CANCER RESEARCH TECHNOLOGY

TRANSLATING RESEARCH IN TO NEW CANCER CURES - THE CRUK/CRT PERSPECTIVE

23rd March 2015

ADVANCING DISCOVERIES TO BEAT CANCER
AGENDA

1. Who We Are – CRUK and CRT
2. CRUK Translational Research Strategy and Infrastructure
3. CRT Development And Commercialisation Models
WHO WE ARE

- World's largest charitable funder of cancer research
- Employs its own scientists and funds research in UK universities
- Entirely funded by donations from the public
- Annual research spend of more than £350 million

- Technology development and commercialisation arm of Cancer Research UK (CRUK)
- Exclusive rights to IP from CRUK funded research
- Provide commercialisation services to institutions worldwide
- HQ in London, US subsidiary in Boston
WHY CRT?

What makes CRT unique?

• Primary focus is cancer
  – Specialist skills and experience

• Discovery and early clinical development capability
  – Greater ability to match customer needs

• Global project sourcing
  – CRUK, other charities and institutes, CRT Inc., CTx Pty

• Focus on patient benefit
WE ARE ENTERING A NEW ERA OF TRANSLATIONAL RESEARCH

• Increasing understanding of cancer cell and molecular biology
• Increasing ability to profile the structure, sequence and expression levels of genes, proteins and metabolites, establishing new potential biomarkers and drug targets
• Advances in sequencing technologies and reduction in costs, with advances in mathematical and computational capabilities to handle the information
• High quality sample collections with associated clinical data
• Innovative clinical trial designs

Continuing progress presents CR-UK with the opportunity to:

Facilitate greater flow of progress from bench to bedside,
Achieve a greater understanding of the biology from bedside to bench
THE NEED FOR INCREASED MULTIDISCIPLINARY COLLABORATION

Challenges in multidisciplinary collaboration

• Requirement of and access to multiple technologies
• Requirement for multiple skill sets
• Culturally different from “traditional” science
• Lack of reward / recognition/ incentives
• Lack of leadership with a translation focus
• Challenging to work across multiple sites
• Challenging to work across multiple organisations (NHS, academia, research funders etc.)
Key success factors to overcome these barriers include…

<table>
<thead>
<tr>
<th>Access to a Comprehensive Set of Capabilities</th>
<th>• A comprehensive set of capabilities (e.g. basic science, surgery, pathology, toxicology, pharmacology, medicinal chemists, trial infrastructure, clinicians, patients etc) for effective translational science</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical Mass</td>
<td>• Interaction is easier if people are located on the same site – connections are made which would not be otherwise, co-ordination is facilitated and accelerated • Some level of critical mass is important to drive the right mindset • Comprehensive infrastructure in a single location facilitates Pharma interaction</td>
</tr>
<tr>
<td>Networking &amp; Collaboration</td>
<td>• Networking and collaboration within and across locations is critical to access a comprehensive set of capabilities and to drive multidisciplinary working; even if the right building blocks are available, they must be joined up • It is also needed to access large patient numbers &amp; rare sub-groups</td>
</tr>
<tr>
<td>Strong Translational Leadership</td>
<td>• Strong leadership with a translational vision and the right mindset is key to driving translation and multidisciplinary working • Strong translational leadership is needed within the leadership team - not just limited to a single individual</td>
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<tr>
<td>Incentives</td>
<td>• Incentives need to be created to drive team science and collaboration, but also to highlight and drive the right areas of research • Funding mechanisms are a critical part of creating these incentives</td>
</tr>
<tr>
<td>Partnership</td>
<td>• Buy-in and partnership with the Trust and the University • Partnership with others e.g. Pharma etc</td>
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</table>
To deliver such research and drive effective translation, multidirectional, multidisciplinary integration of activities is required.

**Illustrative Future Vision**

1. Multidirectional, multidisciplinary integration of research activities

- Biologists need to be involved in all translational activities
- Molecular pathologists provide a key link between the lab and the clinic
CANCER RESEARCH UK’S AMBITION

1 in 4 survival rate
1970s survival rate

2 in 4 today’s survival rate

3 in 4 within the next 20 years
CANCER RESEARCH UK TODAY

WE SUPPORT A UK-WIDE NETWORK OF RESEARCHERS DELIVERING WORLD-CLASS RESEARCH

5 INSTITUTES
7 CLINICAL TRIALS UNITS
15 CENTRES
18 EXPERIMENTAL CANCER MEDICINE CENTRES
79 FELLOWS
100 PROGRAMME GRANTS
250 CLINICAL TRIALS
450 PHD STUDENTS
OUR STRATEGIC PRIORITIES: WHAT WILL WE DO

We will substantially increase our investment in:

- Basic understanding of cancer
- Cancer prevention
- Early diagnosis research
- Cancers of unmet need
- Therapeutic innovation
- Precision medicine
OUR STRATEGIC PRIORITIES: HOW WILL WE DO IT

To help deliver our strategic priorities, we will:

- Develop the best researchers
- Increase investment
- Invest in our translational network
- Launch new funding schemes
- Encourage collaborative approaches
Unique environment supporting key areas:

- Precision medicine
- Stratified medicine
- Biologically-rich trials

Centres Strategic Awards
Recruit Senior Leaders
NEW FUNDING

Programme Foundation Award
New scheme to support exceptional mid-career researchers
Launch July 2014

Immunology Award
New scheme to attract researchers investigating immunology in other disease areas into the cancer field
Launch Summer 2014

Multidisciplinary Award
New scheme to stimulate collaboration between biomedicine and the engineering and physical sciences
Launch Summer 2014

Pioneer Award
New award to support innovative, high risk, high reward research to tackle cancer challenges
Launch early 2015

Additional investment in Centres
• New Centres Strategic Awards to support networking and infrastructure
  Launch Summer 2014
• Assistance to recruit senior leaders

Grand Challenge
New scheme to support research into important, challenging questions in cancer
Launch early 2015

Transatlantic collaboration
Stand Up 2 Cancer support for transatlantic collaborations in translational research
Launch TBC
‘Research councils and charities are increasingly focusing on translational research but the ‘Valley of Death’ is hindering subsequent commercialisation’
TRANSLATIONAL RESEARCH IS IN TRANSITION

‘New normal’ is emerging - Old structures are being replaced with new and potentially more robust funding mechanisms

Pharma
- Internal R+D
- Outsourced R+D

Academia
- Passive licensing to Pharma
- Active licensing efforts, innovative partnering models, proactive pursuit of rights

Venture Capital
- Company financing
- Project financing
TRANSLATIONAL RESEARCH AND DEVELOPMENT

Drug Discovery – Small Molecule and biotherapeutics

Translational funding
Academic drug discovery units
Response mode funding streams

CRT Discovery Laboratories (CRTDL)

Over 80 drug discovery programmes under development
TRANSLATIONAL RESEARCH AND DEVELOPMENT
EARLY CLINICAL DEVELOPMENT

• CRUK Drug Development Office (CDD)
  – Manage and execute preclinical development and Ph I/II trials
    » GMP manufacturing capabilities
    » Clinical studies conducted to ICH GCP
    » Full project, data management, clinical and non-clinical operations teams
  – >120 agents taken into Ph I/II studies
  – 7 products subsequently reached market
  – Access to world-class network of major UK oncology units (ECMCs)

Zytiga for prostate cancer
Temodar for brain cancer
Etopophos for lymphoma, sarcoma, leukaemia, lung, brain and testicular cancers
Alimta for lung cancer
Lentaron for breast cancer
Zinecard or Savene for reducing chemotherapy side effects
Lozoxantrone for leukaemia
EVOLVING DEVELOPMENT AND COMMERCIALISATION ROUTES

- CRUK drug discovery research
- CRUK funded basic research
- Other charities
- Global institutes

- Licence → Development → Market
- Start-up → Company → IPO/M+A
- Academic-Industry Partnerships → Development → Market

Expanded in variety and scope
Changed in nature
MODELS – DIFFERENT APPROACHES FOR DIFFERENT PROJECTS

1. R+D Collaborations
2. Consortia
3. Alliances
4. CRT Pioneer Fund
5. Clinical Development Partnerships

In the last 5 years, CRT have signed >60 agreements in one or more of these models.
DRUG DISCOVERY ALLIANCES WITH CRTDL
NEW CRTDL MODEL: ELIMINATING THE GAP

Academic Research | Project Feasibility | Hit ID | Lead ID | Lead Op to in vivo POC | Development | Market | Patient Benefit

Academia

CRT Discovery Laboratories

Commercial Partner

Academia

Commercial Partner

CRT Discovery Laboratories
DRUG DISCOVERY IS NOT A LINEAR PROCESS (KILL THE CHEVRON!)
WHAT CAN ACADEMIA BRING TO DRUG DISCOVERY?

DEPTH OF KNOWLEDGE AND FOCUS ON TARGET BIOLOGY/DISEASE

ABILITY TO TAKE RISKS:

- Chemistry
- Target MOA
- Screening methodologies
- Level of target validation

PROVIDING “VALIDATED TARGETS” AND DISEASE POSITIONING

DRUGGING THE “UNDRUGGABLE”

PHENOTYPIC/CELL BASED APPROACHES

ACADEMIA IS NOT REDUCED COST OUTSOURCING!
WHAT DOES INDUSTRY BRING?

SCALE AND THROUGHPUT IN MANY STAGES E.G. HTS, CELL SCREENING, MEDICINAL CHEMISTRY

PROJECT MANAGEMENT AND DISCIPLINE

A FEEL FOR WHAT IS DEVELOPABLE - EXPERIENCE

DEVELOPMENT CAPABILITIES EG DMPK IN MULTIPLE SPECIES

NOT JUST A SOURCE OF FUNDING!
ALLIANCES AT CRT’S DISCOVERY LABORATORIES

Model brings together the best of academia and industry:

- World-class CRUK-funded research and PI’s
- CRTDL’s expertise in validating and progressing new drug targets
- Company drug research and development capabilities

Cancer Metabolism
signed Jul-2010
2yr extension Mar-13

Deubiquitinating enzymes (DUBs)
signed Jul-13

DNA damage repair processes (DDR)
signed Sept-13
ALLIANCES AT CRT’S DISCOVERY LABORATORIES

**Consortium of 4-6 World class PIs**
Novel biology, novel targets, technologies, assays, reagents, target biology expertise

**Drug Discovery Alliance**
CRT Discovery Laboratories and/or partner’s in-house team

**Output**
Optimised lead/development candidates in theme area

- Areas of ‘hot’ cancer science
- Focused biology theme
- Multi-target scope
- Integrated joint development
- Company option to acquire programmes at defined stage
- Shared upside
CRT PIONEER FUND

£70M investment fund to bridge the funding gap in the UK between cancer drug discovery and early development
THE CRT PIONEER FUND: RATIONALE

• Early stage venture capital is scarce in UK/EU
• CRT/CRUK want to connect discovery with development
• Fund creates an additional exploitation route for CRT
• Increases amount of value retained in projects for CRT
• Efficient progression- reduces need to find external partner
CRT has exclusive rights to CRUK IP

CRUK provides the majority of IP in the portfolio

Cancer Research UK

CRT’s share of profits gets invested in CRUK

Cancer Research Technology

European Investment Fund

Pioneer Fund (£70 million)  
Managed by Sixth Element Capital

Pharma and Biotech companies

Discovery  Preclinical  Phase 1  Phase II

Licensing revenue  Technology licenses

Public entity  Private entity  Public-Private entity
CLINICAL DEVELOPMENT PARTNERSHIPS

Releasing the untapped potential in cancer drug development
CDP IN A NUTSHELL

• Joint initiative between CRT and CRUK’s Drug Development Office.

• Objective:
  – Bring new life to de-prioritised cancer agents
  – Increase the number of clinical trials being undertaken for the treatment of cancer

• Targeted at leading pharma and biotech companies

• Clinical trial is undertaken at no cost to the company
<table>
<thead>
<tr>
<th>AGENT/TARGET</th>
<th>COMPANY</th>
<th>INSTITUTE</th>
<th>INDICATIONS</th>
<th>DEVELOPMENT STAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temodal®</td>
<td>Schering-Plough (now Merck)</td>
<td>Aston</td>
<td>Glioma</td>
<td>PRECLINICAL</td>
</tr>
<tr>
<td>Zytiga®</td>
<td>Cougar (now J&amp;J); BTG</td>
<td>ICR</td>
<td>Prostate</td>
<td>PRECLINICAL</td>
</tr>
<tr>
<td>Erivedge™</td>
<td>Genentech/Roche; Curis</td>
<td>Harvard; CRT</td>
<td>BCC</td>
<td>PRECLINICAL</td>
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<tr>
<td>PARP</td>
<td>Clovis; AstraZeneca</td>
<td>Newcastle; ICR; Sheffield</td>
<td>Ovarian; Breast; Melanoma</td>
<td>PRECLINICAL</td>
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<tr>
<td>TG4010</td>
<td>Transgene</td>
<td>Guy’s Hospital</td>
<td>NSCLC</td>
<td>PRECLINICAL</td>
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<tr>
<td>HSP90</td>
<td>Novartis; Vernalis</td>
<td>ICR</td>
<td>NSCLC; Breast</td>
<td>PRECLINICAL</td>
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<tr>
<td>SG 2000</td>
<td>AstraZeneca</td>
<td>Portsmouth; London School of Pharmacy</td>
<td>Ovarian; Haematological Tumours</td>
<td>PRECLINICAL</td>
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<tr>
<td>Akt/PKB</td>
<td>AstraZeneca; Astex</td>
<td>ICR</td>
<td>NSCLC; Breast</td>
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<tr>
<td>GSK1070916A</td>
<td>GSK</td>
<td>-</td>
<td>Advanced Solid Tumours</td>
<td>PRECLINICAL</td>
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<tr>
<td>IMA950</td>
<td>immatics biotechnologies</td>
<td>-</td>
<td>Glioblastoma Multiforme</td>
<td>PRECLINICAL</td>
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<tr>
<td>PI 3-kinase</td>
<td>AstraZeneca; Piramed</td>
<td>LRI; ICR; Ludwig</td>
<td>NSCLC; Breast</td>
<td>PRECLINICAL</td>
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<tr>
<td>ONX-0801</td>
<td>Onyx Pharmaceuticals</td>
<td>ICR</td>
<td>Advanced Solid Tumours</td>
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<tr>
<td>AT 13148</td>
<td>Astex Therapeutics</td>
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<td>Advanced Solid Tumours</td>
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<tr>
<td>AZD 0424</td>
<td>AstraZeneca</td>
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<td>Advanced Solid Tumours</td>
<td>PRECLINICAL</td>
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<tr>
<td>AZD 3965</td>
<td>AstraZeneca</td>
<td>-</td>
<td>Solid Tumours; Lymphoma</td>
<td>PRECLINICAL</td>
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<td>DI-B4</td>
<td>Merck KGaA</td>
<td>-</td>
<td>Leukaemia; Lymphoma</td>
<td>PRECLINICAL</td>
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<tr>
<td>RG7813</td>
<td>Roche Glycart</td>
<td>LRI; CRT-DL</td>
<td>Solid Tumours</td>
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</tr>
<tr>
<td>Undisclosed</td>
<td>Roche Glycart</td>
<td>Oxford</td>
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<td>AZD2098</td>
<td>AstraZeneca</td>
<td>-</td>
<td>Renal Cancer</td>
<td>PRECLINICAL</td>
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<tr>
<td>AST-VAC2</td>
<td>Asterias Biotherapeutics</td>
<td>-</td>
<td>Lung Cancer</td>
<td>PRECLINICAL</td>
</tr>
</tbody>
</table>

As of Oct 2014
CRT SPIN-OUT ACTIVITY
CRT’S SPIN-OUT POLICY – WHEN TO?

• Only when it is the optimal route to develop the science and deliver patient benefit

• Strong science and scientist with potential to produce a critical mass of projects

• Propriety IP position/leading science position

• Scientist with commitment

• Management- CEO with track record (VC “approved”) available at formation
CRT’S SPIN-OUT POLICY – WHAT WE WILL “INVEST”

• IP and services

• An IP pipeline of up to 2 years duration with IP under option and licences requiring further consideration (may require University consent)

• Pre-formation services given for equity

• Post-formation services (up to a 12 month maximum) given for cash

• Up to 5% of capital raised (max £100K) to complete a round
CRT’S SPIN-OUT POLICY – PROTECTING OUR INTEREST

• Usually appoint a shareholder director position as long as shareholding ≥ 10%

• Where shareholding ≤ 5% CRT would not require a board seat

• Case by case based on risk/benefit for shareholdings of 5-10%

• Where CRT holds >5%, CRT requires shareholder agreements to cover
  – non-disposal of IP without consent
  – clawback licence in insolvency
  – pre-emption rights on transfer of shares and issue of new shares (CPF)
CRT’S SPIN-OUTS POLICY – START UPS IN FOREIGN JURISDICTIONS

• In general, CRT would not lead when a spin out is not under UK legal/tax regime

• If CRT does lead it requires
  – a local CEO with biotech experience
  – tax and legal advice from a local legal practice
  – director’s responsibilities in the jurisdiction to be evaluated on a case by case basis

• Papivax

• CTx
CRT’S SPIN-OUTS

Notwithstanding the above each opportunity should be judged on its merits and in light of prevailing market conditions.
ANECDOTAL CONCLUSIONS

• Set the hurdle high (especially if going the “maximal” route)

• Resist forcing a NewCo to placate researcher aspirations (especially “me-toos”)

• Adapt to the environment (finance and management availability) - there is no best way

• Remember it is a time consuming and people intensive

• Don’t forget licensing!
## OUR START-UP COMPANIES

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>SUMMARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acublate Limited</td>
<td>Set up in January 2012 by CRT to develop a next-generation High Intensity Focused Ultrasound (HIFU) surgery device to treat a range of solid tumour types.</td>
</tr>
<tr>
<td>BliNK Therapeutics</td>
<td>Founded in June 2011 by CRT and Paris based Kurma Life Sciences Partners to generate monoclonal antibodies using a novel platform.</td>
</tr>
<tr>
<td>Chroma Therapeutics</td>
<td>Discover and develop small molecule drugs based upon chromatin biology. Raised $53m in series C financing.</td>
</tr>
<tr>
<td>CYCLACEL (KuDOS Pharmaceuticals)</td>
<td>Develop agents that target key cell cycle regulators. Merged with Xcyte Therapeutics Inc. and subsequently raised $45m.</td>
</tr>
<tr>
<td>MISSION Therapeutics</td>
<td>Formed in August 2011, the company will translate cutting-edge cell biology research on DNA repair into drugs that will markedly improve the management of life-threatening diseases, particularly cancer. In November 2013, MISSION Therapeutics secured £30M in Series-B funding.</td>
</tr>
<tr>
<td>PIRAMED PHARMA</td>
<td>Develop anti-cancer signal transduction inhibitors. PI 3-kinase programme partnered with Genentech has potential milestones of $230m plus royalties. Acquired by Roche for $160m in 2008.</td>
</tr>
<tr>
<td>Spirogen</td>
<td>Founded in 2001, Spirogen uses ADC technology to optimise the performance of cancer drugs. Acquired by MedImmune in October 2013 for an initial $200m with a deferred consideration of up to $240m.</td>
</tr>
<tr>
<td>Inivata</td>
<td>A clinical cancer genomics company focused on harnessing the potential of circulating tumour DNA (ctDNA) analysis to improve cancer testing and treatment.</td>
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</table>
Concept

Existing therapeutic  Empowered therapeutic

Tumour cells
OUR RESEARCH TOOLS BUSINESS – XIMBIO

Our reagent portfolio is the largest single source of UK academic antibodies

• CRT has been commercialising research reagents created in academic institutes for 30 years
• Our portfolio exceeds 1000 monoclonal and polyclonal antibodies as well as cell lines and transgenic mice models
• The majority of our antibody portfolio is marketed through major worldwide chemical suppliers:
  – Abcam, EMD Millipore, BD BioSciences etc
• Cell lines and transgenics are supplied directly to industry
• We maintain hundreds of licensing agreements with over 60 companies
• > £2m in revenues generate from Research Tools business for the 2010/11 financial year
THANK YOU
WWW.CANCERTECHNOLOGY.COM