

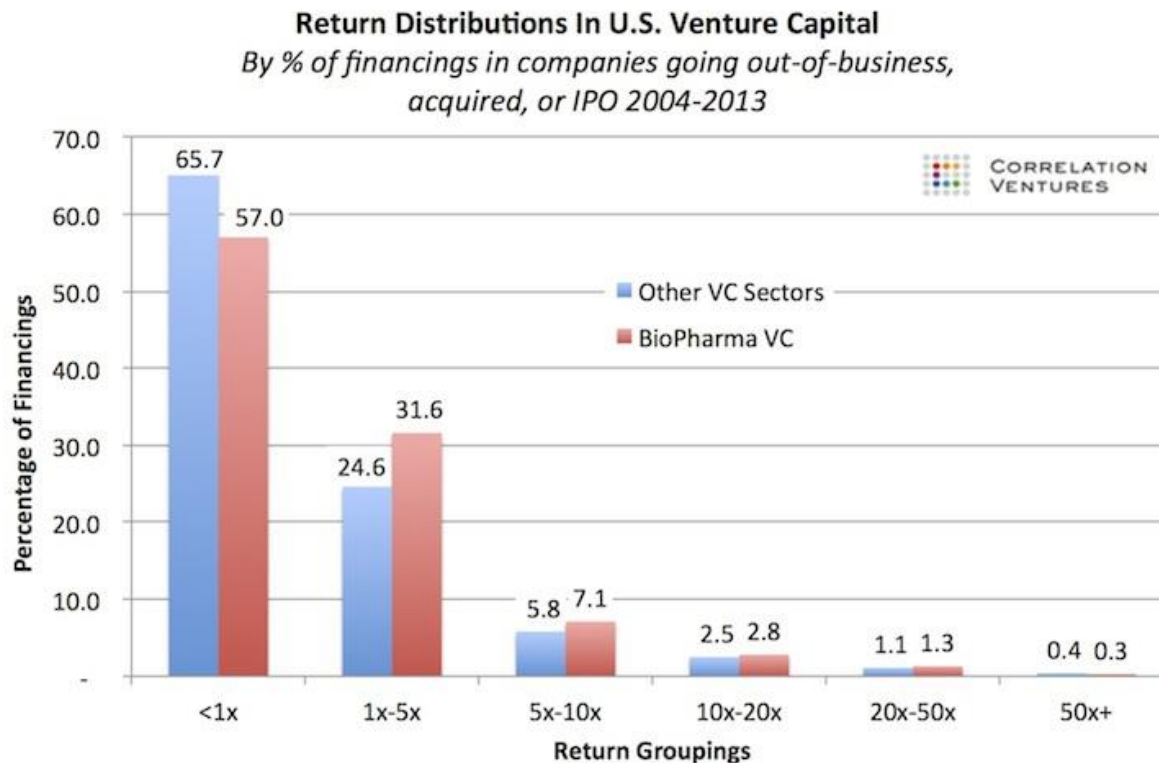
ELRIG 2015

Investing in Early Stage Drug
Discovery – An Investor's
Perspective



SIXTH ELEMENT
CAPITAL LLP

Drug Discovery Investing - Early Stage Investors View



N = 2,228 financings for BioPharma; 19,412 for Other VC Sectors
Includes data from Dow Jones VentureSource and other sources

Drug Discovery Investing - Early Stage Investor's View

- High Risk Science
- Capital Intensive – \$47m - Average Capital ¹ to Exit in 2014
- Time Consuming - 5 Years Median time to Exit² (Range 6m to 12 years)
- Baked in deal structures
 - Preference Stacks
 - Control
 - Non-Aligned Syndicates
- Difficult to execute and make a return for a small fund

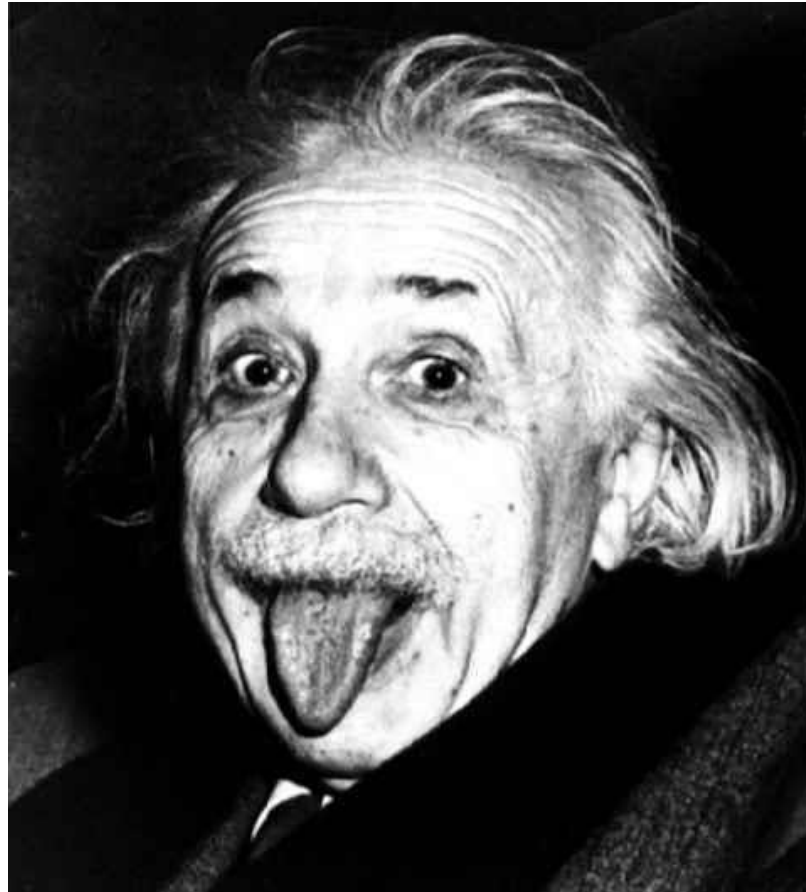
1. HPM BioPharma / Biotech Report 2014
2. Silicon Valley Bank Analytics Insight - 2010

Why Bother?

- Highly rewarding professionally
- Chemists, biologists and clinicians are superstars
- Opportunity:
 - 25% FDA approved drugs 98 – 07 derived from US Universities
 - Rises to 30% if you analyse for ‘innovative’ drugs*
- Pharma is looking for innovation and will pay
- Returns on successful projects can be very significant

*Kneller R. Nat. Rev. Drug Discovery 9,867 – 882, 2010

Insanity?



CRT Pioneer Fund

CRT Pioneer Fund

- £70m Fund ~ 15 investments
- 100% Oncology with CRUK focus
- 2/3 of Fund to be invested in CRUK supported projects
- Asset centric
- Assets developed primarily within CRUK infrastructure – capital efficiency
- Primarily sole funder ~ £10m per project
- Highly flexible funding and deal structures
- Returns primarily generated through licensing

Investors

- Cancer Research Technology
- European Investment Fund
- BACIT

Manager

- Sixth Element Capital

CRT Pioneer Fund – What's New?

- Projects must deliver significant benefit to the cancer patient – novelty and innovation
- Projects not companies – capital efficiency
- Projects developed 'in house'
 - Work supported in CRT/CRUK Drug Discovery Units
 - Clinical trials run via CRUK's Centre for Drug Development (CDD)
 - Non-core work outsourced (e.g tox, scale up synthesis etc)
- CPF does not need co-investors
- In-licensing model – essentially we are buying a value share in a project rather than company equity
- Focussed on developing to end Phase I before out-licensing to pharma
- Returns primarily through milestones & royalties not 'traditional exits'
- 'Patient Capital' – upto 15 Year fund life

CRT Pioneer Fund – What's Old?

- People still at the heart of success
- Projects need to be globally competitive at investment
- Can our investment make a difference?
- Detailed diligence – technical, commercial, IP
- Formal SAB and Investment Committee Investment process
- Tranched investments against milestones – Candidate Nomination, Tox etc,

CRT Pioneer Fund - Rationale

- CRT/CRUK –
 - Bridges gap between discovery with development
 - Creates an additional exploitation route for CRT
 - Builds on existing infrastructure
 - Reduces delays in development
 - Increases value retained in the project
- EIF
 - New ‘financial instrument’ for to bridge specific financing gap
 - Potential high economic and social impact
 - Support existing strong CRT activity
 - Test a new model

CRUK / CRT – World Class Cancer Partners in CPF

CRUK has a history of developing profitable oncology drugs



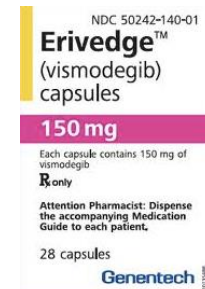
Aston University
Temodar
Licensed to Merck
Launched 1999
\$1000m + annual sales



Institute of Cancer Research
Zytiga
Licensed to Johnson & Johnson
Launched 2011
\$1000m + annual sales



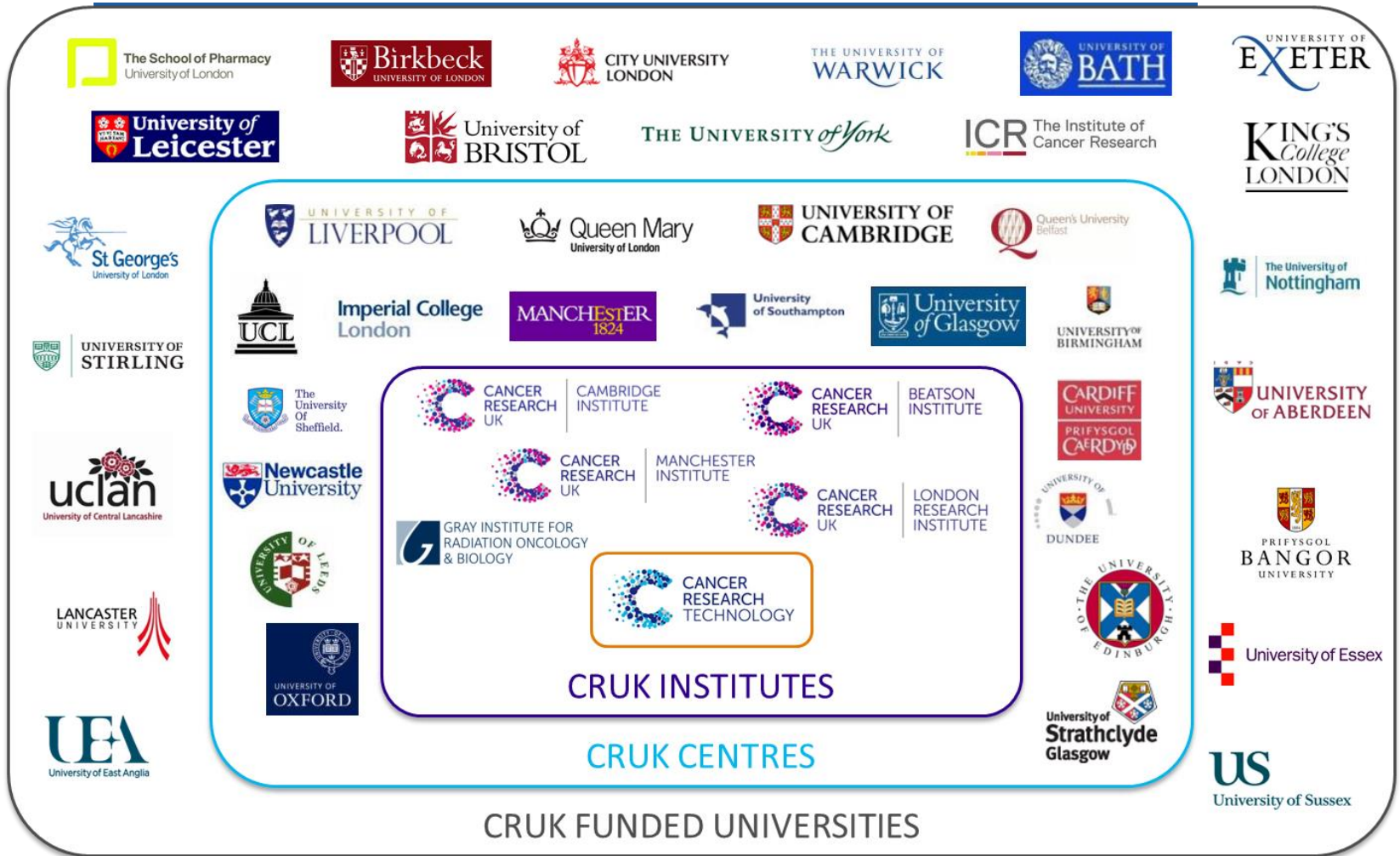
Institute of Cancer Research
Tomudex
Licensed to Astra-Zeneca
Launched 1998
\$100m + annual sales



London Research Institute
Vismodegib
Licensed to Roche
Launched 2012
Est annual sales \$500m

CRUK invest \$500m p.a in UK cancer research
CRT Pioneer Fund has preferential access to CRUK / CRT's drug discovery portfolio

CRUK / CRT: Unique Portfolio of Partners



Investment and Divestment Committee



Ian Nicholson (Chairman)

- Currently serves as NED on several public and private biotech companies in EU.
- Former CEO of Chroma Therapeutics. Raised over £65m from blue chip VC's. Negotiated headline value - \$1bn alliance with GSK and developed early stage projects through to Phase III study.
- Former Senior VP Business Development, Celltech, Acting CEO at Oxford Glycosciences, Commercial Director at Oxford Assymetry and Lonza. Whilst in these positions Ian led multiple significant commercial transactions (in and out licensing and M & A).



Dr Ellen Baron

- Managing Director, Healthios Capital Markets. Healthios is a US boutique Investment Bank and Ellen is establishing the Boston office with a focus in oncology.
- Former General Partner at Oxford Bioscience Partners (7 years), a Boston VC where she led multiple deals across their 149 portfolio companies.
- Former Senior Vice President of Business Development at Human Genome Sciences (HGS). 20 years at Schering Plough (SP) culminating in 8 years as Senior Director Business Development. At HGS and SP she concluded multiple in and out licensing transactions including working on the in-licensing of Temozolomide from CRT.

Scientific Advisory Board

Member	Position
Professor Herbie Newell (Chair)	Professor of Cancer Therapeutics, Northern Institute for Cancer Research (NICR). Expert in the <i>in vivo</i> pharmacology and pharmacodynamics of experimental cancer chemotherapy. Involved in multiple commercial collaborations including the recently announced alliance with Astex Pharmaceuticals.
Professor Ian Collins	Reader in Medicinal Chemistry, ICR. Previously Merck Sharp and Dome. Has led multiple medicinal chemistry projects in various therapeutic fields and his work has led to successful industry collaborations.
Professor Mike Owen	Independent Biotechnology Consultant. Formerly CSO at Kymab, Senior VP and Head of Research, Biopharmaceuticals R&D at GSK, Scientific Staff at Lincoln's Inn Fields.
Professor Peter Parker	Based at CRUK London Research Institute Peter is an expert in the molecular biology cell signalling pathways and their de-regulation in cancer. Founder of Piramed.
Professor Patrick Schoffski	Head of the Department of General Medicine Oncology and Laboratory of Experimental Oncology Leuven University. Practising experimental clinical oncologist and active participant in multiple oncology clinical trials in Europe.
Dr Ultan McDermott	Group Leader and Faculty member Wellcome Trust, Sanger Institute. Medical Oncologist. Current focus is running the Cancer Cell Line Project at the Sanger Institute.
Professor Maurizio D'Incalci	Head of Oncology at Mario Negri Institute, Milan. Widely experienced in the pre-clinical <i>in vivo</i> pharmacological evaluation of novel cancer agents with multiple mechanisms of action.
Dr Martin Drysdale	Head of Drug Discovery at Beatson Institute for Cancer Research. Formerly Deputy Research Director at Vernalis. Expertise in multiple therapeutic areas. Research has led to key relationships with major pharmaceutical companies.

CPF Pipeline – invested since March 2012

Project	Source	Oncology Indications	Rights	Pre-Lead Opt	Lead Opt	Preclinical Devt	Phase I	Phase II
CHR-2845	Chroma	HCC	Worldwide	→				
CHR-2845	Chroma	CMML	Worldwide	→				
Macrophage targeted p38 Inhibitor	Chroma	Multiple	Worldwide	→				
Macrophage targeted CSF1R Inhibitors	Chroma	Multiple	Worldwide	→				
CHK1	Institute of Cancer Research	Multiple	Worldwide	→				
MPS1	Institute of Cancer Research	Undisclosed	Worldwide	→				
ReT	CRUK Manchester Institute	NSCLC, MTC	Worldwide	→				
Undisclosed	Institute of Cancer Research	Undisclosed	Worldwide	→				
Undisclosed	Institute of Cancer Research	Undisclosed	Worldwide	→				

Macrophage Therapeutics Projects based on ESM Technology Platform

In Legals

Macrophage Pharma

- Technology platform and compounds in-licensed from Chroma for use in all indications except GSK carve
- Enables intracellular targeting and accumulation of small molecules to macrophages and monocytes using esterase sensitive motif technology (ESM)
- Manipulation of macrophages enables discovery of novel immuno-oncology therapeutics
- Platform has already delivered 2 orally bioavailable, compounds into clinical trials
- Macrophage Therapeutic's portfolio consists of:
 - CHR-2845 – targeted HDAC inhibitor; completed a Phase I study, currently in Phase I study in HCC and a CMML Phase I study to be initiated in 2015 – investigator led
- Pre-Clinical
 - P38 and CSF1R programmes in lead optimisation – macrophage switching
- Research
 - Opportunities for multiple novel projects exploiting ESM technology

Checkpoint Kinase 1 Inhibitors (CHK1)

- Compounds discovered at the Institute of Cancer Research Cancer Therapeutics Unit and supported by CR-UK in collaboration with Sareum Ltd
- Candidate:
 - is potent, well tolerated and orally bioavailable
 - is highly selective for CHK1
 - shows *in vivo* potentiation of DNA damaging agent induced tumour growth inhibition in solid tumours
 - Shows oral efficacy as a single agent in an *in vivo* N-MYC driven model of neuroblastoma and in an *in vivo* model of AML
 - Shows *in vivo* efficacy in combination with radiotherapy in solid tumours
- Candidate in pre-clinical development prior to entry into two Phase I clinical trials
- Potentially best-in-class compound

Monopolar Spindle 1 (MPS1) kinase inhibitor

- Compounds discovered at The Institute of Cancer Research, London (ICR) and supported by Cancer Research UK and Breakthrough Breast Cancer
- Project is in lead optimisation
- Project hypothesis – Inhibition of the mitotic checkpoint will cause gross chromosomal abnormalities leading to death of cancer cells
- Two advanced chemical series with solid IP protection
- Clearly identified patient populations in breast and colon cancer
- Aim to identify a candidate for pre-clinical development during 2015
- Current plan is to take compounds into Phase I prior to partnering

RET

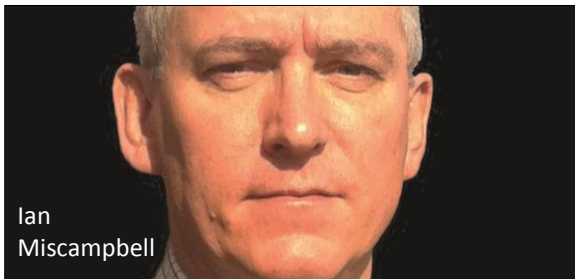
- Compounds discovered at the CRUK Manchester Institute (CRUK-MI)
- RET is a translocation critically associated with development of cancer in subset of NSCLC and MTC. Becoming implicated in other diseases as genetic analysis of other tumour types evolve
- Targets tightly genetically defined population
- Potential for rapid development strategy
- Programme designed to deliver a candidate and back-up to address potential for drug resistance

The Sixth Element Capital Team

Experience prior to founding Sixth Element Capital



- 20 years exploitation of life science IP in licensing and venture capital
- Temodal – Schering Plough, Rukaparib - Agouron, Trovax – Oxford Biomedica
- DNA Research Innovations (LIFE) , Oxford Immunotec (OXFD)
- > \$250m of fund raisings into portfolio companies
- > \$150m raised into venture funds
- Founder Sixth Element Capital



- 7 Public and Private companies & CFO in VC firm
- Stem cells, inflammation, oncology, vaccines, diagnostics, dermatology, consumer
- 13 M&A deals
- 6 licensing transactions
- 12 financings > £100m capital raised
- Founder Sixth Element Capital




- Specialist in drug development asset valuation
- Degrees in mathematics and mathematical finance from Oxford University
- Co-founder Avance, a corporate finance boutique specialised in valuation
- Advised > than 100 fund raising rounds and license deals.
- He is co-author of "Valuation in Life Sciences"
- Founder Sixth Element Capital

CRT Pioneer Fund - Summary

- £70m Fund
- Principally Projects not companies
- Projects developed 'in house'
- Links CRUK Discovery with Development
- Fully funded projects
- Capital efficient
- Creative deal structure
- New paradigm for investing in early stage cancer drug discovery

Contacts



rob@sixthelementcapital.com
ian@sixthelementcapital.com
ralph@sixthelementcapital.com
www.sixthelementcapital.com