interview

Glyn Edwards talks about cancer drug development at Antisoma

Interviewed by Ulrike Knies-Bamforth and Dan Huke

Glyn Edwards
Chief Executive Officer, Antisoma

Glyn Edwards was appointed Chief Executive Officer of Antisoma in March 1998. He has reshaped Antisoma into a focused drug development company with a diverse pipeline of cancer drug candidates and a close relationship with Roche. Edwards is also a Director of Elara Associates. Prior to joining Antisoma, he was with Celltech from 1981 until 1986 and later became Director of Business Development at Therapeutic Antibodies. Edwards received a BSc in Biochemistry from Bristol University and an MSc in Economics from the London Business School.

Could you tell us a little bit about yourself and about your career so far?

I've been involved in the biotech industry for about 25 years now. I joined Celltech when it was just started, it started in 1980 and I joined in 1981, in a commercial role, and I've been involved on the business side in getting biotech and hi-tech products out from the lab into the marketplace for that entire period.

Could you outline Antisoma's philosophy and background?

Antisoma's is quite a simple philosophy to explain; we're an exclusively oncology-development-focused company. Our view is that there's a lot of exciting discovery work going on in the academic and in the biotech communities, but a real shortage of oncology development skills. Therefore, we have put together a team of people that are able to develop drugs from a variety of different technology backgrounds, from the late preclinical stage all the way through the clinical process, to find out if they worked in patients. We thought that if we did that, the pharma industry would be very interested in picking up drugs that had human clinical data and taking them to market. So that's Antisoma's philosophy.

The background is a bit more complicated in that the company originally was a spin-out from what was the Imperial Cancer Research Fund (now Cancer Research UK) and started as a couple of researchers, who carried on doing the work that they had been doing at the ICRF, which means that the development skills really originated in some projects that they were doing.

Could you outline some of the short-term and long-term goals for Antisoma?

Long-term it's really quite straightforward. This is a commercial organization and we will get our return when we get a product to market, and so getting at least one product to market is a medium- to long-term goal. However, we all know what the probabilities of success for any one project are, so what we've tried to do is to put together a portfolio of projects, which are rather different from each other, which is our way of diversifying the systemic risk out of the portfolio. I don't know which one is going to be the one that gets to market, but what I do know is with the portfolio of drugs we've got there is a very good chance of at least one of them doing so. So in the short term, what we've got to do is move all six of our projects forward to try to find out whether they work or not. And in the words of our chairman, Barry Price, who is one of the early inventors of Zantac at Glaxo, 'what you've got to do is get the donkeys off the racecourse', which means that it's not a question of trying to keep these projects going as long as possible, rather it's a question of finding out, as early as possible, if they work or not, so that you can then put the resources behind the ones that have got the good data.

'What you've got to do is get the donkeys off the racecourse'

What do you say is the high point of Antisoma's seventeen-year history and why?

I think the Phase III trial that we carried out of R1549, the product formerly known as Theragyn, was a high point and a low point. It was a high point because we were able to carry out a very well controlled multi-centre Phase III trial across several continents, which was scientifically very robust. The design, the execution and the result of the trial were very

1359-6446/05/$ – see front matter PII: S1359-6446(05)03660-3

interview

good and very clear, despite there being a number of difficulties with the product along the way. The low point obviously was that the results showed definitively that the product didn't work, so commercially it wasn't a success. However, in many companies a major failure would cause the company to crumble and collapse or to be acquired. So, to my mind, the other great success was that at that time we were able to fall back on a good group of people, six other very exciting projects and strong investor support so that Antisoma is now just as strong, even if we're not yet at the same market cap that we were before. I think that the highlights really relate to being able to develop exciting projects and find out whether they work or not.

'It certainly is a character-forming experience when a product fails, but at the end of the day, drug development is a risky business.'

You mentioned the results from the R1549 trials. Do you think these have affected your development strategy for other pipeline drugs?

I don't think so. It certainly is a character-forming experience when a product fails, but at the end of the day, drug development is a risky business. Not every drug that goes into development gets through and according to the latest statistics, one in ten products in clinical trials is going to get through to market. I've seen data recently from Glaxo indicating that the Phase III failure rate has increased for the larger companies, so that figure of one in ten may be an underestimate. In this business you've got to get used to drugs not working; what you need to make sure is that you have scientifically and definitely shown that that's the case. As a result, I think that the things we learnt from that were all positive, and will help us to develop better study designs and be a better drug developer as a result of it.

At the time, the Roche-Antisoma alliance in 2002 was viewed as a new model for a buyout; can you outline for us the benefits of such a model, and how successful has the alliance been in your view?

First of all, it actually was not a buyout, so maybe that's the wrong way of looking at it. It is an alliance and I think it is a new model, but not necessarily applicable everywhere. The proof of the pudding really is going to be whether we get a product to market with Roche, and I'm pretty confident that, out of the portfolio of products that we have, will get to market in the alliance with Roche. On that one metric, the alliance hasn't yet been successful. However, on other metrics, for example, in terms of what it has enabled us to do and what it has enabled Roche to do, I think you can count success on both sides. What the big pharma needs is access to late-stage projects and in our alliance we are developing products until the end of Phase II, with Roche having the option to buy in at the end of that point on fixed terms. This gives them a potential stream of good products without having to put a huge amount of management time into multiple alliances. For instance, we have a meeting next week with Roche to talk about three projects, whereas normally they would go to the biotech company and talk about one project, so in that way it's pretty efficient from their point of view. From our point of view, if we get a product to market, we know that one of the world's best oncology marketers will be marketing it, so it will make good market penetration. Of the revenue that they generate, we will get an appropriate share, so commercially it makes sense as well. And then there are softer issues, such as if we hit problems in development, we can get access to their expertise to sort things out. So I think on all the softer measures it's been a great success from both sides, but the hard measure of getting a product to market hasn't been achieved yet and history will judge us purely on what are the sales of whatever products come out of the alliance.

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We recently spoke to Peter Hug, the global head of Roche Pharma Partnering, and we asked him what the criteria are for successful partnering. Could you outline what Antisoma looks for in a potential partner?

Well, we haven't been looking for partners recently because we're actually very happy with the Roche partnership we have, but I can outline what we were looking for before and what we've learnt from this relationship. Obviously, you've got to look for aligned interest; our interests are in developing products to prove a principle, their interests are in having products that they can take forward and market immediately, so there is an obvious complementarity of interests. And that's not always the case. Especially if you're looking at partnerships between biotech companies you should be very careful that the interests are complementary and not competitive. Secondly, you've got to look at cultural issues. I was at a conference recently and a group presented a case study of alliances that have fallen apart. In this case study, a third of the alliances fell apart because the product hadn't worked, a third of them continued and did quite well. Interestingly, a third fell apart even though the product development was going very well, because of problems between the companies, who just couldn't work very well together. I consider this a high failure rate for alliances where everyone puts a huge amount of investment and effort into it, so a cultural compatibility is very important.

'If you're looking at partnerships between biotech companies you should be very careful that the interests are complementary and not competitive.'

The third important issue with partnerships is systems and structures. In our relationship, there is an alliance manager in Roche who is appointed to focus on looking after this alliance; and Antisoma has appointed an alliance manager to look after their interests. While there are committees and various groups that are operational and meet to discuss things, these alliance managers ensure that the softer issues run smoothly. This is a very important safety valve and works extremely well.

Looking at the other side of the coin, the people partnering with you, could you outline the benefits for academic institutions for partnering or out-licensing to Antisoma rather than going straight to big pharma for the treatment of their compounds?

interview

I think there are a number of issues here. There are going to be some cases where partnering with big pharma is the right thing to do. However, we do have some real strengths that work extremely well for certain types of projects. First of all, we are dedicated to working with partners who have done the discovery. We have no discovery ourselves – every one of our projects has come from someone else. It is very important to realize that for us, it might be one out of six projects, but for them it's their only project that they've put heart and soul into. Being able to give their project the best shot and to handle the interaction with them so they stay involved is really important. If they give a project to big pharma, it may be one of a hundred projects that that company has, but for us it may be one of six, one of seven, one of five; and every single project we do is very important, so it would get high priority. When we dealt with Deutsche Krebsforschungszentrum in Heidelberg, Germany, for a project that ultimately wasn't successful for scientific reasons, we were able to move the project forward and get the data very quickly, whereas in their previous experience with a very large pharma company, the project had been licensed and sat there for five years. We're medium sized now, we're publicly listed, which differentiates us from the very small companies. We've got a team of 65 people here and we've got quite a large amount of money. So if the project needs two or three million Euros spending on it in order just to get manufacturing sorted out, we can do that, that's not a problem. For our customer this means that they get the benefit of the small focus of a team that's dedicated to your project, yet with adequate resources to be able to sort problems out and get things manufactured and do the proper toxicity studies and move it forward with worldwide reach. We have studies today being carried out from New Zealand to Seattle and San Francisco; so we truly have global access to clinics and clinicians.

So, I think for projects where people are looking for a partner, for whom the project's going to be very important, we can do a really good job and they'll get a lot of very professional people resource as well as financial resource. What we actually find is that people who have partnered with us tell other people about us and projects come to us largely because of our reputation.

Can you describe the pipeline at Antisoma, which of these compounds do you see as having the most clinical impact and why?
Yes, that's a really difficult question and I actually think all six of the projects we're investing in have the potential to make a huge difference to patients and are equally exciting. We've got two small molecule projects, three antibody-based projects and one aptamer project, so out of the six there are three very different core technologies involved, organic chemistry, antibody and genetic engineering and then the new field of aptamers.

In the six projects, we've got five different targets; only two of the projects share the same target, mac 1, but even those two have different killing mechanisms, so the six drugs have five different targets yet six different mechanisms of action. So there's a great deal of diversity in technology, in target and in mechanism of action in the projects and that's really important. We've all seen biotech companies where one product fails and the other products are based on the same technology and so they all go down at the same time. In our case, if one of our projects goes down, it's just that, one goes down and it has no impact on the chances of success of the other projects. I guess the flipside is if one's successful then that has no impact on the chance of success of the others but that's a fair risk to take.

'We are exclusively focused on cancer and for us the definition of cancer drug is very important.'

So that's basically how you manage the risks?
When we're looking to in-license something, we give additional emphasis to things that are different to the projects that we've brought in. Now, obviously, if you read all the management literature one of the keys to success with small companies is focus. So trying to run different projects in a portfolio, yet trying to retaining focus at the same time could be a real problem. We are exclusively focused on cancer, which is obvious, but also on cancer drugs and for us the definition of cancer drug is very important. We'll do large molecules, small molecules or aptamers. They all act directly on the tumor and there's a very clear, drug-like action to them. We don't do cancer vaccines, we don't do gene therapy, we don't do cell-based products, not because I don't think those will work, but because it takes different development skills to be able to develop those kinds of products. So, if we just focus on molecules that act directly on the tumor in a drug-like way, that still gives us a very large universe but it means that our regulatory and clinical operations, our manufacturing experts and so on can all understand the projects and we can share resources. So, we have some focus, yet have this very strong diversity in the types of products that we've got.

We understand that you have recently acquired Aptamera and we were therefore wondering if aptamer-based drugs are going to represent a much greater proportion of your portfolio in the future.
Well, they may do. I think aptamers are an emerging area that's starting to look very, very interesting and there's a lot of activity going on. The comfort from looking at aptamers is that we already know that there is an aptamer drug which has been approved. This is Macugen, which is being marketed by Pfizer and Eyetech Pharmaceuticals. What really excited us about Aptamera, though, was not so much the long-term ability to get into aptamer drugs, it was the particular drug, which was formerly called VGRO100, and which we've renamed AS1411. We are excited both because of the science behind it and its drug characteristics. It is different from other aptamers as it kills the cancer cell directly and you don't have to add any other killing agent. Once it gets inside the cancer cell, it itself appears to be causing the toxicity. It had very good data in cell culture and in animal models, but more tellingly, the clinical data from the Phase I study that was carried out by Aptamera show a really good safety profile. There were no significant drug-related adverse events and interesting signs of activity in patients, a lot of prolonged stable diseases in patients with different tumor types and some real signs of tumor regression. AS1411 sits very well in our portfolio, it adds diversity, has a new target, nucleolin. But, at the end of the day we try not

biotech focus

to get excited by technologies; it's clinical data that drives our decision making.

Is there a problem or what do you see as the biggest problem with the future development of such aptamer-based drugs? There are no fundamental problems with it, they are relatively expensive but so are antibodies and recombinant proteins, and people are taking steps towards new methods of synthesis which may drive costs down. There's no doubt that these drugs have interesting pharmacokinetics that are not entirely predictable from the small molecule or even the antibody area, but as we gain experience with them, we'll get a better scientific understanding. I think the future for aptamer drugs is very promising, however, it's early days and we have to wait to see.

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biotech focus

Biomanufacturing: a high-growth industry for North Carolina

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Somewhere in the United States, in a small meeting room complete with a few chairs, a table and a dry-eraser board, biotechnology entrepreneur Anthony Laughrey outlined the attributes for a suitable location for his new start-up company, KBI BioPharma, a contract process developer and manufacturer of biotechnology drugs.

The KBI BioPharma leaders judged six candidate states on a variety of items: excellent universities and community colleges; supporting infrastructure of government and private agencies; extensive workforce training programs; specialized construction and engineering companies; high quality of life.

All these criteria are important to a successful biomanufacturing operation, and, holding a handful of colored markers, Laughrey checked the boxes over and over again under one state: North Carolina.

'None of the other five states measured up, when all of these factors were considered', he said.

Laughrey's choice has proved a positive one. Since selecting Durham, North Carolina, as the base of his company, and receiving a US$1 million loan from the North Carolina Biotechnology Center in 2003, KBI BioPharma has grown from one employee to 32.

'The fact North Carolina has invested in biotechnology for 25 years was a big reason for coming here compared with the other states', Laughrey said.

The state's investments in biotechnology have come via the North Carolina Biotechnology Center, the world's first government-sponsored organization devoted to biotechnology development. The nonprofit corporation, created in 1984, has formed working partnerships with dozens of public and private organizations and channeled more than US$160 million of state investment into biotechnology research, business and education.

This long-term investment strategy has paid dividends to the state. North Carolina's life science industry has grown to include 173 biotechnology companies, 77 contract research organizations and 51 device and life-science related companies, collectively employing ~40,000 people. In addition, more than 200 companies provide products and services to the industry, accounting for thousands more jobs.

About one-third of the state's biotechnology companies are large, multinational operations such as Biogen Idec, Diosynth, Bayer CropScience, Novozymes, Syngenta and GlaxoSmithKline. The rest are small to mid-sized companies that have either moved to the state or sprung from its universities or larger companies (Box 1).

Outstanding universities drive industry's expansion

Education has fueled the life science industry in North Carolina. The state has more than 50 public and private colleges and universities. More than 45 life science companies in

1359-6446/05/$ – see front matter PII: S1359-6446(05)03650-0