

<b>Institution: University of Nottingham</b>
<b>Unit of Assessment: UoA1</b>
<b>Title of case study:</b> Scancell - a successful cancer immunotherapy company
<p><b>1. Summary of the impact</b></p> <p>The University of Nottingham spin out company Scancell Holdings plc is developing novel immunotherapies for the treatment of cancer. By licensing products (£6million) and listing and raising money (£4million) on the stock exchange, it has provided an excellent return for investors. In 2012, in response to good clinical trial results, Scancell's shares showed the greatest percentage increase (10fold) on London's AIM stock exchange, reaching a market capitalisation of £98million. This has encouraged further investment (£6.5million) which is in line with the Government's plan to promote the Biotechnology Industry. As the products progress to market it will save further lives and continue to increase in value providing further profit for investors.</p>
<p><b>2. Underpinning research</b></p> <p>Cancer is the second leading cause of death in the Western world. Worldwide, around 12.7 million cancer cases are diagnosed every year, and this is expected to increase to 21 million by 2030. The drive behind the Cancer Immunotherapy group at The University of Nottingham (UoN) was therefore to improve treatment for cancer patients worldwide. In order to fund the development of these products, Professor Lindy Durrant (Professor of Cancer Immunotherapy, UoN, 2003-2013) spun out Scancell and, in 2008, listed on the Plus and then AIM London stock market. Durrant is the joint CEO of Scancell.</p> <p>Durrant developed both novel oncolytic monoclonal antibodies (mabs) which recognised unique glycolipids, and pioneered novel cancer vaccines targeting dendritic cells <i>in vivo</i>. All of these immunotherapies were licensed to Scancell. The company prioritised three mabs - SC100, SC101 and SC104 - for further development and patenting. SC100 recognised epidermal growth factor receptor and inhibited binding of its growth factor, resulting in significant inhibition of tumour growth. SC101 recognises a glycan, Lewis <sup>y-b</sup>, and shows direct tumour killing. SC104 showed good <i>in vivo</i> anti-tumour responses, recognised a unique glycolipid antigen sialyltetraosylceramide and mediated apoptosis (1). In collaboration with Peptech/Kyowa Hakko Kirin, SC104 was therefore humanised, defucosylated and further patent protected. SC104 subsequently entered Phase I clinical trials in the US in December 2011 for the treatment of gastrointestinal tumours. The Cancer Immunotherapy group has recently been awarded £500k in grants from the UoN with matched funding from Cancer Research UK, Pancreatic Cancer Research fund and Lewis Trust to set up a Centre of Excellence in Therapeutic Antibodies. The aim is to produce and license further anti-tumour antibodies to the Pharmaceutical industry to promote rapid clinical trials and to allow the centre to become self-financing.</p> <p>As part of the research, Durrant also developed cancer vaccines. The lead product, 105AD7 was produced in collaboration with Professor John Scholefield (Professor of Surgery, UoN 1998-2013) and was shown to stimulate T cell responses in over 300 colorectal cancer patients with no associated toxicity (2,3). In collaboration with Professor Kathy Pritchard-Jones (UCL) a similar trial was performed in osteosarcoma patients. Two of the 28 patients were cured of their disease and survived for at least 10 years post treatment (4).</p> <p>Scancell have now shown that it is possible to replace the T cell epitopes within 105AD7 with a range of different epitopes and stimulate high avidity T cell responses targeting other cancers (5,6). This vaccine worked as a protein but is more effective in DNA form. The vaccine is superior to traditional DNA vaccines, peptide vaccines and peptide pulsed dendritic cell vaccines, as it directly targets antigen-presenting cells and cross presents the antibody via the high affinity Fc receptor, CD64 (5,6). This approach, termed "ImmunoBody<sup>®</sup>", has been patent protected.</p> <p>The lead product emerging from this research, SCIB1, is a DNA vaccine for melanoma. In collaboration with Professor Poulam Patel (Professor of Oncology, UoN, 2003-2013), SCIB1</p>

successfully completed Phase I (2012), and has just completed recruitment for Phase II, clinical trials. Phase I results showed no toxicity and at the highest dose one of four advanced melanoma patients showed tumour regression of most lesions, including complete regression of lung lesions in one patient. Scancell is continuing to develop a range of ImmunoBody<sup>®</sup> vaccines for treatment of other cancers. They have recently developed a new vaccine platform based upon modified self-peptides with the patent filed in August 2012.

### 3. References to the research

1. **LG Durrant**, SJ Harding, NH Green, LD Buckberry, and T Parsons (2006). A new anti-cancer glycolipid monoclonal antibody, SC104, which directly induces tumour cell death without immune effector cells. *Cancer Res.* 66(11) 1-9. <http://dx.doi.org/10.1158/0008-5472.CAN-05-3812>
2. S Amin, RA Robins, CA Maxwell-Armstrong, JH Scholefield and **LG Durrant** (2000). Vaccine induced apoptosis: a novel clinical trial endpoint? *Cancer Res.*, **60**; 3132-3136. <http://cancerres.aacrjournals.org/content/60/12/3132>
3. GJ Ullenhag, **I Spendlove**, NF Watson, AA Indar, M Dube, RA Robins, C Maxwell-Armstrong, JH Scholefield, and **LG Durrant**. A neoadjuvant/adjuvant randomized trial of colorectal cancer patients vaccinated with an anti-idiotypic antibody, 105AD7, mimicking CD55 (2006). *Clin Cancer Res.* **12**: 7389-7396. <http://dx.doi.org/10.1158/1078-0432.CCR-06-1003>
4. K Pritchard-Jones, **I Spendlove**, C Wilton, J Whelan, S Weeden, I Lewis, J Hale, C Douglas, C Pagonis, B Campbell, P Alvarez, G Halbert, and **LG Durrant**. Immune responses to the 105AD7 human anti-idiotypic vaccine after intensive chemotherapy, for osteosarcoma (2005). *Br J Cancer* . **92**: 1358-1365. <http://dx.doi.org/10.1038/sj.bjc.6602500>
5. VA Pudney, RL Metheringham, B Gunn, I Spendlove, JM Ramage and **LG Durrant** (2010). DNA vaccination with T cell epitopes encoded within antibody molecules induces high avidity CD8 T cells which are capable of efficient anti-tumor activity. *Eur J Immunol* 40(3) 899-910. <http://dx.doi.org/10.1002/eji.200939857>
6. VA Brentville, RL Metheringham, B Gunn and **LG Durrant** (2012). High avidity CTL to tumor associated antigens can be selected into the memory pool but they are exquisitely sensitive to functional impairment. *Plos one* 7(7):e41112 <http://dx.doi.org/10.1371/journal.pone.0041112>

### Grants underpinning this research and awarded to Professor Durrant:

- Cancer Research UK programme grant - £400K; 1993-1997
- Cancer Research UK funding for antibody development - £500K; 2008-2015
- Lewis Trust funding for anti-Lewis y mabs - £250K; 2008-2016
- Pancreatic Cancer Research Trust funding for anti-pancreatic mabs - £250K; 2010-2014.

### Patents:

- Specific binding members; patent awarded in Europe (EP1745077;2012), Japan (JP4944016;2012), US (US8343490;2013;US7915387;2011), Australia (AU2005240837;2011; AU2011200487;2013), China (CN1961004;2012), India (6191/DELNP/2006;2011), Korea (KR2007008511;2012), New Zealand (550738;2011).
- A human anti-idiotypic antibody 105AD7; patent awarded in Europe (EP0440689;1995), Japan (JP3095169) and USA (US6042827).
- Binding member which binds to both lewis-y and lewis-b haptens, and its use for treating cancer. Patent awarded in Europe (EP1385547;2009), Australia (AU2002307934;2007), Japan (JP4559030;2010), USA (US7267821;2007; US7879983;2011; US8273349;2012).
- Humanised antibodies to the epidermal growth factor receptor. Patent awarded in Europe (EP1278851; 2006), China (CN1239701), Korea (KR100480985;2005).
- Polypeptides stimulating T cell responses; WO02058728 (A2). Patent awarded in Europe (2005), US (2012), Australia (2007).
- Denatured antigen DNA vaccine; PCT 08735583; awarded in Europe in 2013.
- DCIB68 DNA vaccine; PCT10152624.2; patent awarded in Europe in 2011.
- Anti-tumour responses against modified tumour antigens; PCT/GB2013/052109.

#### 4. Details of the impact

Scancell Holdings Plc (a) has legitimised an exciting new model for Biotechnology investment; demonstrating that floating on the stock market at an early stage can realise good returns for private investors. This unlocks greater potential for the private sector to invest in a wide range of research and development. In line with the Government's plan to promote the Biotechnology Industry, this provided a good opportunity to translate more novel products into the clinic and onto the market. Scancell out performed shares in the biotechnology industry as indicated by the FTSE All-share index for Pharmaceutical and Biotechnology and all shares in AIM (see graph). Cancer immunotherapeutics, such as those developed by Scancell, are predicted to bring in \$35 billion in annual sales for the Pharmaceutical industry (b) and, by 2018, 4 of the top 5 cancer products are expected to be immunotherapies.

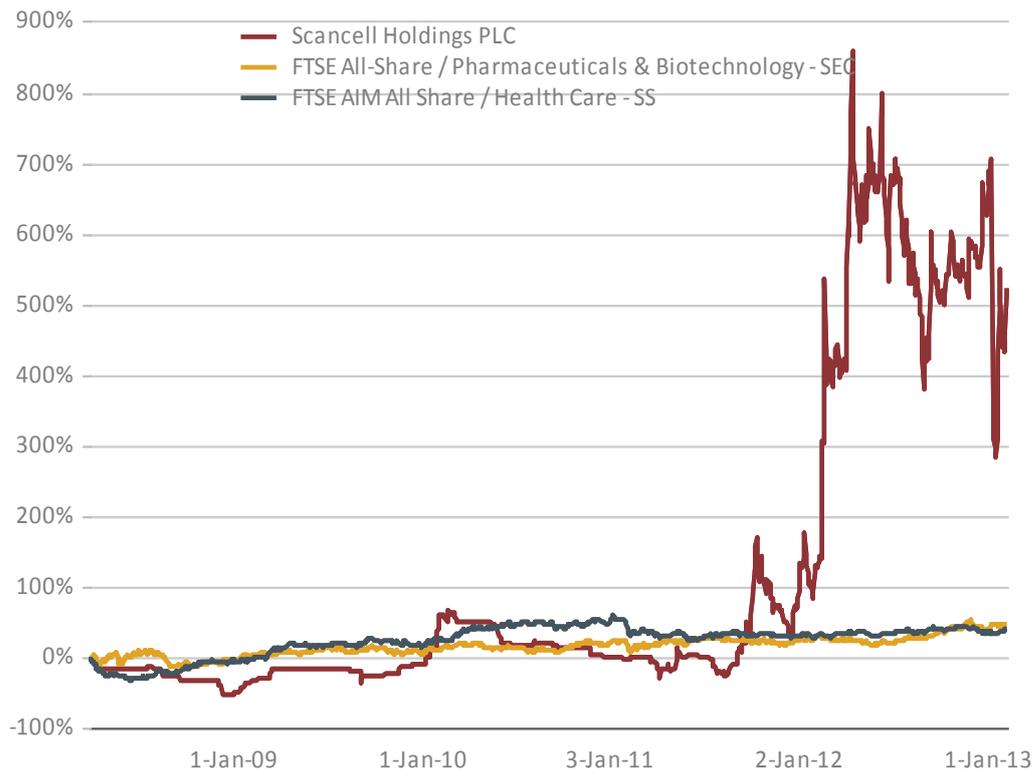


Figure showing the % increase in share price from Jan 2009 until Jan 2013.

Scancell has generated licensing income of £6million from US/Japanese/Korean companies from its patent portfolio (c). It filed patents on the three most promising mabs, SC100, SC101 and SC104. SC100 was then licensed to a Korean company ISU. Scancell sold its cancer killing mabs including SC101 and SC104 to the Australian biotechnology company, Peptech Therapeutics (now part of Teva). The lead candidate antibody, SC104 (CEP-37250/KHK2804), was humanised by Peptech and defucosylated by Kyowa Hakko Kirin in Japan and both these companies are co-developing it. It entered phase I clinical trials in the US in December 2011 (d). These international deals have all helped to increase the profile of UK Biotechnology around the globe. Scancell continues to develop its vaccine platforms and currently holds four patent families protecting cancer vaccine platforms targeting solid tumours and infectious diseases (e). It filed its initial protein vaccine platform in 2006 and this was awarded in Europe in 2007 and in the US in 2012. In 2008, it filed its DNA patent portfolio. The first patent on its lead vaccine SCIB1, which is currently in clinical trial (f), was awarded in Europe in 2012. In 2012 it developed a novel platform on modified peptides and filed a patent in August 2012.

Scancell financed its expansion with an innovative approach, which has legitimised a new model for Biotechnology investment. After spinning out and raising private equity funding (£4 million) it acquired a PLUS listing in 2008 and an AIM listing on the London Stock exchange in 2010 (g). In 2012, in response to the successful clinical results for SCIB1, Scancell holdings plc shares

increased by the highest percentage on the London stock exchange, generating significant press coverage for both the company and the University. From its initial market capitalisation of £10m it reached a value of £98 million which provided a tenfold return for investors (h). As indicated in the PraxisUnico annual report 2013 (i), Scancell is one of the few University start-up companies to provide not only reward for early investors but also a vehicle for further investment and profit.

As a result Scancell has clearly demonstrated the potential for private sector investors in small scale Biotech to realise strong returns within reasonable time scales. This provided a new successful model for Biotechnology investments whereby individuals can invest at different stages of a product's life history and still get value on their investment. Additionally, as the companies mature, there remains a large upside for new investors as the products are licensed/sold to the pharmaceutical industry. In July 2013, Scancell raised a further £6.5 million and although the share price dipped it has come back strongly and its market capitalisation has remained stable at around £80 million during 2013 (g).

Scancell has thus created significant value from modest investments of £10.5 million. It has done this through innovative science, a novel business model and by keeping overheads low. By listing on the stock market it has released significant value for its initial investors. Along the way Scancell has contributed to the local economy, employing 9-10 highly skilled people during the period 2008-2013 and supporting other UK businesses through its outsourcing of manufacturing, development and clinical work.

In line with the Government's plan to promote Biotechnology Industry, Scancell's model provides an example of how to promote investment in this sector.

#### 5. Sources to corroborate the impact

(a) All financial and corporate governance details are corroborated by accounts filed by Scancell holdings plc at companies house and on the company website <http://www.scancell.co.uk> (also available as a pdf on request).

(b) News article: <http://www.cnbc.com/id/100757009> (PDF available on request.)

(c) The licensing deals and revenues are all publicised in press releases, copies of which are found on the company website <http://www.scancell.co.uk>. Examples (in pdf format) are available on request.

(d) Clinical trials of SC104/CEP-37250/KHK2804: <http://clinicaltrials.gov/ct2/show/NCT01447732>

(e) Patents. See:

[http://worldwide.espacenet.com/searchResults?compact=false&ST=advanced&IN=Durrant&locale=en\\_EP&DB=EPODOC&PA=Scancell](http://worldwide.espacenet.com/searchResults?compact=false&ST=advanced&IN=Durrant&locale=en_EP&DB=EPODOC&PA=Scancell) (a pdf of patents is also available on request).

(f) Clinical trials of SCIB1: <http://clinicaltrials.gov/ct2/show/NCT01138410?term=SCIB1&rank=1>

(g) Its current share price and market capitalisation can be verified at the London Stock exchange linked via the website: <http://www.scancell.co.uk/Apps/Content/HTML/?id=133>

(h) News articles: <http://www.thisismoney.co.uk/money/investing/article-2254089/Stock-market-winners-losers-2012-Small-proved-beautiful-energy-firms-helped-shares-shine.html>  
<http://www.thetimes.co.uk/tto/business/markets/article3644511.ece>

(PDF available on request.)

(i) PraxisUnico Spinouts UK Survey: Annual Report 2013 (PDF available on request).