

Deirdre Gillespie, Oxxon Therapeutics

Early days

Oxxon Pharmaccines was set up in 1999, after a very eminent group of scientists identified and began work on a technology intended to develop preventive vaccines for terminal diseases. Three were professors, Andrew McMichael, Adrian Hill and Geoffrey Smith. The technology, as they developed it through mice, to monkeys and to man appeared very potent – a very strong way to stimulate the immune system to prevent infection. Deirdre Gillespie says, “It was actually Dr Joerg Schneider, back in 1997 who asked whether this could be applied in a therapeutic setting. Given its strength, could we use it to treat patients whose immune systems are failing, as well as using it to prevent infection?”

Oxxon Pharmaccines (now Oxxon Therapeutics) was formed to apply the technology in this therapeutic setting, the name being changed to Oxxon Therapeutics (OT) in 2004. “Joerg was therefore founder of the company; it was his idea; he was the first employee. He became Director of Research in June 1999, Oxxon’s first employee but based in Oxford University, and he and the seed investor focused on getting the IP spun out from ISIS Innovation, the technology transfer part of the University.

“Joerg then moved the company into “the Shack” a portacabin at the Bio-Business Centre in Littlemore Park where small companies have often started, with an assistant and a third employee who, for a while, was the first CEO. The three were there to work, design the lead products, acquire needed assets, get some manufacturing set up, to get the company going. This first CEO was a sales and marketing man but there is not much to sell in a start-up biotech! It’s more a matter of getting technology licences and filing patents. So he took another more sales-oriented job and I (Deirdre) joined as CEO in 2001.”

Deirdre Gillespie

“I was born in the UK and am a physician trained in London. I was a medical registrar to the Nuffield Department of Medicine in Oxford. A senior registrar I met at that time later became the CEO of a venture capital group formed in 1998 in London. It is called MVM and has first call on all new technologies coming out of the MRC. I left Oxford to join the pharmaceutical industry and then moved into biotech. Ultimately I was the Chief Operating Officer at a publicly- traded biotechnology company in Southern California. So I was very pleasantly surprised when I received a call 15 years later from MVM to consider coming back to Oxford to manage Oxxon.”

Funding

“Oxxon has successfully raised money”, Deirdre explains: “There was seed money, then a Series A round in November 2000 which raised £4.7 million from existing shareholders and some business angels, plus £500,000 from the Isis College Fund in Oxford. Then an open venture capital round, early in 2003. Not only was there a bear market when the second VC round took place, but it was undertaken during the middle of the Iraq war when there was every risk that the US investors would pull out if events in Iraq went badly.”

Getting so much finance was therefore a big achievement. “Indeed”, says Deirdre “we raised more in our VC round than we had sought - £15 million instead of £12 million.” Including the seed money, in total, Oxxon has so far raised about £22 million. Deirdre is “extremely careful with the money and is as stingy as they come on things that do not add value.” Nevertheless, in the summer of 2004 OT was spending around £5 million a year.

The Science

Over the last 20 years there have been breakthroughs, and Andrew McMichael here in Oxford has been a major figure in them. Critical for Oxxon is that the cellular immune system, which operates through T cells, has been elucidated this part of the immune system attacks problems inside cells, intra-cellular infections – AIDS, malaria, hepatitis B, cancer and so on.”

"We all have T-cells and they roam around our bodies, checking out the state of health of other cells. If T-cells "see" a cancerous cell, they can punch a hole in it, pour in chemicals and kill the cell. T-cells prevent sick cells existing. It is a clean-up job: they are the waste disposal people. There are various reasons why this process may not work. Diseased cells have ways of "hiding" from the T-cells, or of suppressing the immune system so that it cannot fight back. But if the T-cells are not working well in a cancer patient and you can stimulate them that should be a good thing."

"Among others, both Avidex and Oxxon are working on T-cells. The immune system has evolved two effector arms: T cells and antibodies. T cells evolved to recognise antigens that are inside a body cell. The antigens can derive from tumours or viruses. Following antigen recognition T cells destroy their target cells by secreting toxic molecules thereby eliminating tumour cells or virus harbouring cells. In contrast antibodies bind and recognise antigens in body fluids outside cells or on cells thereby preventing viruses from entering cells."

"Oxxon's approach uses its proprietary immunisation method (heterologous PrimeBoost) to induce and stimulate high levels of antigen-specific T cells. These antigen-specific T cells will then seek out tumours or virus-infected cells and eliminate them from the system. PrimeBoost is aimed at helping a patients' immune system to fight the disease by amplifying the natural immune response. By contrast, for example, Avidex's approach is to use one part of the T cell: the receptor that recognises the antigens. These receptors are produced synthetically and coupled with a toxic or radioactive agent to combine recognition with an effector molecule. The idea is that this "magic bullet" finds its way in the body and accumulates around tumours or virus-infected cells. The therapeutic effect is mediated by the toxic or radioactive component of the drug."

An exciting phase

Deirdre continues, "Several of our products are now in Phase 2 trials which is where things become exciting. Although the company was established to evaluate PrimeBoost to treat disease, initially the only data we had related to preventive vaccines. The founders had used PrimeBoost in healthy subjects to see if they could prevent the subjects getting malaria or HIV, and had observed very potent immune responses in the subjects. The company was formed to test the technology in patients with diseases so, very early on, the company was seen as a malaria or HIV vaccine company, because that was the only data we had. Over the last couple of years we have pushed our therapeutic programmes forward and are no longer dependent on data from the vaccines being developed by our founder collaborators. We have also changed our name to emphasise our focus, though in addition many interested parties found 'pharmaccines' difficult to handle – and to spell!"

"Our strategy has been to test our PrimeBoost approach in clinical trials as early as we could to demonstrate clinical benefit – this is critical to Oxxon's success. In addition we have driven our patent estate very aggressively and, in 2003, the patents on our core PrimeBoost technology were granted in Europe and the US – a very major milestone. Now with data close at hand we are evolving a manufacturing capability which is time consuming and expensive. This should be in at the time when a product moves into the later stage clinical trials."

The company

"After having a staff of 16 in the summer of 2003, there are now 36, including three new senior managers. Five of the 36 are based in Boston in the US, where we will establish commercial capabilities in a similar way to the groups in Oxford. But our full research capability will remain in Oxford." The 36 does not include the board directors or the scientific advisory board, but does include Joerg and Deirdre.

"Dr Roger Brimblecombe is the non-executive chairman of the board, having previously been Head of R and D for SmithKlineBeecham. He worked for years in Philadelphia for them, and is a "big pharma guy". He has also been on the board of smaller companies like Oxford GlycoSciences and Vertex, a big biotech in Boston. Dr John Brown has recently joined the board, having been the CEO of Acambis, a very successful – originally British – vaccine company."

"There is no ISIS representative on our Board, but Quester Capital Management - a London-based VC company – is represented. They manage the ISIS college fund. Incidentally, the university still has a very small shareholding in Oxxon, but its value has been diluted as other shareholders have increased their share of the equity."

Oxxon's employees are all well qualified, but not all are scientists. "The policy is to keep the key people in-house and to contract out as much as we can. We now contract out all the running of clinical sites, hospitals and trials, the statistician, data management, QA etc. Sub-contractors provide essential flexibility."

"Over 50% of the headcount is in Research. The scientists make the product for us before it is sent to the contract manufacturer to be scaled up, and we also do the sophisticated immunological assays to measure the effect of our PrimeBoost products on T cells and the immune system".

When asked to define Oxxon briefly, Deirdre says

"Oxxon Therapeutics (OXTI) is focused on advancing the next generation of commercially viable innovative drugs for the treatment of chronic infectious diseases and cancer."

"OXTI has harnessed the power of the immune system to help improve the well-being of patients. The Company's lead clinical programs are bringing new treatments to patients with Hepatitis, HIV and Melanoma. www.oxti.com"

Becoming a US company

OT is very unusual, as Deirdre explains, " in having 'flipped' from being a British company to becoming a US company, so we have US shareholder agreements and US stock option plans and are about to get US accounts. The reason we have done that is that it is very hard to float a bio-tech company in Europe in 2004 - the markets are just not interested now and may not be for some time. There is much more money for investment in bio-tech companies in the US and most of our potential operational partners are in the US too. And investors are more comfortable interacting with a company which is operating with the same legal structure as their own."

" In a sentence", says Deirdre, "I am following the money." Terrorism concerns have led to additional funds being made available to vaccine and immunotherapeutics companies."

"Oxxon is the first biotech to do a complete flip as far as I can establish. "So", says Deirdre, "I work for two weeks in the UK and then two in the US."

As for procedures, "first, the board decided to establish the US subsidiary and then considered ways of handling the legal agreements that two companies must have to work together. So we needed a service agreement and, after analysing the options, we identified that we could become a US company in three months for £140,000. Comparing this cost with the potential benefits, the board agreed we should become a US based company. A huge proportion of the A and B shareholders voted in favour, plus about two-thirds of ordinary shareholders. And no-one voted against - very unusual for shareholders! So, the whole company was behind the change recognising the higher potential of the US market place"

Risk – but fun too!

"The biotech world is not for everyone. It is high risk, high return. To appreciate the potential, you need to understand stock options and thrive on change. From management's perspective you have to do much, much more with much less than would be the case in a large company. One person off on maternity leave in a group of 36 really impacts productivity and puts additional pressure on others - and overall the workforce is young. But, on the upside, each individual can have a real impact on outcome, everyone is involved in all aspects of a rapidly growing business, great and close relationships are built and it really is great fun."

Douglas Hague and Christine Holmes, September, 2004