Institution: Imperial College London

Unit of Assessment: 01 Clinical Medicine

Title of case study: Creation of Thiakis Ltd and Profitable Sale to Wyeth Ltd.

1. Summary of the impact (indicative maximum 100 words)

Imperial College research on the gut hormone, oxyntomodulin, showed it caused considerable weight loss in man. A powerful long acting analogue suitable for daily human administration (TKS1225) was developed. This was licensed by Imperial to a spinout, Thiakis Ltd, for successful human toxicity testing and then sold to Wyeth for $30 million initially and $120 million on meeting milestones. Wyeth Pharmaceuticals and the full legal agreement was subsequently acquired and developed by Pfizer in 2009.

2. Underpinning research (indicative maximum 500 words)

Key Imperial College London researchers:
Professor Sir Steve Bloom, Professor of Medicine (1974-present)
Professor Mohammad Ghatei, Professor of Peptide Endocrinology (1977-present)
Dr Caroline Small, Senior Lecturer (2000-2007)
Dr Rachel Batterham, Wellcome Trust Clinical Training Fellow (2000-2003)

The obesity pandemic has proved difficult to treat due to chronic side effects of central acting drugs. In an attempt to deduce the side effect profile, the Imperial team, Professor Bloom's group has pioneered the use of gut hormones as natural appetite regulators. In 1996 the group demonstrated that the gut hormone, GLP-1 injected into the brain inhibited feeding in rats (1). This established this gut hormone as naturally regulating satiety after every meal. In 2002, they demonstrated that a second gut hormone PYY3-36 inhibits food intake and reduces weight gain in rats (2).

A third gut hormone, oxyntomodulin, was then discovered by the group to similarly reduce food intake but uniquely to also increase energy expenditure and thereby reducing body weight (3). This hormone is elevated in many natural human situations where low body weight is a feature.

Ground breaking studies by the group in 2003, demonstrated that oxyntomodulin reduced food intake in man. Administration of the gut hormone oxyntomodulin in human volunteers resulted in weight loss of 0.5kg per week over four weeks, greater than for any other therapy with the advantage of having no side effects (4, 5). The weight loss was due to oxyntomodulin's dual effect of reducing food intake and increasing energy expenditure, an effect not documented with other therapies. Oxyntomodulin was thus a strong lead for development of an obesity therapy.

Oxyntomodulin is rapidly degraded by the body as it is inactivated by enzyme action. Studies therefore focused on developing a long acting oxyntomodulin analogue which became the drug TKS 1225 (6). As a result of this research work a number of patents were filed and an Imperial College spin out company Thiakis was founded in 2004.

In 2006, Thiakis undertook a venture capital funding round jointly led by leading life science venture capital groups, Novo A/S and Advent Venture partners and including the Royal Society. Thiakis used this £10 million investment to undertake toxicity testing of the drug TKS 1225 in animals and then undertook successful testing in man.

In 2008, Wyeth acquired Thiakis for $30 million cash with additional payments of $120 million payable upon the achievement of development milestones. Wyeth Pharmaceuticals and the full legal agreement was subsequently acquired and developed by Pfizer in 2009.

3. References to the research (indicative maximum of six references)

(1) Turton, M.D., O'Shea, D., Gunn, I., Beak, S.A., Edwards, C.M., Meeran, K., Choi, S.J., Taylor, G.M., Heath, M.M., Lambert, P.D., Wilding, J.P., Smith, D.M., Ghatei, M.A., Herbert, J., Bloom, S.R. (1996). A role for glucagon-like peptide-1 in the central regulation of feeding. *Nature*, 379, 69–72. DOI. Times cited: 927 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 36.2

(2) Batterham, R.L., Cowley, M.A., Small, C.J., Herzog, H., Cohen, M.A., Dakin, C.L., Wren, A.M., Brynes, A.E., Low, M.J., Ghatei, M.A., Cone, R.D., Bloom, S.R. (2002). Gut hormone PYY3-36 physiologically inhibits food intake. *Nature*, 418, 650-654. DOI. Times cited: 988 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 36.2

(3) Dakin, C.L., Small, C.J., Batterham, R.L., Neary, N.M., Cohen, M.A., Patterson, M., Ghatei, M.A., Bloom, S.R. (2004). Peripheral oxyntomodulin reduces food intake and body weight gain in rats. *Endocrinology*, 145, 2687-2695. DOI. Times cited: 147 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 4.45

(4) Cohen, M.A., Ellis, S.M., Le Roux, C.W., Batterham, R.L., Park, A., Patterson, M., Frost, G.S., Ghatei, M.A., Bloom, S.R. (2003). Oxyntomodulin suppresses appetite and reduces food intake in humans. *J Clin Endocrinol Metab*, 88, 4696-4701. DOI. Times cited: 186 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 5.96

(5) Wynne, K., Park, A.J., Small, C.J., Patterson, M., Ellis, S.M., Murphy, K.G., Wren, A.M., Frost, G.S., Meeran, K., Ghatei, M.A., Bloom, S.R. (2005). Subcutaneous oxyntomodulin reduces body weight in overweight and obese subjects: a double-blind, randomized, controlled trial. *Diabetes*, 54, 2390-2395. DOI. Times cited: 121 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 8.28

(6) Druce, M.R., Minion, J.S., Field, B.C.T., Patel, S.R., Shillito, J.C., Tilby, M., Beale, K.E., Murphy, K.G., Ghatei, M.A., Bloom, S.R. (2009). Investigation of structure-activity relationships of oxyntomodulin (OXM) using OXM analogues. *Endocrinology*, 150, 1712-1722. DOI. Times cited: 26 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 4.45

Patents:

- WO2004062685. Modification of feeding behaviour and weight control by oxyntomodulin. Bloom, S.R., Ghatei, M.A., Small, C., Dakin, C. http://bit.ly/diYY5o
- WO2006134340. Oxyntomodulin analogues and their effects on feeding behaviour. Bloom, S.R., Ghatei, M.A. http://bit.ly/cRJADi
- WO2003057235. Modification of feeding behaviour. Bloom, S.R., Small, C., Batterham, R., Ghatei, M. http://bit.ly/d6LAvM

Key funding:

- Medical Research Council Programme (G7811974) and two Wellcome Trust Programme Grants have supported this work.

4. Details of the impact (indicative maximum 750 words)

Impacts include: economic, commercial
Main beneficiaries include: industry

Our researchers have developed and sold a spin-out company, Thiakis Ltd, which investigated analogues for obesity therapy. It is the commercial company development and financial benefit of the sale that has had significant economic impact.

In December 2008, Thiakis Ltd was sold to Wyeth Pharmaceuticals to develop Thiakis' lead

product TKS 1225, a synthetic analogue of oxyntomodulin. Wyeth acquired Thiakis for approximately $30 million with additional payments of $120 million conditional on the achievement of set milestones. Wyeth Pharmaceuticals was subsequently acquired by Pfizer in 2009 [1].

In 2010 the intellectual capital and analogue modification knowledge developed by Professor Bloom at Imperial has resulted in further peptide hormones (Pancreatic Polypeptide) being developed at Imperial as an anti-obesity treatment. An award from the Wellcome Trust Seeding Drug discovery was made to Professor Bloom to develop further gut hormones as anti-obesity therapy. This award utilises the knowledge base of analogue development that has been created as part of the Imperial research programme [2]. This has lead to the employment of 5 people at Imperial who perform this analogue research programme.

The success of Thiakis was used as a model by Imperial Innovations Ltd during its flotation on the stock market. Thiakis demonstrated to investors that Imperial Innovations Ltd could take inventions from the initial academic discovery through the patenting and venture capital phase and into the commercial arena. Thiakis was utilised by Imperial Innovations Ltd as a successful case study that allowed investment to be raised. This investment round in Imperial Innovations Ltd has provided investment capital for further spin out and commercialisation of academic research [3].

The work described has stimulated a new area of pharmaceutical research and development. International drug companies such as Merck, Novo Nordisk and Lilly have developed Oxyntomodulin research programmes following the success of Thiakis and the Imperial research programme described [4]. These programmes demonstrate the commercial adoption of the new technology of obesity analogue originally preformed at Imperial.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[1] Wyeth acquire Thiakis
http://www.adventventures.com/about-us/news-events/news-lifesciences/41-press-release/175-wyeth-pharmaceuticals-acquires-thiakis-in-a-transaction-worth-up-to-100m. Archived on 7th November 2013

[2] Wellcome Trust Seeding Drug Discovery Award
http://www.wellcome.ac.uk/News/Media-office/Press-releases/2010/WTX059169.htm. Archived on 7th November 2013

[3] Innovations Interim Report 2009

[4] New pharmaceutical development
http://www.clinicaltrials.gov/ct2/show/NCT01055340 (archived on 7th November 2013)
http://www.google.com/patents/US8367607 (archived on 7th November 2013)