interview

Alice Huxley and Nick Miles of Speedel on the company's pipeline and future plans

Interviewed by Christopher Watson and Stephen Carney

Alice Huxley
CEO and Founder, Speedel

Nick Miles
Director of Communications and Investor Relations, Speedel

Alice Huxley is CEO and founder of Speedel. She studied biochemistry and received her doctorate from the University of Bratislava, Slovakia. After her post-doctoral fellowship at the biotechnology department of Ciba-Geigy, she joined Ciba-Geigy as a research scientist and held various positions with increasing responsibilities in both research (endocrinology) and clinical development (cardiovascular and cancer). Following the merger of Sandoz and Ciba-Geigy to create Novartis, she assumed the role of a global project manager, in which she led several multidisciplinary teams developing new drugs in cardiovascular and transplantation therapeutic areas. In 1998 Alice Huxley, together with her husband Marius Sutter, who also serves as a member of the Board of Directors, founded Speedel Pharma and was first elected as Delegate of the Board of Directors in 2000. As Delegate of the Board of Directors and as Speedel's CEO, Alice Huxley is an executive member of the Board of Directors.

Nick Miles is Director of Communications and Investor Relations. His experience covers a broad range of corporate issues and financial transactions. He joined Speedel in 2003, after five years at Serono, where he held two senior positions as director for investor relations and director for media and public relations. Prior to this, he was a director at Gavin Anderson & Co, a top tier financial communications agency based in London, England, where he advised a wide range of companies on such transactions as privatisation, flotation, and merger and acquisitions activity. Nick Miles' first career was as an international banker with HSBC in Asia and the Middle East, where his experience was gained in retail banking, foreign exchange, trade finance and internal organizational consulting.

For those not familiar with the company, could you talk a little bit about about Speedel?

AH: The company was created in 1998 around one specific compound (and actually still our flagship compound) called SPP100 or aliskiren, the first oral renin inhibitor, a new mode of action for the treatment of hypertension and related cardiovascular diseases. This compound was not further supported in the development pipeline of Novartis after the merger of Ciba-Geigy and Sandoz. As often happens when two companies come together, a pipeline review results in a new pipeline and a few projects simply do not make it. The SPP100 compound was dear to my heart and I did not want to see it 'die', if you will. The compound was at a very early stage, at the beginning of phase I, and was not entertained further by the newly merged company because there were a few issues with the molecule, the main one being that the synthesis of this relatively complex molecule was estimated to be too expensive for it to ever become a commercially viable drug. Combined with the fact that the project work was at a relatively early stage, so there was no clinical proof of concept and there had never been a successful renin inhibitor in phase II, this led the management of Novartis to the decision to not support the compound in their new pipeline. I used to work on this project previously at Ciba-Geigy and obviously I was upset about this and came up with the idea to approach the Novartis top management with a proposal to licence out the SPP100 to a (yet to be created) company. This company would be a 'virtual' drug development company and would try to further develop this drug candidate until the phase II stage, when Novartis would be able to evaluate first, whether we did manage to

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interview

develop a new commercially viable synthetic process and second, whether we did deliver successful clinical proof of concept. To cut a long story short, between 1999 and 2002 the young company (Speedel) did accomplish these two major tasks and Novartis exercised the call-back option and took the compound back. The compound is now at the phase III stage, the first phase III data are now available, and the submission of the first registration file is planned for early 2006 for hypertension. Rather than being a one-product company we then wanted to develop a sustainable business and we now have a rich pipeline of products. This includes SPP100 in phase III trials as a monotherapy for hypertension and phase II trials as a combination therapy, for example with irbesartan, the endothelin receptor antagonist SPP301 will start phase III trials in the second half of 2005 for diabetic nephropathy and SPP630 and SPP635, our own renin inhibitors, are in early human testing.

What are the company strengths?

NM: First, we are targeting the largest therapeutic areas which have a significant unmet medical need and a high commercial potential. Second, as Alice has mentioned, we have a mature and diverse product pipeline that contains potential blockbusters. Third, SPP100 is a significant breakthrough in the treatment of hypertension and end-organ protection. Fourth, SPP301 offers a novel mode of action for the treatment of diabetic nephropathy. Fifth, our global leadership in renin inhibition, which is going to keep us busy for a few years going forward. We have got the big pharma partnerships with Novartis, Roche and with Abbott Laboratories and finally, we've got a highly experienced, entrepreneurial management team here who combine the best of both worlds – top quality standards from big pharma together with biotech entrepreneurialism.

In the past, many companies had been incapable of developing orally available renin inhibitors. What was it that made you confident that you would be able to do so?

AH: First, the availability of clinical data from several phase II as well as one phase III trial showing that SPP100 does lower blood pressure in patients with mild to moderate hypertension clearly shows that the compound works. Second, the safety and tolerability profile seems to be identical to placebo, which is very important for a chronic treatment such as hypertension therapy. Furthermore, we have developed a manufacturing process that promises to be good enough and efficient enough to be used in a large scale.

Could you outline what you see as the benefits of renin inhibition over current therapies for hypertension?

NM: The key benefit, in addition to lowering blood pressure, is end organ protection, which is reducing the damage to kidney and heart, primarily, as a result of increased blood pressure. Renin inhibitors are practically the only class of agents that lower plasma renin activity, a factor associated with increased incidence of myocardial infarction and kidney disease in hypertensive patients.

Do you think that this will trigger a response from other companies to chase the renin inhibitor market?

AH: They are already. There is the alliance between Merck and Actelion centred on renin inhibition and they recently announced that they have reached their first milestone, which was the identification of a renin inhibitor to undergo full pre-clinical investigation. We have also seen patent applications coming out from Pfizer and we have heard of one or two other companies that are actively pursuing renin inhibition research again.

Could you explain the relationship between Speedel and Speedel Experimenta? How do they work together and what advantages have you found that Experimenta offer you?

NM: Experimenta is a wholly owned subsidiary of Speedel. Operationally, it is a research unit; it is a research department of Speedel. The business model that Alice and her team originally started off on was founded on in- and out-licensing. Obviously Alice and her team were pretty far-sighted because they realised that for a sustainable business you have to actually roll up your sleeves and do the creativity yourself at some stage or another. As a small private company you do not have the deep pockets that you need to outbid big pharma for in-licensing candidates - you cannot carry on doing that. So from a risk diversification point-of-view and from a growth platform point-of-view, it was sensible for the company to establish Experimenta. Alice benefited from having around her in Basel a pool of very experienced scientists and technicians, particularly the same core teams that developed diovan and that had worked on the whole renin inhibition programme at Novartis and also some people from Roche. Putting all that together, it made sense to then establish our own labs, which was done in 2002 and that has been gradually ramped up so that now there are 34 scientists and technicians covering the whole remit of disciplines – medicinal chemistry, pharmacology, toxicology, data management, modelling – all of these people are now in-house. So that was the rationale for that and I think the proof of the pudding has been the SPP630 and SP635 data that we came out with earlier this year. These were the first set of molecules that were actually produced from the in-house team.

You have stated that you partner with big pharma post phase II. Have you any plans in the future to develop the capability to be a stand alone company as far as commercialisation is concerned?

NM: SPP301 is the first potential candidate for us to commercialise ourselves in some way or another because this is the first candidate compound we are taking into phase III and we will be evaluating the commercial opportunity depending upon the results of the phase III trial. You could see a scenario where we could strike a deal where we co-promote SPP301 to the specialist diabetologists and nephrologists, for example, and a big pharma could do the mass marketing to the GP population. That is a potential scenario that, assuming the company is in financially strong enough shape and is big enough to take on that new marketing type role, would be quite fun to do. There are some indications, for example hypertension, where a company of our size cannot possibly contemplate taking on that marketing role itself. For those big, general indications we would have to rely on striking some form of commercial partnership with a big pharma where they would do it all

interview

themselves. It will depend upon the indication ultimately and the scale of the company at the time.

Your endothelin A receptor antagonist SPP301 has just completed phase II trials for diabetic nephropathy, a formidable breakthrough in this area. How do you think that success in this field will shape the future direction of the company?

NM: We are cardiovascular and metabolic focused and there are some similar pathways that we are exploring here to get to diabetic nephropathy so it makes sense from that perspective. It makes sense from an indication point of view – it is small enough for us to focus on as a potential commercial opportunity. What is really exciting is that this is the first time that an endothelin has been developed for this indication. All the other endothelins out in the market or in development are being developed for pulmonary arterial hypertension and prostatic cancer, for example. We are the only company who has taken an endothelin into phase III for this indication and, interestingly, it might be one of the first products that is specifically labelled and indicated for diabetic nephropathy because the current treatment regime are anti-hypertensives, which do not have a specific label for diabetic nephropathy but because of their blood pressure lowering effect are being used in order to alleviate the symptoms of diabetic nephropathy. SPP301 is being deliberately developed for this indication and as an addition to the current standard therapy. Our trials have shown that there is a significant improvement in the reduction of proteinurea in people receiving both an anti-hypertensive and SPP301. So this is bringing exciting medical benefit to a severely chronically diseased group of patients. It is a huge unmet medical need with the explosion of diabetes in the world. We estimate that on a conservative basis, there are about 8 million diagnosed diabetics that have got diabetic nephropathy in the seven key major markets. It really is a terrible disease and the prognosis is terrible at the moment. Anything that can dramatically slow down the progression of the disease has got to be good and that is ultimately what we believe SPP301 can do.

You have recently used a microdosing approach for your renin inhibitors SPP630 and 635 and you have stated that it helped with your fast tracking of the SPP600 series. Could you give me some idea as to how much time and money you have saved from the approach and whether it will continue to be used in your future drug discovery?

AH: Microdosing is a methodology in which, at a relatively early stage of development, very small doses of a drug candidate are administered to human volunteers and with an extremely sensitive methodology (accelerator mass spectometry) one is able to measure several pharmacokinetic parameters of the test compound. We know from the history of renin inhibition research and development that the key issues were the bioavailability and the pharmacokinetic profiles. With microdosing, one can assess these parameters at a relatively early stage of development at the transition point between the practical research and classical clinical development. We use microdosing as a screening filter for those projects in renin inhibition where we had a few derivatives that showed promising profiles in animal testing in order to pre-screen them before entering the classical, expensive and lengthy human clinical testing. So what we try to do is to increase the probability of success of the expensive clinical undertaking to best reduce the attrition rate in Phase I. We did it with the SPP600 series where we tested three molecules and two of them we found to have an attractive enough profile to be considered for classical phase I. In the future will we use these methods? Most probably, yes.

How difficult was it for you personally to break away from big pharma and to go it alone?

AH: Well, it was not easy but I had to do it. I really, really wanted to save the SPP100 compound, otherwise it would have been put on the shelf and so I had a very strong motivation to fight. The pieces fell into place at the right time; there was an attractive compound, progressive management of a new and creative company, Novartis, who were open to these entrepreneurial proposals, the availability of risk capital and so on. So, on the one hand it was easy because there was strong motivation but on the other hand it was difficult after 16 years with big pharma to be on your own and to have to secure a work place, job and money yourself, before you actually can start to work on a project.

How easy have you found partnering with big pharma? Are there any pointers that you can give us that would help in a successful partnership?

AH: I have only one recipe for success, if you will. Regardless of whether it is with external partners, internal collaborators or an investor, there is always one common denominator that predetermines success and that is alignment in philosophy. Sharing a similar working philosophy and having mutual respect between companies is essential when partnering.

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