Interview with Massimo Di Martino, President & Managing Director, Abiogen

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Tags: Abiogen

You created Abiogen in 1997, following the acquisition of Istituto Gentili by MSD, in order to maintain your family's entrepreneurial tradition, keeping building on the legacy of your great-grandfather Commendatore Alfredo Gentili, combining it with your personal innovative vision to create a "new reality".

To have a better understanding of the company strategy to success in only 12 years, could you expose the main milestones and achievements of Abiogen's young though rich history?

At the time when MSD presented the opportunity to create another company, Istituto Gentili's former management had difficulties in analyzing the evolutions of the Italian pharmaceutical market. Indeed, starting from the early nineties, cost rationalizations started to be implemented in the country, the reimbursement schemes were completely re-shuffled, and pharmaceutical companies entered a period of troubles and uncertainties. But whereas the former management considered this turning point as the end of a period, I personally decided to perceive it as the beginning of a new era, offering other opportunities requiring customized strategies.Therefore, Abiogen started building on Istituto Gentili's traditional assets- R&D know-how, and a strong portfolio in the osteoarticular, diabetes and respiratory areas- leaving aside the cardiovascular field in which the competition was fierce and the opportunities were already decreasing. And the company quickly became the first player in the world to present 3 biosphosphonates on the market, with a fourth still under development.The second guideline has been to differentiate the

company from other players by maintaining and increasing the manufacturing activities. In a context of global delocalisation, Abiogen’s vision was to rely on its skills and experience to offer very high quality levels of production in a very specific niche, in order to work with multinationals in need to outsource this small share of their total production. As these players also require periodical audits regarding quality standards, the facility is continuously inspected by the authorities and upgraded according to global standards in order to remain highly competitive. FDA approval will certainly be the next step, following a pre-audit to be realized in the coming months.

Looking at how such strategy has been converted into success, and as a result of your ability to quickly react to market trends- how do you assess Abiogen’s performance in terms of growth and revenues?

The first investment plan was set up in 97, for the renewal of both the plant and the headquarters. As the old manufacturing site of Istituto Gentili -located in the historical building of a former pediatric hospital from the 19th century- was not adequate anymore for Abiogen’s activities, a total of Euros 40 million have been invested to build the new one, starting from 1998 until the inauguration in July 2001. Consequently, the first five operational years have been heavy for Abiogen from a financial point of view.The second step has been the launch of a consistent R&D program on the long term, closing agreements with foreign universities in order to quickly develop a promising biotech pipeline. For instance, an ongoing project is currently focusing on the development and evaluation of anxiolytic and antidepressant activity of two new CNS agents coming from the British Technology Group.Therefore, from an initial turnover of Euros 35 million, the performance progressively improved thanks to these main investment lines, combined with strong agreements such as the one with BMS to whom in 2000 we out-licensed patent rights for the exploitation of an oral anti-diabetic agent.Overall, Abiogen’s start-up phase has been outstandingly smooth and successful, as the company could rely from its very beginning on years of experience and excellent skills. The only real obstacle came from the political level and the restrictive policy towards the pharmaceutical industry implemented between 2001 and 2006 –with13 successive price cuts during these six years, resulting for instance in a total price reduction of 11% for the only year 2006.Indeed, it seems that the Italian industry is victim of a prejudice: the government is convinced that pharmaceutical companies are more focused on the commercial aspect than on research, and that their profitability has to be limited by institutional tools.Such governmental interventions make it difficult to stick to long-term plans, as forecasts and amortization plans can suddenly become irrelevant overnight, with new parameters to be taken into account. In such an unstable context, Abiogen can nevertheless rely on more than 50 years of research tradition, and keeps building its traditional core area of osteoarticular drugs, yet also increasingly covering CNS

and degenerative diseases.

In this process of combining the traditional study of connective tissues developed in the 70’s with the new frontiers of biotechnology, in which therapeutic areas do you see more remaining unexploited potential?

Indeed, in terms of R&D pipeline, the heritage from Istituto Gentili was mainly covering the osteoarticular area – including both cartilaginous and bone affections. But when starting up Abiogen, there was a need to find new fields in which the company could compete accordingly to its dimension, know how and history- in other words, areas of high unmet medical need, such as CNS for anxiety and depression, as well as oncology. For this reason, new paths have been explored.But even through such process of diversification, Abiogen is not willing to expand its research facilities, and wants to maintain its capacity to coordinate each project, working with highly specialized centre for specific trials.CNS investments are currently orientated towards an anxiolytic agent, currently in phase II in an Austrian centre, as well as a compound targeting panic disorders, developed in Pisa.The oncology area is rich of four ongoing projects; the most promising resulting from an agreement with the Wistar Institute of Philadelphia, and looking to develop the first European heterologous cell therapy targeting metastatic cells. In the same way, the M.D. Anderson Cancer Center in Huston asked Abiogen to try such cells for leukaemia patients who remain insensible to Glivec.

As Abiogen has a steady focus on unmet medical needs, in a context of lack of synergies between public and private, how would you describe the challenge of convincing a bureaucrat, who might play a crucial role in getting treatments ultimately reimbursed, but who might not be as informed as an industry insider?

The main issue is that whereas all the innovative products, especially biologicals, are submitted to European procedures, the Italian National Agency (AIFA) is not following the same pace as other European countries- as delays in national regulatory procedures can last up to one to two years. Opportunely, AIFA should work it out by the recruitment of 100 new employees. One further issue is that new products price often has to be decreased to allow the compounds to enter the Italian reimbursement list. As a result of such an unfavourable regulatory framework which makes it very hard to successfully develop biological products, Italian companies suffer from a lack of experience in this field.For instance, Abiogen started the clinical development of its cell therapy in Italy, and soon had to face the difficulty to establish a dialogue with the Health Authorities about clinical protocols and GMPs procedures. The main issue was really to find an interlocutor that would be aware of the importance of our very innovative project. Finally this cell manufacturing lines

obtained the Italian GMP authorization – but there is undoubtly room for improvement in the Italian authorities' level of contribution to the pre-authorization phase of new biological products. Abiogen's knowledge and skills for research and product development also enable the company to develop strong partnerships with third parts.

What is your approach to R&D partnerships and what makes Abiogen a point of reference for such collaborations?
In 2007, the management team analysed the past 10 years of Abiogen Research operations in comparison to the trend of the R&D agreements of the last three years, which are mostly in the early discovery and late development stages.Therefore, Abiogen analysed its pipeline and decided to modify the model of development for its compounds, both in terms of technical approach and strategic planning.As an example, we decided to enhance the preclinical package of the compounds with all the data that could be interested to a third party instead of rushing to the clinical phases as soon as possible. In the same way, the biological projects in the oncology field, which are co-developed with the South Western University of Dallas and with the Wistar Institute of Philadelphia, are aiming at creating a pool of development, starting from Abiogen's existing assets to find other companies or investors. Beyond such development partnerships, Abiogen's roots lie in the collaboration with important national and international players through licensing activities that enabled the company to succeed.
In the process of expanding out-licensing collaborations, how will you select the most promising partnerships?

Considering our dimension and position, finding new partners is not easy, and the process is always different according to each single project.But Abiogen is extremely present in international meetings dedicated to licensing opportunities, in order to showcase its projects to multinationals that could be interested in learning more about new opportunities.And as a result of this successful strategy, five multinationals have recently signed a confidentiality agreement about Abiogen's anxiolytic agent, in order to analyse the feasibility of a potential partnership. Indeed, as anxiety is a social pathology and represents a high- potential market, such compound is very attractive for Big Pharma that are mainly interested in potential blockbuster products,But in such case, the potential partners mainly look at their own interest, much beyond the product's specificity. For this reason, opportunities to discuss with smaller biotech companies can appear more adequate in terms of synergies, and this is why Abiogen is also present in international meetings at this level. In terms of image and brand recognition,

what does Abiogen stands for today in Italy and worldwide and where is there further room for improvement?

Abiogen developed strong relationships with US Universities; accurately worked with the most important opinion leaders in the osteoarticular field already brought a high level recognition; and has been present in all the international meetings targeting its core therapeutic areas in the last 10 years- a number of initiatives which enabled to acquire a high level of recognition in the global scientific company, and to transform long-term relationships into concrete trials and development projects.Indeed, such a continuous exchange of contacts with potential partners resulted for instance in the M.D. Anderson Cancer Center's solicitation to work on cell therapy, as well as a request from a German group to co-develop a new orphan drug, among many others scientific partnerships.But it is also worth mentioning that Istituto Gentili has always considered research as a main part of its mission- which even resulted, back in times, in a poor consideration for marketing activities and commercial strategies. Abiogen started building on this legacy, maintaining the same research focus applied to new molecules and substances, as a prevalent core R&D commitment more than focusing on restyling activities or extension lines of old compounds.And this is also why we have a good relationship with the national research institutes and extremely good reputation in the scientific world.

Keeping bringing innovation to Istituto Gentili's legacy, what are your personal ambitions for Abiogen in the next three to five years?

Abiogen would like to have the possibility to add value to the research investments conducted in the past 10 years, improve its capability to develop new drugs and close new agreements with other players.I personally don't believe in future growth through direct commercial activities in other countries. The real immediate goal is to reach a level of revenues in adequation with the research investments- even tough commercialization could come as a second step, when Abiogen will be able to build on the successful results obtained from the R&D operations.

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