Investors back NovImmune's antibody strategy

On 12 May 2009 a privately-owned company based in Geneva, Switzerland called NovImmune SA announced that it had raised CHS 62.5 million ($54.8 million) in a private share placement with existing and new investors. The announcement was unusual for at least two reasons. At a time of tight credit, it was an exceptionally large financing for a European biotechnology company. And second, it was an endorsement of a business strategy focusing on antibodies, a very competitive segment of the new medical products market.

The immediate reason for the financing was the ending of a licensing agreement between NovImmune and Merck Serono. In 2005 Serono SA acquired exclusive worldwide rights to two of NovImmune's compounds and took an equity stake in the company. The compounds were two fully human monoclonal antibodies which were being investigated for a range of auto-immune diseases. Diabetes was one of the possible indications, and after Merck KGaA acquired Serono in January 2007, the merged company decided to drop its work in diabetes to concentrate on other therapeutic areas.

Small companies in partnerships with larger concerns often get pulled up short when the bigger company changes its research priorities. This happened in January 2008 when Novo Nordisk A/S of Denmark decided to divest its global oncology assets, thereby changing the focus of its multi-year research collaboration with Innate Pharma SA of Marseilles, France. Innate eventually negotiated a product swap with Novo Nordisk which enabled it to take control of a key cancer asset (see the November/December 2008 issue of *MedNous*).

By comparison, NovImmune has known since October 2007 that Merck Serono would be changing its research priorities. This gave it time to put together a financing package that covered both the cost of buying back the two compounds and taking over Merck Serono's equity stake – with cash to spare for product development. But in a difficult financial climate, the company had to make a strong business case to its existing investors which included BZ Bank Aktiengesellschaft, Ingro Finanz, Varuma and the Pictet Private Equity Fund.

To find out more about the company's strategy and how it succeeded in winning over its investors, *MedNous* interviewed the company's chief executive officer, Jack Barbut, and the director of business development, Luca Bolliger, at the company's offices in Geneva shortly after the financing was announced.

In a nutshell, the business case is that NovImmune has a pipeline of seven products, some of which could potentially be developed for more than one indication. Its lead product, an anti-CD3 molecule, has what the company considers to be superior properties to two other antibodies under development by competitor biotechnology companies. And these companies have significant Big Pharma support.

Mr Barbut has an unusual background for a biotechnology chief executive. Educated in engineering at the Ecole Polytechnique Fédérale de Lausanne, Switzerland, he spent nearly 20 years in contract research in the US before being asked to lead NovImmune. He is the founder of both Chrysalis International Inc, now part of MDS Pharma Services, as well as of Synarc Inc, a leading pharmaceutical services organisation. He was recruited to NovImmune in 2001 by the company's founder, Bernard Mach, a renowned immunologist.

Dr Mach founded the company in 1998 on the basis of intellectual property generated at the University of Geneva where he was professor and director of the Department of Genetics and Microbiology. He is described as the inventor of cDNA cloning, which is a way of isolating DNA that are complementary to messenger RNAs that encode proteins. This has important applications in the production of monoclonal antibodies. He has also written extensively about the molecular and genetic basis of deficiencies of the immune system. For example, he has described how the genetic regulation of a protein complex known as the major histocompatibility complex (MHC) plays a role in controlling immune response. Defects in the regulation of a specific part of this complex, MHC class 2, can play a role in immune disorders.

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>
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Dr Mach has applied his scientific expertise in more than one commercial setting. He is one of the eight co-founders of Biogen (now Biogen IDEC) and was chairman of the scientific advisory board of the Lombard Odier Immunology Fund when the fund financed a record number of successful immunology-based companies. He currently chairs NovImmune's scientific advisory board and is also a special member of the Swiss Academy of Medical Sciences and a member of the French Academy of Sciences.

Since its founding, NovImmune has raised CHF 154 million. The company did its first round of financing in 2000, just before Mr Barbut joined, raising CHF 15 million from the Lombard Odier Darier Hentsch Immunology Fund and from the Novartis Venture Fund. In 2005, it did a Series B financing of CHF 14 million, which brought Serono in as a shareholder and also resulted in Serono taking out an exclusive license to develop and commercialse the company's

two lead antibody products. In 2006, it did another Series B round of CHF 58 million led by BZ Bank, and then in May of this year, the CHF 62.5 million round, again led by BZ Bank. In between the main rounds, it raised bridging finance of about CHF 4.5 million. After the most recent fundraising, BZ Bank and its syndicate are the biggest group of shareholders in the company, Mr Barbut said.

From the very beginning, management's idea was to develop products, and specifically to develop monoclonal antibodies directed at treating auto-immune disease, the mechanisms of which had been elucidated by Dr Mach's research.

"It was clear from the beginning that we would build a company that was focused in one particular area which was immunology. We would not go for platform technologies, but we would go for products and we would build a product pipeline around that biology," Mr Barbut said.

If NovImmune has a peer, he said, it would be Genmab A/S of Denmark. "Genmab has a certain number of compounds which have been generated internally against targets and that's how they have built value. From that point of view, we are very similar in having a product strategy. We believe that we will create value for our shareholders through products and not just through a platform," he added.

NovImmune's current product portfolio consists of seven therapeutic antibodies of which six are fully human, which is to say they contain no mouse material, and one which is a very early-stage humanised antibody. With the exception of the very early humanised antibody, all of the candidate therapies have been developed using in-licensed technology. The company has licensed in transgenic mice technology from Medarex Inc and phage display technology from Cambridge Antibody Technology, which is now part of AstraZeneca Plc.

Where it has added value is pulling together leading immunologists to decide on drug targets and development strategy. One of the company's key strategists is Marie Kosco-Vilbois, the chief scientific officer, who joined NovImmune from the Serono Pharmaceutical Research Institute in 2002.

As a principle, management decided that it wanted to look at some well-known targets where there was an existing therapy which they believed that they could improve upon. Their lead product therefore targets a protein complex known as cluster of differentiation 3 (CD3).

The first ever therapeutic monoclonal antibody to be approved by the US Food and Drug Administration was in fact an antibody that targets CD3. Called OKT3 (muromonab), it is an immunosuppressant for administration to patients undergoing organ transplants. "As a target, CD3 has been around for a very, very long time. But because it is so toxic it hasn't moved into the chronic indications," Mr Barbut said.

He said that the challenge for NovImmune is to develop a second-generation antibody that can overcome the side effects of the existing compound while meeting a large medical need. The company is therefore investigating a new anti-CD3 monoclonal antibody for early onset type 1 diabetes. The compound, NI-0401, is the company's lead product. It targets the CD3 antigen, a key regulator in the activation of T cells. T cells belong to a group of white blood cells that play a key role in immunity.

"Normally your T cells are there to protect you. If you get attacked by a virus, normally your T-cells will eliminate that. But in a small percentage of cases, the T cells will actually turn against you, and that's what's called an auto-immune disease," Mr Barbut said. Anti-CD3 molecules are designed to 'reset' the T-cell receptor.

Under its now defunct licensing deal with Merck Serono, NI-0401 was investigated in Crohn's disease and in renal transplantation. Type 1 diabetes is a new indication with a much broader application.

In developing NI-0401 further, NovImmune is in competition with the US companies MacroGenics Inc and Tolerx Inc. MacroGenics is in a collaboration with Eli Lilly to develop and commercialise teplizumab, and Tolerx is collaborating with GlaxoSmithKline to develop and commercialise otelixizumab. Both products are anti-CD3 humanised antibodies.

"In the indication of type 1 diabetes they are currently ahead of us because they are humanised compounds and they started much earlier than we did. On the other hand, we will have a better safety profile and significantly less immunogenicity," Mr Barbut commented. Low, or no immunogenicity, means that the antibody is less likely to be rejected by the body. Early clinical work on NI-0401 was done by Serono. NovImmune is about to take the compound into a Phase 2/3 trial.

Next in line in the portfolio is NI-0801, which is intended to neutralise the activity of IP-10. IP-10 is a chemokine, or type of protein, which is expressed in inflammatory disease. NovImmune is developing the antibody for auto-immune and inflammatory diseases. NI-0801 is expected to start an early Phase 2 study in the beginning of 2010.

"If we look two years down the line, by late 2011, we will be a company, if everything goes well, with a compound in Phase 3, two compounds with solid Phase 2 data in hand and two more compounds which will be in Phase 1 and Phase 2. So there is a very deep pipeline, all of which have been generated by the two different platforms," Mr Barbut said. The executive said the recent private placement gives NovImmune about 18 to 24 months of cash, excluding any external partnerships.

"And as I have said to some other people, I would be very surprised if we don't announce a partnership in the next 12 to 16 months," he commented.

At the end of the day, what are NovImmune's unique attributes? Mr Barbut said the company has been able to assemble "under one roof" the biologists, the microbiologists and the clinical development experts who can focus single-mindedly on the challenge of developing new antibodies for immune-related disorders. From the very beginning, Bernard Mach understood the components of a successful company. "The only thing he didn't realise is that it would take seven years to do this," Mr Barbut commented.

Jack Barbut and Luca Bolliger were interviewed by *MedNous* in Geneva, Switzerland on 15 May 2009.