Professor Graham Richards, Oxford Molecular and Inhibox

This is Graham Richards's account in his own words…

I became a graduate student in 1961 - a member of the first generation to use computers – and when, in 1966, I became a University lecturer, my research required theoretical computer calculations on molecules found in interstellar space. Unexpectedly, in about 1967/8, SmithKline & French, the pharmaceutical company wrote to me, sending a paper with calculations about histamine molecules, and asking "Is it any good?" I read it, and it was awful.

A scientific question leads to an IT tool

The histamine molecule has two main effects. First, it makes your eyes water and your skin itch - allergies. The second reaction, for which there was then no anti-histamine, makes your gut secrete acid. SmithKline & French were looking for a drug to stop acid secretion, which they ultimately did. But this paper said the histamine molecule had two shapes so that one shape affected your gut while the other upset your eyes. I replied saying; "This is rubbish. The calculations are poor and, without a computer but simply by looking at the molecules, one can see that two shapes are possible. SmithKline & French wrote back saying; "That is important to us, come and talk". So I became their part-time consultant for a few years involved in computer calculations on drugs and pharmaceuticals. Academic colleagues sniggered, saying this was off-the-wall and silly, though nowadays they are doing the same things.

I wrote a book about this in the mid-seventies and, soon, my little sideline became my main research topic. I also gave talks about my research and people from pharmaceutical companies would ask for a copy of my software. I either gave it to them free or asked for £50, because I could not maintain the software myself or even document it well. But, by 1980, I realised that we were producing marketable software.

An entrepreneurial student

Then I got a crucial graduate student – Tony Marchington - who had been my undergraduate pupil and who had an entrepreneurial background. His father was a hill farmer and Tony is a natural dealer. Even as an undergraduate he helped to write a film script about C. S. Lewis and was paid £3000 – a lot in 1979!

With that money he bought a steamroller. I thought the boy had gone off his head until I discovered that he took his steamroller to steam rallies and was paid, say, £250. So Tony did a DPhil, linked to a CASE studentship - a Co-operative Award in Science & Engineering - where his industrial collaborators were ICI's Plant Protection division. When Tony finished the DPhil our approach was becoming fashionable and ICI were keen to hire him and also use my technology, even though there was a recession and ICI had a no-hiring policy. And they paid him the highest starting salary they had thus far ever paid to anyone at that level.

Showing his letter of appointment, Tony borrowed £35,000 from his bank and bought two steam ploughs which he took to steam rallies, and got paid even more then the £250. Then, being an entrepreneur, he thought: "If they are paying me so much money they must be doing rather better themselves". So he organised his own steam rally, made £40,000 profit in a weekend, and set up a company which he still has - Buxworth Steam Group. And he has gone on buying steam engines. At the height of our success he bought the Flying Scotsman – the famous steam railway engine – and spent about £1.5 million doing it up.

We thought and talked about setting up a company to deal in computer software in the early eighties, but Tony had the good job at ICI, was newly married with a mortgage, so I firmly said: no. We would have called the company Molecular Design Limited but very soon, through the mail, came a flyer from a company in Haywood, California, calling itself Molecular Design Inc and doing roughly

the same thing. It is a pity we missed the boat. Three years later that company was sold to Maxwell for £49 million!

Intellectual property

In 1987, Mrs Thatcher crucially changed the position of Intellectual Property (IP), which was now to belong to Universities. Oxford therefore needed a mechanism for exploiting it and set up Isis Innovation. I was involved and have been a director of ISIS for most of its life. Being on the Board as ISIS planned spin-outs, I thought Tony and I should exploit our idea.

Soon after, in November 1988, my wife died of cancer, leaving me with two teenagers. My personal way of getting out of a miserable situation is to work harder, so I rang Tony, who had left ICI and was working only with his steam engines. I said to him, "Let's have a crack at starting that company". Things were clearer with the IP side sorted out. Moreover, we had new ideas. So we decided to try to raise venture capital and, though that was difficult, we raised £350,000.

Spinning-out Oxford Molecular

That took until the summer of 1989, when we started the business in a hut right outside my own lab - a prefabricated hut, which we called Terrapin House. We had three employees. Tony was CEO and everything else commercial and managerial; another former graduate student handled technology; and we employed a secretary. We split the equity – a third each to the University, the VCs and the founders. It does not go that way these days.

The £350,000 would keep us going for six months and we depended on Tony's skill as a great trader and dealer. We sold things we hadn't got and did deals with big companies. With Tony working full time, we grew quickly and successfully and after 18 months had 15 employees. We were bursting at the seams, had convinced our venture capitalists that we actually could run a company and, indeed that there was a business to be run. We also got second round funding from the same VCs.

They tried to cheat us this time, but we won. The initial money the VCs put in was at £1.17 a share and they were going to double it up at £2.34 a share. Everyone would be happy. So with all agreed on that, we moved to the Science Park and committed the money in about July. Then came the September Board meeting, where all the legal issues were going to be formalised. The night before, the financiers rang and said: "You haven't sold what you said you would over the summer. We still think you have a good business there, but we will only put the money in at £1.17 a share". Tony, the dealer, said "OK, then, we will buy you out. We have another backer". They weren't sure if he was bluffing - though he was – and did put the money in at £2.34. But we learned a lesson – VCs are not your friends.

So we moved to the Science Park and, with a bit of a struggle, opened a US office as was not uncommon. We came to good agreements with some Japanese companies and took over our only credible European rival - a French company called BioStructure - which was in Strasbourg. Interestingly,most of its money came from the Remy Cointreau family, whose president was our biggest shareholder for a while.

Floating in a crazy period

By the summer of 1993 things were going nicely. We numbered 30-odd and were growing steadily, but then came one of those mad cyclical periods. Dud companies were being floated on preposterous prospectuses and financiers approached us, offering to take us public. In the end, we did go public in 1994 through Henry Cooke Lumsden of Manchester, who were relatively small. They did us well and we "got it away" in April 1994, just before the shutters came down on that crazy period.

We floated in 1994, selling a third of the company for £10 million, thus valuing the whole company at £30 million. From 1989 until 1994 I was chairman, but the City wanted a proper City gent as

chairman. One of our VCs with his own money - Rod Hall – therefore became chairman and we had to find a new managing director, a new finance director, and so on. Immediately after the flotation, we did a lot of takeovers and grew quickly. Some takeovers were very smart, but we did seven in the USA, which was perhaps too much.

In the 1980s was big companies were diversifying. So, oil companies got into pig rearing, software production etc. Then the pendulum swung in the 1990s and the slogan became: "concentrate on your core business".

Growing through acquisitions

There were therefore many opportunities to buy nice software companies which had received a lot of investment from big multinationals. And it was from them that we made the bulk of our acquisitions. We bought with paper and I think we overdid it. We ended up with seven sites in the US, coping with different accounting systems, and integrating new people. By about 1998 we had some 400 employees – 200 of them in the USA. We also had the biggest slice of the Japanese market, and for two consecutive years we were the second fastest-growing share on the main board of the London Stock Exchange. It was an incredible success story, and my paper wealth was considerable.

We could not sell shares then because we were locked in for two years during which we switched brokers from Henry Cooke to Cazenove. We were getting a bit big for Henry Cooke, and moved to the prestigious firm of Cazenove. Cazenove did do one thing brilliantly at the end of the lock in, which was in April 1996, when all the founders immediately wanted to sell some shares, and this was achieved without a fall in the share price.

Again, the VCs screwed us a bit because having implied that Tony and I - who were doing the road show - could sell half our shares, rang on the night before the lock-in ended. They said: "Sorry, the City will only let you sell a quarter". By this time Tony had spent all his potential gains on a farm and the Flying Scotsman.

By 1997/98 we had a very good business plan that has since been copied by other people. We started with a software company because they are cheap to set up.

We were just selling tools, the sort of things that draw pretty pictures. A better idea, when you have enough cash, is not to sell the software to a drug company, but to use the software yourself both to design molecules and to screen them. You earn much more that way. So we developed the strategy of having a group with three companies. One would be a software company; a second would use the software to design and synthesize molecules; and a third would test them. The three companies could work in concert or individually, or any two of the three together.

This would keep us very much in pharmaceuticals and biotech, which was coming in at that time. Indeed, we did set up a second company which we called Cambridge Discovery Chemistry and that caused us problems.

Selling out

With hindsight what we should have done is this. Tony is a brilliant entrepreneur and starter of companies but, after we floated, he should have gone. That is received wisdom really. But the board of which I was a member let him stay, so I am culpable along with everyone else. The share price was high and everything was going wonderfully, but there is a difference. If you run a small company, you can carry everything in your head, live on your wits and charm - and sell the products successfully. But running 450 people, handling the regulatory authorities and so on was not Tony's forte, so things unravelled. The share price started to go down. Furthermore we suspected that brokers were playing games with our share price and only wanted it to move – either way, up or down.

Inevitably, there was tension in the Board with whom Tony fell out. He wanted to do a management buy out at the existing share price but the board wouldn't hear of it, yet within a year they had sold the company for less than that.

The company was sold in two bits. The experimental side went to an American company - Millennium - and the software side to another American company - Pharmacopeia. The shareholders who hung on got a poor price and I was one of them getting about 40-odd pence a share. On the other hand, given the way similar companies have gone since 2000, maybe 40p a share was quite good!! And the University made about £10 million from their shares.

The company itself is now called Accelrys, owned by Pharmacopia and still producing software. Oxford Molecular had bought a lot of genetics software and had the world's biggest share of this hugely-growing market. Unfortunately the company is no longer ours.

New entrepreneurship

Since then, I have moved to other entrepreneurial things. I set up a dot.com company to organise internet conferencing, but that failed. My latest venture, two years old is a company, Inhibox, which provides a screensaver. Any computer user can sign up, get my screensaver and, every time they connect to the Internet, get molecules to test to discover if they fit as potential drugs. 2.5million people now work for me - in 227 countries, so I have already had 250,000 years of free computer time and have access to more computer power than the entire world pharmaceutical industry.

Inhibox

About 10,000 people a week join the screensaver, all of them giving their time for nothing. They don't have to understand the chemistry: they don't have to do anything. I can only use them while their computers are unused, but most computers do nothing for much of their time. Some people are surprised that the number is so large, but we have the support mainly from, initially, considerable publicity for our venture from the media – especially television across the world – and since then very large interest has come simply my word of mouth among our supporters.

My screensaver begins from a protein structure and tries up to 3.5 billion little molecules, one at a time. If someone gets a hit, a message goes to a big server in Texas and then back to me. But the IP and the structures of these molecules belong to Oxford University, with whom we set up Inhibox to hold the IP. And these are structures for potential drugs.

Inhibox is very small - almost virtual. But it has prospects for growth, because it will take the IP and do deals with it. And the people whose screens we use have to sign the IP away when they join us, philanthropically.

The coming game?

What we get from the process are lists of molecules that might bind to a particular enzyme and be drugs. We need to produce a more a manageable list, and then the farther pipeline down the pipeline we go, the more income we would get. We could just sell these structures to drug companies for what they would pay. Or we could sell them cheaply, but arrange to take a percentage if they turn out to be successful. Or we could make the drugs ourselves or by sub-contacting manufacture. Testing them and patenting them would take us further down the line, but the more valuable the products were the more investment you would need.

Setting up a subsidiary is a real possibility. If we test some molecules and get really good results, then we could raise more money. Inhibox was founded with just £400,000, and £300,000 is still in the bank. We haven't spent much, but nor have we earned much. We are still at the proving stage.

The company is at present just me and another former student. He is employed by a pharmaceutical company and works part time on this. If the future looks good and we get more money, he will become a permanent employee. We can then build the business.

All this is very timely and fits well scientifically because, with the human genome complete, we have sequences for proteins and they are what really matter, not genes. If you have structures of proteins, and they have a binding site, the drugs tend to be little molecules fitted into the binding site. As you get protein structures you can use them as targets and that is currently very fashionable - finding new protein targets - and they are coming on stream quickly. Exploring the potential for rational drug design is self-evidently a coming game.

Douglas Hague, December 2003.