Interview with Eduardo Bravo, CEO, TiGenix – Belgium

05.10.2012

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eduardo-bravo-ceo.jpg

Bravo, in relation to your previous career in big pharma companies, you have recently made a shift into much smaller entities including Cellerix and TiGenix. What motivated you to make such a dramatic and bold shift in your professional life?

I was young and ambitious and despite having a successful career in the big pharmaceutical industry, I opted for a more entrepreneurial path where I could contribute to building something from scratch. Before doing so, I met with Cristina Garmendia (she has recently served as the Minister of Science and Innovation in Spain) who created the Genetrix Group, a successful biotechnology group based in Madrid. She was instrumental in convincing me to join Genetrix.

Shortly after that, we recognized that within the group, Cellerix was the jewel in the crown and thus decided that it needed to be financed independently. After discussions with knowledgeable investors, it became clear that we needed to shift the management from a holding company to Cellerix that was being financed independently. Consequently, Claudia D'Augusta – former CFO of Genetrix – and I moved to the management of Cellerix. Following that, we received our first financing round and Cellerix was formed within the Genetrix Group.

You were appointed CEO of TiGenix in 2011 following its combination with Cellerix to create a new European leader in cell therapy. Can you tell our readers more about the strategic objectives of this combination and the expected synergies from this union?

What distinguishes TiGenix and Cellerix from other companies is its common vision: that cell therapy will be the next revolution in healthcare. Both TiGenix and Cellerix decided to develop their products as drugs — conducting clinical trials to demonstrate their potential as value added

products.

Moreover, both companies had the ambition to become worldwide leaders in cell therapy. Put differently, we aspired to become the Genentech of cell therapy. Of course, there is always the possibility of becoming an acquisition target but that was never our goal. Instead, we have the ambition to build a solid and leading company within our field, rather than building a company with the intention of simply attracting acquisition interests.

As both companies were confronted with the same challenges, the merger helped us to share our technology platforms and our regulatory and scientific expertise. Another advantage was that TiGenix was already a listed company with a very strong base of investors, facilitating finance needs. Moreover, at the time TiGenix also had the only cell therapy approved in Europe, contributing to the company's revenue stream.

In conclusion, I think the merger has turned out extremely well, and has resulted in a "new" TiGenix that is much more than the sum of its parts. I am also very optimistic about our growth prospects, and am pleased that our customers and other stakeholders agree that the companies form a perfect combination.

In the 1.5 years since you took charge of TiGenix, what would you classify as the company's main milestones and what are your proudest achievements?

Our proudest achievement is perhaps the fact that we have been able to retain our high-value employees, demonstrating their confidence in the future of the company. Furthermore, I believe that high quality staff is a critical element of our operations.

On the other hand, from an industry perspective, our proudest achievement is the progression of our main product ChondroCelect®, which is the first cell-based product that successfully completed the entire development track from research to clinical development to approval by the European Medicines Agency as an Advanced Medicinal Therapy Product. Just after the announcement of the merger we obtained national reimbursement for ChondroCelect® in Belgium. We have recently received national reimbursement in the Netherlands and we are close to securing it in other countries as well.

Moreover, as the CEO of the company, I am proud to say that we have delivered on every single milestone we communicated to the public. It has taken some time but after one and a half years we see the market starting to recognize that we deliver on our promises. We are not there yet but our investors are becoming ever more confident in the company's future.

Science and clinical research forms the backbone of your company, which is based in one of the world's most attractive pharmaceutical and biotech markets, Belgium. What in your opinion makes Belgium a mecca for biotech companies?

An aspect that we try to communicate to stakeholders is that Belgium finds itself in a privileged position for cell therapy due to the concentration of cell therapy companies located in the Benelux region, particularly in Belgium.

Recently we have established a private association among the companies active in cell therapy to try to raise the profile of the relatively small sub sector. One of the association's goals is to retain Belgium's favourable position that obviously derives from the quality of its universities, especially with regard to the quality of the spin-offs they produce.

Likewise, the government has invested substantially in the biotech sector. In addition, there is huge interest by private investors as well as capital derived from life science funds and other funds that have helped speed up the sectors development.

Not only does ChondroCelect® represent the company's lead product but it also the first and only approved cell-based product in Europe. Can you provide our reader with a brief description of this product and what its expected benefits are to patients in need of cartilage repair in the knee?

ChondroCelect® is not for any cartilage defect. The cartilage is a stiff yet flexible connective tissue that does not regenerate itself and is found in many areas in the body, such as the elbow and the knee. If a person suffers a defect after a sports injury or a trauma, for instance, and develop a hole in the cartilage, they are then faced with two options: to do nothing and risk developing osteoarthritis over time which often ends with requiring synthetic joint replacement, a major and traumatic intervention.

An alternative for patients is micro-fracture surgery. This involved performing a repair of cartilage that works by creating tiny fractures in the underlying bone. This fills the gap in the cartilage, helping to decrease their pain levels. However, this procedure simply delays the problem and does not offer a cure.

On the other hand, it was discovered in the University of Leuven that it is possible to grow the cells of the cartilage to create new cartilage. Of course, this process has been patented and led to the creation of TiGenix. After obtaining positive animal data, TiGenix decided to test it applicability to humans and so took the tough road of five years clinical trials comparing micro-fracture surgery with ChondroCelect®. Within one year we managed to demonstrate that the cartilage obtained with ChondroCelect® is almost identical to natural cartilage while the cartilage coming from micro-fractures is not. Moreover, after three to five years there is a significant difference in improvement between micro-fracture and ChondroCelect®. So far, ChondroCelect® is the only product in the world that has demonstrated such results.

Importantly, by the end of 2007, legislation related to cell therapy was introduced. It was decided that when cells are either modified or used for a different tissue than when extracting the cells, they become a pharmaceutical drug. Since there were several drugs like this on the market a transition period has been created. Meaning that suppliers of these drugs have been provided with a period of five years to conduct trials in order to get the product approved before the end of the transition period — 31 December 2012. As a consequence ChondroCelect® is competing with products that have not demonstrated safety and efficacy in well controlled clinical trials and that are produced on a less stringent quality system. Fortunately for us, now that the end of the transition period is approaching these competing products will be removed from the market, since ChondroCelect® is the only drug in its class that received approval by the European Medicines Agency and the European Commission.

How would you describe the performance of ChondroCelect® so far on both a local and European level? Do you think it's achieved the level of penetration it deserves?

It took us one and a half years to receive reimbursement rights from the government. One reason for the delay was that we were unable to devote enough resources to this task. Another reason was the fact that ChondroCelect® was the first cell therapy drug going through the system, which by definition did not put us in a favourable position. The pricing commission for example had never seen a cell therapy before; hence we can say that it was a learning process for both parties.

On addition to this, the price per vial seems high — approximately €20,000 apiece. Nonetheless, we eventually received reimbursement rights in Belgium and later in the Netherlands. Now, I believe that we have started to break the ice and remain optimistic to soon receive national reimbursement in other countries as well.

Are you apprehensive about any 'me too' products from competitors?

I believe that the cell therapy environment is too large for companies to compete with each other; there are far too many unexplored areas within the field for that. Hence, for the time being, I do not see any other companies competing directly with us. Moreover, it is a general feeling among the cell therapy companies that rather than reinventing the wheel it is wiser to share our knowledge for our mutual benefit, and there are certainly a lot of growth opportunities within our domain.

Considering the relatively fledgling nature of the stem cell industry and TiGenix's pioneering role within it, what would you highlight as the main lessons learnt as you progressed?

The first thing that comes to mind is that biotech companies in general are underfunded, especially in Europe. Indeed, we certainly would have been better off doing more things in parallel with more capital.

Furthermore, one of the main differences between companies in Europe and the United States is that European companies are always probing for sources of capital, while in the US companies are generally funded for three years to provide them the freedom to concentrate on their core business.

Besides ChondroCelect®, TiGenix also boasts an array of advanced clinical stage pipeline of adult stem cell programs. Can you illuminate our readers on the latest developments within your pipeline and highlight the products you are most excited about?

Our most advanced product is Cx601, which is the local delivery of cells for the treatment of complex perianal fistulas in Crohn's disease patients. A perianal fistula is the connection between the rectum and outside skin surface with an important and potentially negative impact on quality of life. It is a painful disease that still lacks successful treatment. Currently we are conducting phase III trials in Europe and once we have received positive results we will file for registration approval.

Our second most advanced therapy is Cx611, an intravenous infusion of cells in patients for the treatment of rheumatoid arthritis. We have targeted this disease because it has undisputed clinical endpoints, meaning that no one can argue whether it works or not; it is a directly observable result. We are looking at long-term effects of the cells and after injecting the cells, we follow-up with the patient for a period of six months without any further treatment. If we can demonstrate that the cells have the memory effect that we believe them to have, it will be a quantum leap in the treatment of autoimmune disorders. We expect the final clinical results in April 2013.

The last one – my preferred program – is Cx621 which is also for the treatment of autoimmune diseases. I am most excited about this because it is a proprietary way of injecting the cells directly into the lymph nodes. We believe that a lower dose will produce higher efficacy and lower side effects. We have filed a patent for the administration procedure and have already conducted Phase I clinical trials. So far, the administration method has proved to be feasible and safe.

Healthcare systems around the world are changing, increasingly taking added value and health-economic benefits into consideration. In your experience, what is your view on the state of the healthcare system?

The problem that we are facing is that as life expectancy increases, people want to live healthier lives and the industry keeps introducing new products that require more investments. At one point however, governments will have to decide whether to reimburse certain drugs or not and can lead to a philosophical discussion on the subject. For instance, should we provide a smoker patient, with a donor heart? Or should the drugs of overweight related diseases be reimbursed for patients who lead unhealthy eating habits or lifestyles?

This debate is surely ahead of its time but government budgets are shrinking and the cost of healthcare is rising. Responsibility will have to be shifted to the population. Instead, the healthcare

sector should place more emphasis on preventative healthcare rather than curing diseases. It is a huge debate and a big issue that is inevitable.

Where would you like to take TiGenix over the next 1 to 2 years and how do you aim on achieving that goal?

For the next couple of years we want to keep delivering on the milestones that we have set and hopefully that will give investors the confidence that our strategy is the right one. Beyond that, we may want to add other assets to the company, not only focus on internal growth.

The last additions to our board demonstrate that we are ambitious; that our objective is not to remain a mid-sized company but that we want to develop from a technology leader into a full-fledged commercial cell therapy company.

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