

Aravis Venture looks to get a step ahead by finding the right targets

Around 15 years ago, Jean-Philippe Tripet came to the conclusion that investment in early-stage biotech companies was a good idea. Then he had a better idea. He should invest in early-stage immunology companies. And it was his get-a-step-ahead outlook that turned him into one of the more successful investors in this sector.

At that time, in late 1994, Mr Tripet was head of research for institutional investors at Lombard Odier in Geneva. Lombard Odier's wealth management business, originally founded on the savings of French Calvinists fleeing Napoleon, has grown into a modern, research-oriented investment house with worldwide connections.

Lombard Odier's management was receptive when Mr Tripet proposed a fund to invest in immunology, which was just starting to emerge as a very dynamic sector of biotechnology.

"There was a strong belief in the mid '90s that immunology was going to be a very important theme with the emerging research into monoclonal antibodies," Mr Tripet said in an interview with *MedNous* editors in London on 23 February 2009.

The Lombard Odier Immunology Fund initially raised CHF 60 million but by the time Mr Tripet left in 2001 to start his own fund, LOIF had assets of around CHF 4 billion. In six years or so he had produced an outstanding performance.

Evolva SA, a Swiss company that genetically re-engineers natural compounds to make small molecule drugs, has thumb-nail biographies of its directors on its website. Its entry for Mr Tripet gives a flavour of his financial acumen. It says that between 1994 and 2000, Mr Tripet was responsible for 70 private investments by the immunology fund totaling CHF 400 million, which produced an internal rate of return of 70% per annum. Not even Wall Street's gun-slingers of the 1960s were able to match that.

One ingredient of Mr Tripet's success was that his fund was allowed to invest between 20% and 30% in venture capital companies, which he did almost entirely in the United States at a time when biotech was expanding rapidly.

"I would say that in the immunology fund about 90% of the investments were done in the US and were really the basis of our focus," Mr Tripet commented.

However, he didn't ignore Europe entirely. For instance, he was a Series A investor in Cambridge Antibody Technology, which has now been acquired by AstraZeneca and a Series B investor in Genmab, which became prominent in developing antibody treatments for cancer.

"We did Cytos in Switzerland and a few other companies,

so reasonably early we had a good taste of how Europe developed over the years."

Aside from investing in the fast-growing US biotech market, the Lombard Odier Immunology Fund had another advantage. It recruited a scientific advisory committee that was not only composed of prominent experts in the field of immunology but one which would play a role in the selection of investments.

"I think that is one of the big strengths that we have, and one which is unusual for asset management, is that we gave the scientists some say on early investment decisions. The idea is to collaborate between the financiers and the scientists. The scientists provided the input on the science and my colleagues provided input on the financial side."

Members of the advisory committee included Richard J. Ulevitch, former chairman of the Department of Immunology at the Scripps Research Institute in La Jolla, California and an expert on the innate immune system; David H.

Sachs, professor of surgery and immunology at the Harvard Medical School and a specialist in immune tolerance in transplantations; Bernard Mach, formerly the director of the department of genetics and microbiology at the University of Geneva, who invented cDNA cloning; Rolf M. Zinkernagel, formerly head of the Institute of Experimental Immunology at the University of Zurich and a pioneer in research on self-nonsel discrimination in immunology; François L'Eplattenier, a former chairman of the Novartis Venture Fund, which is often a coinvestor with Mr Tripet and Tak W. Mak, a professor of immunology at the University of Toronto who discovered T-Cell receptors in 1984.

His relationship with these scientists was strong enough for him to be able to persuade them to join him when he set up his own

company in 2001.

Called Aravis Venture Associates after a range of mountains near Mont Blanc, Mr Tripet's venture capital organisation now operates two funds, Aravis Biotech I and Aravis Biotech II.

"We started replicating the strategy of the immunology fund which was basically worldwide investing. Aravis Biotech I is about 40% invested in the US, 20% is in Asia and 40% is in Europe, mostly Switzerland."

Mr Tripet says the first fund is now at a fairly mature stage and has already had three trade-sale exits. His second fund is orientated towards Europe and is currently only about half-invested.

"When we looked at the market and how the market was

"The number one reason why companies fail in Europe is because they run out of money; it is not because the science is bad."

Jean-Philippe Tripet

evolving we saw that it was becoming really very difficult for us to find slots in the good companies at the seed stage or Series A in the United States as we had done in the past. US venture funds had just got too big and we decided that it was best for us to concentrate in Europe.”

As an investor in Europe, Mr Tripet makes use of his experiences with US investments. This means that he takes a hands-on approach towards his investments. His firm is nearly always represented on the boards of the companies he supports.

“We like to lead financing rounds, which means that we like to set the terms at which we invest. It also means that we are also very often represented on the board of the company as well as compensation committees and audit committees.”

Mr Tripet watches money like a hawk.

“The number one reason why companies fail in Europe is because they run out of money; it is not because the science is bad.”

Importance of money

Mr Tripet said it was very important to bring a sense of urgency to venture capital investment as is done in the United States.

“I think that if you bring that sense of urgency and explain to the founders that when they are starting a company for a pharmaceutical drug they are going into a business that is more capital intensive than a nuclear power plant construction. Money is very important. If you run out of money you are dead.

“We try to make sure that our companies don’t fail for that reason. They are allowed to fail on the science, but not on the money.

“On day one, you need somebody who has a great idea, but day two and over the next 10 years you need somebody who is disciplined, every morning looking at every penny.

“I think you need to make clear to management that they will get money to spend but that it needs to be spent to achieve certain very precise results. You are allowed to fail, as long as you fail early, that’s okay. And you need to fail for good reasons which means that the scientific concept doesn’t work, there is toxicity that was not expected, there was an issue that was not foreseen when we invested.”

Mr Tripet urges the companies he is supporting to diversify their funding sources.

“I think we have learned, again from the US, that you can find money from a great variety of sources including charitable institutions such as the Wellcome Trust which for Europe is a great source of non-equity money for companies that work in the immunology field. Even if you are a European company you can find some non-equity money in the US with the Army, with the various defence agencies. One of our companies has been very successful in that; it raised about \$80 million from the military institutions.”

He was referring to Evolva SA, which is headquartered in Allschwil near Basel, Switzerland, and which is a holding of Aravis Biotech I.

As an investment strategy, Mr Tripet is generally on the look out for platform companies in the immunology and cancer areas, but he says it is hard to find companies that are one-step-ahead in these fields.

“Looking backwards over the last 15 years, I would say cancer was never easy. Most of the big drugs in cancer have been found by serendipity and most of the novel extraordinary targets that have been publicised in the last 10 years have not delivered what we had hoped for.”

He said some of the more recent cancer drugs, such as HDAC inhibitors, are really co-drugs that are taken if a lot of other treatments don’t work. He said these drugs are a kind of last resort for a patient and have tiny markets.

So if efficacy is a problem in cancer, how about antibodies? He foresees few investment opportunities for the first generation of fully human, monoclonal antibodies which will be marketed in the next five or ten years.

“I think there are a very limited number of targets available for these antibodies. They have all been (patent) protected and they are just not available.”

As for the second generation, which is producing antibody fragments with greater penetration power than first generation antibodies, Mr Tripet says that relatively few companies are involved in this area, such as Ablynx NV in Belgium, ESBAtch AG and Molecular Partners AG in Switzerland, the Domantis Ltd subsidiary of GlaxoSmithKline and a few companies in Germany and Denmark.

“I think that they (antibody fragment companies) are all being financed and we don’t see much new in that area. I think the issue is picking the right targets because it is much more difficult with antibodies than with small molecules to change your mind along the way. Once you have started antibody production, you are basically done. You’ve burned \$10 million. It’s a very expensive proposition.”

He says the third generation antibody companies may provide the best investment opportunities. These will be vaccines where the body will make its own antibodies to whatever target is required.

In general, a lot of Mr Tripet’s investment strategy revolves around picking companies with the right target. “Intellectually, it is not producing more targets. There are plenty. It is picking the right one which is difficult.”

Some companies are better at finding the right targets than others. As an example, Mr Tripet cited S*BIO Pte Ltd, a Singaporean oncology target specialist. Aravis Biotech II participated in its Series B financing in October 2008.

“If you look at what this company is doing, it is nothing special. They have one HDAC, they have one JAK2, but where they are very good is at identifying the relevant target for the disease, not the one that’s going to be the next fashionable one, but the one where people are going to get excited.”

He noted that in January 2009, S*BIO announced a North American licence and option deal with Onyx Pharmaceuticals Inc of the United States for two JAK2 inhibitors. The transaction has a potential value of \$550 million, including \$25 million upfront, and the possibility of double-digit royalties.

MedNous interviewed Jean-Philippe Tripet in London on 23 February 2009.