Institution: The Institute of Cancer Research

Unit of Assessment: Clinical Medicine UoA1

a. Context

The Institute of Cancer Research (ICR) is committed to carrying out research in such a way that it can be exploited to its maximum potential for the benefit of the public. The ICR's approach to impact is driven by this philosophy and has the aim of ensuring appropriate and effective exploitation and dissemination of research findings to maximise speed to patient benefit. Our highest priority is to achieve direct improvement of patient care and health outcomes through earlier diagnosis, more targeted and effective treatments, the reduction in side effects and improved quality of life. However, in pursuing these aims we also create considerable commercial impact, particularly in the biotechnology and pharmaceutical sectors.

Within our core research programmes, and in collaboration with colleagues in UoA5, we aim to identify new targets for therapeutics and we aspire to have the most successful academic cancer drug discovery programme in the world. We also lead on the development of radiotherapy. We work in partnership with our colleagues in the Royal Marsden NHS Foundation Trust (RM) to carry out translational research, experimental medicine and phase I/II clinical trials. We collaborate with biotechnology companies and the pharmaceutical industry to take lead compounds through all phases of drug development and work with equipment manufacturers to develop the technologies for diagnostics, imaging and therapy. We also engage widely with clinical practitioners through our leadership of large multi-centre Phase III trials and provide education and continuing professional development updates. We not only carry out our own development of research leads but also facilitate the development of our findings by others through our approach to commercialisation of intellectual property. We participate in national policy development and work with cancer charities to support fundraising and public awareness.

b. Approach to impact

The ICR's aim is to ensure appropriate and effective exploitation and dissemination of research findings to maximise speed to patient benefit.

The ICR and RM were awarded NIHR-BRC status in 2007 as the only specialist BRC dedicated to cancer, and this was successfully renewed in 2012. This funding, together with that derived from being a Cancer Research UK (CRUK) Centre and an Experimental Cancer Medicine Centre, enables us to support an infrastructure in which we systematically take the findings of basic scientific cancer research in cancer gene discovery, cell and molecular biology, targeted cancer therapeutics discovery and radiotherapy and physics through translational steps of tumour profiling, molecular pathology diagnostics, predictive and pharmacodynamics biomarkers into phase I proof of concept studies and molecular imaging supported tumour specific phase II clinical trials. Transition into large-scale network-adopted clinical trials is facilitated by the CRUK-funded, NCRI accredited, ICR Clinical Trials & Statistics Unit which has particular expertise in Radiotherapy, Breast, and Urology trials.

Where necessary, we work in collaboration with commercial organisations to facilitate the development of the product or service, and we monitor progress even after the formal collaboration period has ended to ensure that the impact is being realised. If partner organisations discontinue development, we have mechanisms in place to ensure that the results are returned to us so that we can seek other opportunities to exploit them. Where the lead on commercialisation is being taken by another organisation, for example Cancer Research Technology or Wellcome Trust, these principles are enshrined in our agreement with them and they are obliged to ensure relevant terms are included in contracts. For example, our prostate cancer drug, abiraterone, was returned when the original commercial partner discontinued development, allowing a new partner to be identified and this drug now has regulatory approval.

The ICR sets up commercial agreements that leave scientists freedom to operate and therefore able to help multiple companies in the same field. The consequence of the non-exclusive arrangements is less income but a greater likelihood of patient benefit. For example, the ICR has led on all aspects of the development of intensity modulated radiotherapy (IMRT) from the underpinning theoretical physics to large-scale multi-site clinical trials. The quality assurance

processes on the trials have served to cascade technical development and training throughout the UK and the trial results have led to changes in NICE guidelines for radiotherapy. This work has led to the development of accelerators that are focussed on delivering IMRT. By signing non-exclusive deals, the ICR has worked with Elekta AB and other manufacturers in the development of such equipment.

Although achieving commercial impact from our intellectual property is important, we do not necessarily maximise this. Before making any decision to commercialise, an assessment is made of whether this would provide the maximum benefit to patients and in some instances it is decided they would be better served by making the technology widely available through publication. However, we have learned we may need to act pre-emptively. For example, our initial policy was to publish novel cancer genes but others may patent before the publication comes out. Current ICR strategy, therefore, is to file early patents that can either be dropped after publication once it is clear that no one else has patented (eg BRIP1, PALB2), or the patent is maintained but multiple non-exclusive licences are granted. Between 2008 and 2013, the ICR granted over 91 licences and assignments of intellectual property resulting from our research in UoA1 and received invention income of over £17 million from 19 distinct inventions.

Interaction with industry is vital for taking promising new drugs through the various stages of development, approval and launch on to the market. An exclusive licence has to be offered, otherwise the company would not invest in the drug development, but we seek a fair return and aim to sign a collaborative licence agreement rather than simply “selling off” the programme. We have found the most effect way of accelerating progression to the clinic and ensuring maximum patient benefit is for the ICR to continue laboratory research to identify markers of response, possible mechanisms of resistance and other indications where the drug might be effective and that this research can be critical to the overall success the drug programme. Since 2008, we have discovered 7 drug candidates, the majority of which are being actively developed by industrial partners. We have major drug discovery collaborations with AstraZeneca, Janssen, Merck Serono and Genentech. The research of the CRUK Cancer Therapeutics Unit and the ICR/RM Drug Development Unit has been recognised by the receipt of the American Association for Cancer Research’s Team Science Award 2012. The citation highlighted the team’s world-leading discovery of 16 innovative drug candidates, and the progression of six of these drugs into Phase I clinical trials, including highly promising inhibitors of HSP90, PI3 kinases, protein kinase B/AKT and cyclin-dependent kinases. The AACR also recognised the team’s work on BRAF and its inhibitors, the identification of inhibitors of CHK1 and Aurora/FLT3, and the discovery and development of abiraterone acetate. Also in 2012, Professor Workman received the Royal Society of Chemistry “Chemistry World Entrepreneur of the Year Award” in recognition of his success at taking pioneering drugs out of the laboratory and into commercial development.

Our ability to conduct “smart” and efficient clinical trials has made us a partner of choice for pharmaceutical companies worldwide both for the development of drugs first discovered at the ICR and also for their own drugs, particularly when identifying trial sites outside of the US. We have developed a prognostic score that has enabled better selection of patients for trials. During the period of assessment, in UoA1, we have had 58 collaborations with industry resulting in research income of £4.9 million. We have also concluded 699 separate agreements to set up 41 new clinical trials and entered into alliance agreements with two companies to enable multiple trials and collaborations without the need for separate agreements for each project.

The ICR’s preferred strategy is to license directly to a commercial partner where this is likely to lead to faster product development, for greater patient benefit, and also produces a greater commercial return to the ICR. However, in certain circumstances the ICR will create a spin-out company. For example, this may be a better route than licensing to commercialise a technology or it may be necessary to develop the concept further before commercial partners are willing to invest. The ICR created Piramed Pharma to commercialise its work on PI3 kinase inhibitors. Piramed Pharma was acquired by Roche in 2008 for $160 million, with a later milestone payment of $15 million.

Traditional grant funding supports projects in the discovery phase. In many cases, however, the potential new product or technology at the end of this academic phase is immature. This means that it is sometimes difficult to attract an industrial partner, or, if one can be found, the financial return is often quite modest. If the product or technology were to be developed further before being partnered, its value might increase considerably and the chance of finding a partner would be enhanced. However, the work required to develop the project in this way is often outside the remit of academic grant funding. The ICR has developed two sources of funding designed to bridge this funding gap for ICR projects. During the current period, the Faringdon Fund has provided up to £50,000 for initial proof of concept studies and in future ICR researchers will also have access to BACIT Innovation Investment Funding (see below) to develop projects with commercial potential to increase their value and attractiveness to commercial partners. The ICR also encourages external applications for translational awards and, during the period, in this UoA has had 3 awards totalling over £8 million from the Wellcome Trust to develop BRAF and LOX inhibitors.

Our involvement in consultations, public policy committees, professional bodies, and charity advisory boards allows us to assist in enabling the transition of research evidence into public policy. For example: we played an important role in persuading NICE to review its initial decision in 2012 to turn down prostate cancer drug abiraterone for use in the NHS - and it is now delivering benefits to thousands of men in the UK; a member of ICR Faculty chaired the International Commission on Non-Ionizing Radiation Protection 2009-12; and we have highlighted to policy makers the barriers our researchers face in setting up clinical trials in children.

A key part of our strategy to create impact is to recruit Faculty who have experience of working in industry (8 team leaders in this UoA). Around 7% of all ICR researchers have a background in industry and all are provided with opportunities to develop commercial and entrepreneurial skills. The ICR runs workshops on how to develop successful interactions with industry and exploitation of IP as well as training in related skills such as public speaking and science communication. During the assessment period almost 200 researchers undertook this training. All research students are provided with information on commercialising research through a novel web based platform. Researchers can utilise up to 6 hours per week of their time for external activities such as providing consultancy services for companies or sitting on policy committees. Researchers may set up these interactions either independently or through the ICR's Enterprise Unit. Within the period, 56 such consultancies were set up. The Enterprise Unit, part funded by HEIF and part funded by the ICR's own resources, is staffed by highly trained and experienced business development professionals who have familiarity both with the ICR's research base and of working with industry.

c. Strategy and plans

For the next period, as before, the ICR's aim is to ensure appropriate and effective exploitation and dissemination of research findings to maximise speed to patient benefit; our strategy for impact will therefore remain as described above.

- Our primary objective for the ICR's discoveries is that they are developed for patient benefit, though we seek to achieve a fair financial return as an outcome for any exploitation by commercial organisations. If a discovery such as a diagnostic or bio-marker can be used widely with little or no further development it will be made available freely or through non-exclusive licensing. Exclusive licensing will be limited to those discoveries, primarily new therapeutics, which require substantial further investment from an industrial partner to realise patient benefit.
- Whilst continuing to work in close partnership with our clinical partner RM, we will also seek to form broader alliances across London to bring more of the population into stratified trials.
- We will continue to promote and increase our interactions with the business community to ensure that our research discoveries can be developed in the timeliest manner. Training of ICR scientists, particularly early career researchers, in intellectual property and commercialisation issues and in seeing impact as part of their role will continue.
- Identifying funding for our translational work will continue to be important. In the next period, we will be able to draw on funding arising from our innovative alliance with the Battle Against Cancer Investment Trust (BACIT) a fund of funds investment trust that does not charge fees but instead makes donations to a number of charities, of which the ICR is the major one. Each year BACIT will donate 0.5% of NAV (over £2 million) to the ICR and additionally may invest up to 1% (£4.5 million) to acquire interests in ICR drug development and medical innovation projects

(http://www.bacitltd.com/wp-content/uploads/BACIT-FactSheet-Jul-2013.pdf).

- We are increasingly viewing influence on public policy not simply as a consequence of conducting high-quality science, but as an objective we must actively work towards to maximise the impact of our research. Our new communications strategy strengthens our focus on policy and public affairs as a way of helping maintain a supportive environment for medical research, and ensuring our research delivers benefits for patients. We have recently formed a new communications directorate to pro-actively pursue these aims.

d. Relationship to case studies

Abiraterone, designed and synthesised at the ICR, is an example of a model we have found highly successful. We formed a partnership with a biotechnology company to share ongoing risk after the first clinical testing. The first commercial partner decided to stop development but was required to return the rights. Following further ICR research, the compound was re-licensed to another biotechnology company and finally licensed to a major pharmaceutical company. An exclusive licence has to be offered otherwise the company would not invest in the drug development, but ICR has had a fair commercial return, evidenced by payments to date, and has also continued laboratory investigations into biomarkers and resistance mechanisms.

The HSP90 project is another example of how the different strategies can be employed on a single project. ICR researchers first validated HSP90 as an important cancer drug target and identified biomarkers for use in clinical trials. These results were published to maximise patient benefit by enabling a number of pharmaceutical companies to develop their own in-house drug discovery programmes. At the same time, ICR scientists continued their research and independently discovered the pyrazole resorcinol series, from which, in collaboration with a biotechnology company (Vernalis), a clinical candidate was identified and subsequently licensed to a pharmaceutical company (Novartis). The ICR remains involved in the development of this candidate, AUY922, by supporting key phase I and II clinical trials.

The PKB project is another example of where we have issued multiple licenses and in parallel pursued an ICR-driven drug discovery programme to maximise the chances that the scientific breakthrough ultimately results in patient benefit. In this case six international pharmaceutical companies were licensed with reagents to enable them to begin PKB drug discovery programmes. In the meantime, the ICR team used their structural biology expertise to progress the ICR's own PKB inhibitor programme as a result of which two series of inhibitors are now licensed (AstraZeneca and Astex) and in clinical trial.

The PI3 kinase case is an example where the ICR set up a spin out company, Piramed, in order to progress the research to a stage where commercial partners could be found. Piramed licenced the project to a pharmaceutical company (Roche) and was sold.

Development of aromatase inhibitors for use in breast cancer is an example, where by taking a non-exclusive approach to the application of prognostic testing, ICR/RM researchers have been able to work with a number of companies to shorten the time taken to conclude clinical trials and gain regulatory approval of their drugs, so maximising speed to patient benefit. The ICR also retained rights to the IP for the Oncotype DX test, so that researchers could go on and develop improved tests.

The **Genetics and screening** case shows how peer reviewed publication can lead to impact, in this case the introduction of frequent monitoring of those identified through genetic testing to be at high risk of cancer. It also demonstrates how the ICR systematically takes research findings and follows them through in translational and clinical studies to introduce changes to health service practice and where necessary works with a commercial organisation to facilitate the development of a product, in this case a test to allow the simultaneous screening of an array of cancer susceptibility genes.

Radiotherapy dose fractionation is an example where wide public dissemination achieved the best results for patient benefit. The ICR devised, led and published the results of a large-scale long term clinical trial, which led to changes in clinical practice for the delivery of radiotherapy to treat breast cancer. As a result, patients benefit from needing fewer hospital visits and there are health service savings through reduction in treatment costs.

Intensity modulated radiotherapy (IMRT) is another case where widespread dissemination was the key to maximising patient benefit. No patent was filed and the equipment manufacturers did not have exclusive rights to the basic technology. ICR and RM scientists were free to work with a number of companies on the development of the new accelerators.