them the unique ability of labelling their surrounding cells.

Following the publication of the vector in Nature, 10 global working groups have begun using the vector in a variety of research areas including breast cancer metastasis and leukaemia. With the addition of the vector to the on-line ximbio.com catalogue, Ximbio has received over 70 enquiries from researchers around the world for access to the research tool.

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I think it's really important that people who do translational research have the possibility to translate it, but they need support. Scientists don't necessarily have the skills to translate their research by themselves - they need support to be able to do the next step.



PROF. LUIGI OMBRATO Francis Crick Institute

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Our business unit Ximbio is the world's largest non-profit dedicated to making academic research tools of all kinds available to the global research community.



ROBERT BONDARYK Global Head, Ximbio

Ximbio License Activity





Case study of a diagnostic

Inivata – Using ctDNA to improve cancer testing and treatment.

Inivata is a clinical cancer genomics company focussed on harnessing the potential of analysing circulating tumour DNA (ctDNA). This fragmented DNA derived from a cancer is used to improve cancer testing and treatment.

The company was formed in 2014 based on the research of Professor Nitzan Rosenfeld at the CRUK Cambridge Institute, University of Cambridge. Novel applications of ctDNA are enabled by Inivata's technology platform which includes its proprietary, enhanced TAm-Seq[™] technology. Inivata's lead product, the InVisionFirst[™]-Lung test, is commercially available and the development of tests for other cancers is ongoing.

During the year Inivata announced the launch of a clinical trial to evaluate the impact of its lung biopsy test in advanced lung cancer as well as receiving accreditation from the American College of Pathologists for its CLIA laboratory in the USA.



Harnessing the precision of ctDNA analysis to improve personalised healthcare in cancer

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Forming a startup is exhilarating and exhausting, but ultimately very satisfying.



PROF NITZAN ROSENFELD, CRUK Cambridge Institute

Objective 5: Invest in our people and promote diversity

At CRUK we believe that our success in supporting the researchers we fund stems from our staff, and that the more diverse our team is, the better it will perform.

Supporting our staff

This year we undertook a staff survey and actively listened to our staff's comments and suggestions on how we could improve. Having listened, we then committed to act on such comments. We recognise that we need to be open and honest if we are to continuously improve, and by being public about these initiatives, we expect our staff and customers to hold us to account and to challenge us to keep improving.

Our staff told us about the following areas for improvement within Commercial Partnerships:

- Train staff on change management and resilience;
- Improve effective delegation;
- Increase the number of staff development initiatives;
- Create secondment opportunities for staff;
- Improve and implement a culture of calling out poor behaviour.

We committed to and initiated the following actions to enact change:

- Transition to new organisational structure and operational model;
- Delegation is now managed at a functional level;
- Our first 'manager development programme' cohort was initiated;
- Specialist training courses were initiated and delivered by our own staff to our own staff;
- The R&I University was launched at a divisional level, staff are now encouraged to spend 1 day a month developing themselves;
- Secondment opportunities were highlighted (internally and externally) to allow employees to stretch themselves and develop their careers.

Staff development success case story - Dr Michael Salako on his secondment with Start Codon

"I'm very interested in ways in which we can promote entrepreneurship within the life sciences amongst early career researchers. The chance to go on secondment at a start-up accelerator, which was just starting out to invest in early stage life science companies (about 10 companies a year), was a great opportunity to see how accelerators work, their benefit to budding entrepreneurs and whether companies can be successful. This is insight I could never have got from checking in now and then with accelerators and the information I am gaining can help in my new role within Commercial Partnerships as we spin companies out, and also in my role supporting the Entrepreneurial Programmes team."



Promoting equality and diversity

It is well known that diverse teams perform better than less diverse teams. CRUK takes the promotion of equality, diversity and inclusion very seriously, driven by a firm belief that it is not only the right thing to do, but will also ultimately lead to being more successful in our core purpose of beating cancer. CRUK has committed to a broad range of staff EDI objectives which can be found on the CRUK website*. In addition, CRUK has agreed to a number of EDI targets and objectives with our research community, include via our entrepreneurial programmes. With these wider goals in mind, the Commercial Partnerships team has committed at the team level to a series of EDI and minority ethnic related goals for our staff which we set out below.

Our commitments

- 1. We will move to utilising diverse interview panels and being thoughtful about the candidate experience during interview.
- 2. Every person in Commercial Partnerships should attend a course on EDI organised by CRUK to highlight the issues and to minimise unconscious bias.
- 3. To regularly review our recruitment diversity data and to be alert for trends that signal any move away from diversity (rather than towards it).
- 4. To showcase the power of diversity, provide a case study of a highly achieving, diverse team within our CRUK division (R&I).
- 5. To ensure senior management have EDI objectives that align with the overall EDI agenda within CRUK.
- 6. We will look to review our progress against these objectives on an annual basis.

CRUK's solidarity with the black research community

Since the financial year ended the saddening events relating to George Floyd and others has highlighted the systemic racism faced by black people all over the world including the UK. As a funder of research, CRUK stands in solidarity with the Black Lives Matter movement and has issued a statement to that effect, acknowledging that we are part of the problem when it comes to the underrepresentation of minority ethnic researchers within academic cancer research. Going forward we will hold ourselves to account on our commitment to support a positive research culture for all, take actions as a research funder against racism and make our research funding ecosystem more inclusive for Black people and other underrepresented groups.

Visit our website to read our EDI commitment statement. [Link here] Female staff in Commercial Partnerships 54%



A third at Associate Director level are female

21% Minority ethnic representation in Commercial Partnerships team



Objective 6: Invest, leverage and return capital to the charity

CRUK's primary objective is not to make money from commercialising intellectual property. It is to achieve benefit for cancer patients. This ethos runs at the heart of everything we do.

Nonetheless, as the commercial arm of a charity, it is standard business practice to ask for a fair and reasonable return from any intellectual property that the charity's funding has helped create, even if such returns are incidental to our core purpose and many years downstream. Any revenues that accrue in this way are shared with those that participated in its creation (e.g. universities, institutes, inventors, NHS trusts etc.) thus helping to fuel further cancer research and patient care.

Revenue

Revenue for the financial 19/20 year for Commercial Partnerships related activity was £96m with a Net Contribution via gift aid back to CRUK of £43m. Over the last decade, income from our partnerships with industry has continued to grow to the mature level now seen. We expect this income to begin to decline over the next few years as some of the therapeutic drugs come off patent. Nonetheless, we expect the net positive contribution to the charity from Commercial Partnerships' activities to continue for the foreseeable future.

Net income since 2004 has been over **£0.5bn** of which CRUK's share is reinvested back into Cancer Research.



Over the last 5 years we have shared over **£215m** with our partner institutes and universities, who in turn have also reinvested such proceeds back into academic research. In addition, this year our collaborations and alliances with Industry leveraged an additional **£17m** from industry against our CRUK spend during the course of the year.

Investments and new spin-out activity

In addition to licences and collaborations with industry, spin-out companies represent another mechanism for getting early stage technology out of the research lab and on the path to being developed towards a product or service. CRUK has an established track record with spin-outs, either leading their formation or supporting our university partners to form them.

Our portfolio

At the conclusion of the 2019/20 financial year there were 29 **spin-out** companies in the CRUK portfolio. The portfolio is valued at **c£2.5bn** and the value of CRUK's existing equity stakes is **c£15m**. As these companies grow, they may exit the portfolio through listing publicly, being acquired via trade sale, or sometimes they just don't make it due to technical failure. CRUK has seen a number of successful exit events over the years exceeding **£500m** in total exit value and returning many millions in additional returns to the charity. Some examples are included below:

Kudos Pharmaceuticals. Acquired by AstraZeneca for **\$210m** USD upfront. This company was developing DNA repair including the PARP inhibitor olaparib (Lynparza®) which is now on the market for cancer patients around the world.

Piramed Pharma was acquired by Roche for **\$160m** USD upfront. This spinout was developing PI3K inhibitors, research which has since spawned a number of programmes in the clinic.

Spirogen Ltd was acquired by AstraZeneca for \$200m USD upfront. Spirogen has been retained as a division of AstraZeneca, developing antibodydrug conjugates for cancer.



During the financial year we invested more than £1m into patent filings and seed funding early stage projects.

DR STEPHEN SHAW, Associate Director Opportunity Sourcing and Translation

But we don't want to stop there. We believe that as our Entrepreneurial Programmes Initiative [See Page 19] establishes itself and our funded researchers become more translationally minded, we will see the opportunities to form new spin-outs rise. As such, this year we took the decision to form a dedicated "New Ventures" team tasked with building new spin-outs, managing our seed funds, forging relationships with investors and monitoring our portfolio of existing companies.

Over the course of this financial year, our spin-outs raised over £400m, the highest total ever and reflecting the vibrancy seen in the market for biotechnology companies addressing cancer. This brings the total cumulative amount raised by our spin-out portfolio to date to over £1.5bn.

INVESTMENTS AND NEW SPIN-OUT ACTIVITY, CONTINUED

New companies and investments

During the year we gained equity shareholdings in two new spin-outs.

- Adaptate Biotherapeutics. A new company derived from technology originally developed at Kings College London developing therapeutic antibodies against a special subtype of T cell. [See page 22].
- Myricx Pharma. A drug discovery spin-out from Imperial College London and the Francis Crick Institute targeting PTM pathways in childhood cancers. [See page 20].

Pre-Seed Funding: We funded **11** exciting new projects via our Project Development Fund. This fund provides early stage validation and preseed capital to help bridge the gap between a new idea and some validating data.

Seed investments: During the year we assessed **33** new opportunities, **17** at a detailed level. **9** of these went to our independent seed investment committee for review and we funded **3**, committing **£1.24m** to new and exciting ventures with the potential to help beat cancer.

Accessing scale-up funding

Our new partnership with SV Health Investors has had a sizeable impact on the amount of funding available to new cancer therapeutics companies emerging from the CRUK research base. This **\$265m** fund became fully active over the year and assessed over **30** opportunities, **11** of which were assessed in detail during the year. A new spin-out from Edinburgh University was identified for development and is expected to be funded in the following financial year.

Diversifying our portfolio

In keeping with our objective to further diversify our overall portfolio to reflect the way that product innovations are changing to encompass mobile tech and data, the proportion of our spin-out portfolio occupying the medical device, diagnostic, dataset and software spaces is steadily growing. **17%** of our company portfolio is now made up with companies developing non-therapeutic innovations and we expect this to grow to around **25%** over the next few years.



This year our spin-outs raised over £400m, bringing the total raised to date to over £1.5bn.

DR PHILIP MASTERSON, Associate Director, Business Development



SPIN OUT PORTFOLIO



Financial contribution to CRUK & partners

Where Commercial Partnerships income came from in 19/20 (£'000s)



CRUK Commercial Partnerships generated total income of £95,643k for the year. Of this, £84,010k came from three key royalty streams; Abiraterone (£76,169k), Olaparib (£4,133k) and Rucaparib (£3,708k). There was £6,402k generated from other licensing activities and £4,493k from royalties, licenses and sales by Ximbio. There was £738k of other income generated from recovery of patent and other costs.

£43,151k Net contribution to CRUK generated in 19/20



Where Commercial Partnerships income went in 19/20 (£'000s)



During the year CRUK Commercial Partnership distributed £44,012k of income back to academic and industry partners in line with IP agreements. Other significant costs include £4,495k on staff costs, £904k on patent acquisition and retention and £1,536k on other operating costs. Specific project costs during the year include £504k on the PACE initiative and £1,042k to fund the development of KRAS inhibitors as part of the multi-year collaboration with the Beatson Institute and Novartis.

| COMMERCIAL PARTNERSHIPS INCOME | £'000S | COMMERCIAL PARTNERSHIPS EXPENDITURE | £'000S |
|--|--------|---|--------|
| Key Royalty Streams | 84,010 | Distributions to Partners | 44,012 |
| Other Licensing Activities | 6,402 | Staff Costs | 4,495 |
| Ximbio Reagents Business | 4,493 | Patent Expenditure | 904 |
| Other Income | 738 | Drug Discovery Project Funding | 1,042 |
| Total Commercial Partnership Income | 95,643 | Investment in PACE* | 504 |
| | | Other Operating Costs | 1,536 |
| | | Total Expenditure | 52,492 |
| | | Net Contribution to CRUK | 43,151 |

Our impact

Ultimately, the CRUK Commercial Partnerships team exist to ensure that what matters most is how many patients benefit from the new ideas our funded research helps to create. Everything we do is aligned with this mission. With our focus on the nearterm creation of new patents, spin-outs, licence agreements and collaborations with industry it can be easy to forget that, what matters is how many patients get tested earlier, or receive better treatments for their cancer. With that in mind, we have put together the following infographic - to illustrate CRUK's impact.

All figures cumulative to date.



OUR IMPACT CONTINUED

Zytiga®

Our impact - Transforming advanced prostate cancer care

Our researchers' discovery and development of Zytiga® has transformed treatment for advanced prostate cancer, helping >330,000 patients worldwide since first approved in 2011.

Initially discovered by Professor Mike Jarman at what is now the Cancer Research UK Cancer Therapeutics Unit at the Institute of Cancer Research (ICR), vigorous clinical testing was led by Professor Johann de Bono. Early studies were sponsored by our Centre for Drug Development and latterly enabled by our commercial partners, BTG International Ltd. Zytiga® is now sold by Janssen Pharmaceuticals. The CRUK part-funded STAMPEDE trial also found that adding Zytiga® to hormone therapy at the start of treatment improves survival for men with high risk prostate cancer.

> >330,000 patients helped worldwide

The Abiraterone team with Professor Johann de Bono, Dr Florence Raynaud, Professor Mike Jarman, Dr Elaine Barrie and Professor Ian Judson

Lynparza® and Rubraca®

Our impact - A new approach to ovarian and breast cancer

Our scientists have played a key role in developing these new drugs for the treatment of some types of ovarian and breast cancers. A critical breakthrough came from two teams of our researchers – one led by Professor Alan Ashworth whilst at the ICR. The drugs strike a genetic weakness in cancer cells, including those with faulty BRCA1 or BRCA2 genes.

Lynparza®

We set up KuDOS Pharmaceuticals with Professor Steve Jackson and the University of Cambridge to commercialise his academic work on DNA repair. KuDOS went on to discover Lynparza® and be acquired by AstraZeneca.

Rubraca®

Discovered by our Newcastle University team led by Professor Herbie Newell in collaboration with Pfizer, Rubraca® became the first ever PARP inhibitor to enter the clinic with the help of our Centre for Drug Development. Rubraca® is now developed and marketed by Clovis Oncology.

Lynparza® has treated over 20,000 patients worldwide





Our people and how to contact us

We can't fit all the profiles of our wonderful team on one page, but if you would like to contact us to discuss any matter, please feel free to use the contact details on this page and ask to speak to the relevant team member listed below so we can help direct you to the right person:



TONY HICKSON Chief Business Officer



ROBERT BONDARYK Global Head Ximbio (supporting researchers with research tools and reagents)



JULIE COMPTON

Head, Business Operations (support for queries around existing partnerships, spin-outs and agreements)



LAURA FLETCHER

Associate Director, Strategic Alliances (supporting longer term alliances with industry)



STEPHEN SHAW

Associate Director, Opportunity Sourcing & Translational Support (first responders for researchers in our community around new ideas or accessing translational grants)



ANDREW WALDRON

Director Legal, (transactional and legal support to the research directorate of CRUK)



PHILIP MASTERSON

Associate Director, Business Development (support with creating new spin-outs, as well as new transactions and agreements)



We need your help – tell us about your amazing ideas and let us help you to develop new products so that we can beat cancer together.



Registered charity in England and Wales (1089464), Scotland (SC041666), the Isle of Man (1103) and Jersey (247).

