What a Chemist needs to know about Technology Transfer

How we all work together to get a licensing deal done

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The Institute of Cancer Research

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Objective

To create a valuable product that can be licensed

- From academia to industry
- From small company to large company

Technology transfer and the scientific team need to work closely together to achieve this objective.

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Key Steps to Achieving a Good Licensing Deal

- Pick the right project to work on
- Protect intellectual property strategically
- Monitor competition and develop a unique selling point
- Design excellent marketing materials
- Select target customers wisely
- Value the product realistically
- Pursue potential licensees diligently
- Sell the product well in personal meetings
- Negotiate efficiently and fairly

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Chemists can help at all these stages

Work in partnership with the

rest of the scientific team and your technology transfer office

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Pick the Right Project to Work On

- What is the competition?
- What is the likelihood of chemical success?
- What is the likelihood of commercial success?

Technology Transfer offices need help from the scientific team to work all this out.

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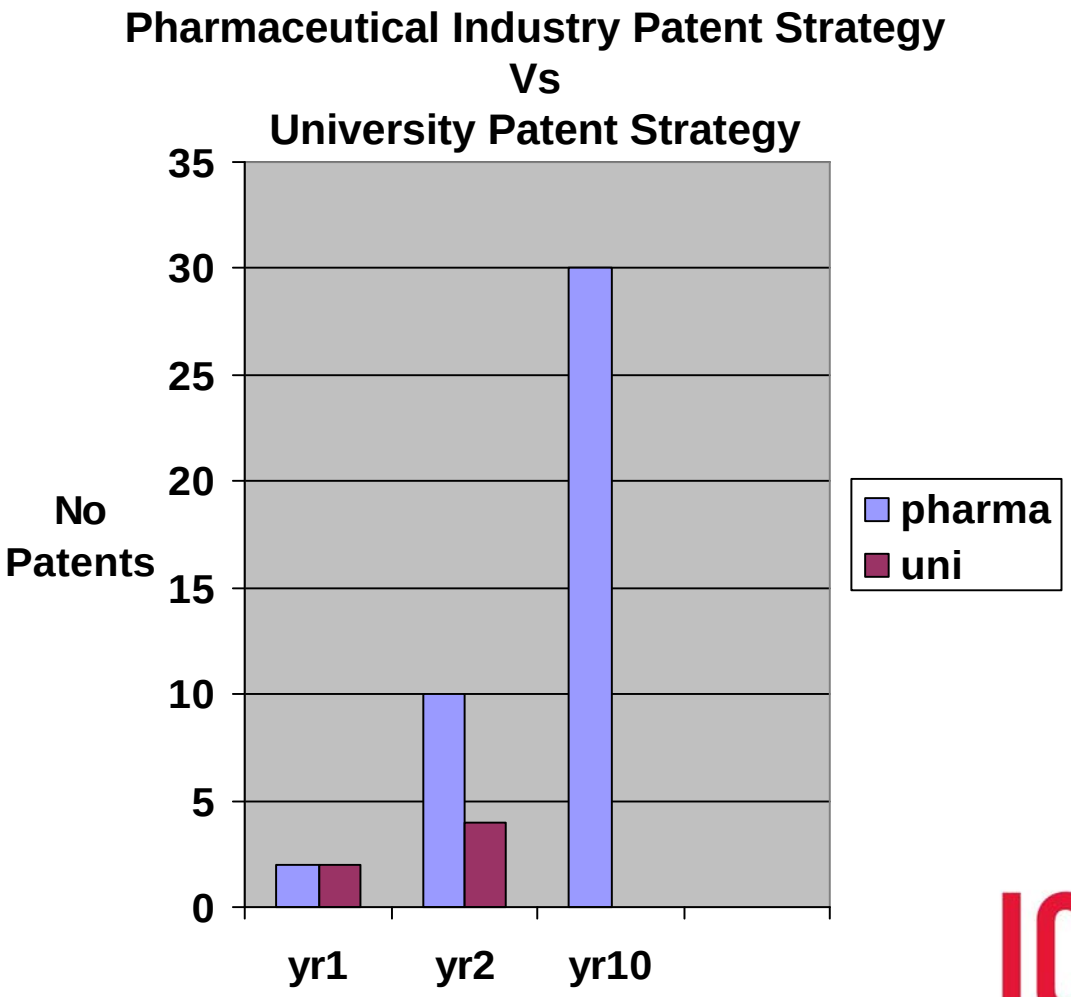
Patenting Novel Chemistry in a Drug Discovery Programme



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Protect Intellectual Property Strategically

- What is the patent budget
- When are you likely to partner

These are important questions for technology transfer offices.

- When should we drop patents
- How much can we get in one patent
- How late can we patent (publications!)

A university strategy is very different from a large company's strategy

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Monitor Competition and Develop a Unique Selling Point

The chemists can really help here. You know your molecules – you know why they are better.

- Toxicity
- Synthetic route
- Solubility
- Solid patent position (chance of grant)

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Design Excellent Marketing Materials

- Project List
- Flyer
- Confidential Data Pack
- Presentation

Chemists should review these documents carefully not just for scientific accuracy but from the point of view of a customer

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The Institute of Cancer Research

Currently there are a number of licensing and collaboration opportunities that the Enterprise Unit would be pleased to review with interested parties

THERAPEUTICS

- Aurora Kinase Inhibitors
- Chaperonin CCT Inhibitors as general Anti-Mitotics
- B-RAF Inhibitors
- BGC9331- A TS Inhibitor
- GDEPT - Gene Directed Enzyme Prodrug Therapy
- CHK1 and CHK2 Cell Cycle Checkpoint Kinase Inhibitors

DEVICES

- High Resolution Gamma Ray Imaging Device
- PETRRA - Novel PET Camera
- Device for tissue processing
- Variable Aperture Collimator (VApC) for Radiotherapy Delivery

PLATFORMS/SOFTWARE APPLICATIONS

- Oligonucleotide Microarray Synthesis Technology
- Software for Analysis In MR Imaging
- Ultrasound Targeted Gene Delivery Technology
- Domain Hunting Technology - Domainex

TARGETS

- Glypican-5 a Novel Cancer Target
- HDAC9 - A novel Histone Deacetylase

DIAGNOSTIC/BIOMARKERS

- Monoclonal Antibodies against Cerb-B2 and EGFR
- Chronic Lymphocytic Leukaemia (CLL) Markers

Gene Directed Enzyme Prodrug Therapy (GDEPT)

KEY FEATURES

- **Targeted therapy enabling localised activation of a cytotoxic prodrug in tumours**
- **All components patented and owned by or licensed to The Institute for GDEPT**
- **Significant efficacy demonstrated in several xenograft models**
- **Prodrug, enzyme and vector have already been safely used in man**
- **First product in preclinical development; due to enter planned and funded Phase I trial in 2010**
- **Extensive patent portfolio will enable development of multiple follow-on products**

GDEPT

GDEPT is a gene-based two-step treatment for cancer. In the first step, the gene for the bacterial - and so wholly exogenous - enzyme carboxypeptidase G2 (CPG2) is targeted to the tumour by the use of a selective vector. This is then followed by the administration of a non-toxic prodrug which is activated locally to a powerful cytotoxic by the enzyme.

The lead product in our GDEPT programme is currently in preclinical development and is due to enter an approved, planned and funded Phase I clinical trial in 2010. The first trial will be in head and neck cancer, which is a challenging and as yet largely unmet medical need. The product will also be capable of application in a range of other oncology indications.

The vector is an adenovirus and has been developed so that its replication is under the control of a cancer selective promoter.

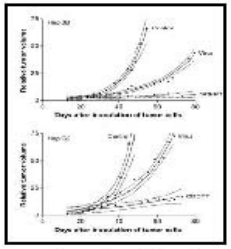

Figure: Xenograft models have demonstrated lead product efficacy.

As a consequence CPG2 expression, and thus prodrug activation, is restricted to cancer cells. The prodrug, enzyme and vector type have all been used safely in man in separate non-GDEPT products.

Human cell line xenograft models treated with a single intravenous systemic dose of the GDEPT vector show tumour-selective replication of adenoviruses and expression of CPG2. As shown in the figure subsequent administration of prodrug causes a dramatic decrease in tumour volume. Many cures have been observed and even those tumours that re-grow after initial treatment respond to further administration of the prodrug, indicating that the gene is stable and active in the long term.

Further to this, *in vitro* characterisation has demonstrated excellent specificity of prodrug activation towards CPG2 expressing cells. Once activated the prodrug diffuses out of cells and can act over the local tumour area. Good bystander cytotoxicity has been shown, only 2% of the cells needed to express the enzyme in order to achieve total cell ablation in a tumour.

Follow-up Products

We are developing a number of follow-on products which are enabled by our GDEPT technology. In the first instance these are being realised through the use of prodrugs with different profiles and/or alternative vector systems. The team continues to investigate new ways of applying the technology and is interested in forming collaborations in this area.

Inventors

Professors Caroline Springer and Richard Marais are the principal investigators leading this programme. Professor Springer is the leader of the Gene and Oncogene Targeting team based in laboratories of the Centre for Cancer Therapeutics of the Institute of Cancer Research in Sutton, Surrey. Professor Marais is the leader of the Signal Transduction team in the Section for Cell and Molecular Biology based at the Chester Beatty Laboratories of the Institute of Cancer Research in Chelsea, London.

Key Publications

Schepelmann, S. et al. Systemic gene-directed enzyme prodrug therapy of hepatocellular carcinoma using a targeted adenovirus armed with carboxypeptidase G2. *Cancer Res.* **2005**, 65, 5003-8.

Davies, L.C. et al. Novel fluorinated prodrugs for activation by carboxypeptidase G2 showing good in vivo antitumour activity in gene directed enzyme prodrug therapy *J. Med. Chem.* **2005**, *48*, 5321-8.

Intellectual Property

The Institute has a broad GDEPT patent portfolio which not only covers the lead product but also enables further GDEPT products to be developed (eg. WO2004020400, WO9603151). Some of these patents are already granted. This protected IP includes the use of CPG2 in GDEPT; composition of matter patents for a spectrum of prodrugs as well as methods of their chemical synthesis; and also liposome and lipoplex vectors for gene delivery. Some components of the lead product are protected by external patents but The Institute has rights to these.

In addition the Institute has a considerable body of expertise and know-how surrounding GDEPT and drug development which will enable the development of a commercial product to be progressed rapidly.

Commercial Opportunities

The Institute is seeking:

(a) an industrial partner to continue clinical development of the lead product. The partner would receive exclusive worldwide commercialisation rights to the lead product. An option agreement pending the Phase I results could be considered.

(b) commercial collaboration partners to enable the development of follow-on products.

The Institute of Cancer Research

The Institute works in a unique partnership with The Royal Marsden Hospital forming the largest comprehensive cancer centre in Europe. The Institute spends on average 75 million pounds a year on research and employs over 1100 scientists and support staff.

It has a world-wide reputation for excellence based on a continued tradition of achievement. We are a winner of the Queen's Award for Technological Achievement and in the most recent review of university research in 2008, The Institute was ranked 1st in the UK for biomedical research.

The Institute is also responsible for many of the scientific advances which have made a difference to people's lives in recent decades.

The Enterprise Unit

If you would like to discuss our GDEPT programme or any other Institute licensing and collaboration opportunities please contact:

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Select target customers wisely

Help the technology transfer team. Tell them who is active in the field. A company with a programme in this area may still be interested in buying yours (if it is better)

Do you know any particular likes and dislikes of possible customers

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Value the Product Realistically

How much work will your licensee have to do to get the product to market? – cost and time.

What is the chance that the product will fail in development?

What is the likely market size?

What is the patent life?

What have other similar deals achieved?

Chemists can help The Technology Transfer office understand all the variables here

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Pursue Potential Licensees Diligently

Technology Transfer offices are often very busy but a classic mistake in selling is to let a lead go cold.

Keep Nagging

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Sell the Product Well in Personal Meetings

Should the Scientists be there?

Why not?

Remember we are selling the product not the university.

Do you want to collaborate or just do an arms length licence?

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Negotiate Efficiently and Fairly

The Licensee and the TTO needs to know:

Do you still want to research on the technology?

Who has rights to improvements?

What are your publication expectations

Do you intend to research in competing areas?

Who are the other stakeholders?

Any contaminating MTAs?

To do any a good deal be very clear up front what your requirements are.

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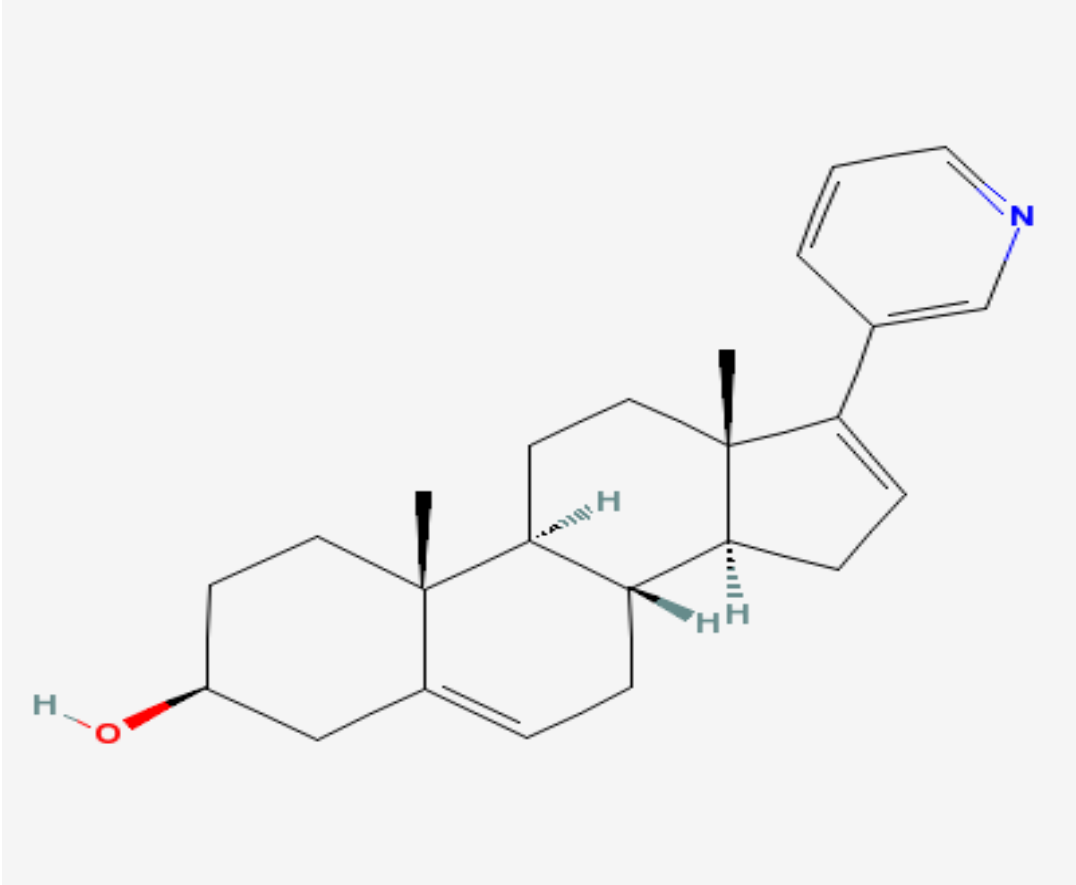

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