

BioXell: an Italian biotech success story?

Although BioXell's successful initial public offering (IPO) on the Swiss Exchange SWX on June 22, which grossed CHF 57.8 (\$46.9) million, can be considered a relatively unremarkable event for a company at its stage of development, it could have a wider significance for the Italian biotech sector. Indeed, Italian biotech has so far struggled to convert the country's strength in life sciences research into a thriving commercial industry. Other, less heralded developments, including a series of regional initiatives and the entry of new investors into the sector also provide some grounds for optimism on the part of the industry's supporters, but it still faces considerable financial and cultural constraints that could choke further development.

BioXell's decision to seek a listing in Zürich rather than its hometown of Milan underlines the lack of development of a fully fledged investment infrastructure for Italian biotech. In a similar vein, Villa-Guardia-based Gentium, a 2001 spinout of Crinos Industria Farmacobiologica, raised cash in recent, successive offerings on the American Stock Exchange and on Nasdaq in New York City, whereas the Italian founders of NiCox opted to establish that company as a French entity, located in Sophia Antipolis and quoted on the Euronext exchange in Paris.

A Milan IPO "wasn't really considered" says BioXell CEO Francesco Sinigaglia, whereas the Zürich exchange is home to several biotech successes and has the support of investors who understand the sector. Even so, the share offering, which was launched shortly after the general decline in global stock markets in early June, was priced at the bottom of the indicative price range of CHF 44–CHF 48 (\$35.5–\$38.8)

that the company published and investors took up the minimum number of shares on offer. However, the share price has held up since the IPO, hovering close to the initial offering price for the first six weeks of trading.

The BioXell success remains a largely isolated one in the Italian landscape. Despite its prominence in fields such as oncology, immunology and neuroscience, Italy has been Europe's most egregious underperformer in biotech during the past decade. Italy was bottom of a league table of 14 western European states that measured each country's gross domestic product against its total number of biotech companies, according to the 2006 Ernst & Young biotech report "Beyond Borders."

An absence of risk capital, deficits in areas such as patenting and technology transfer, a historic inattention to the sector on the part of government and a general lack of interest in commercial biotech on the part of academic scientists have all contributed to this state of underdevelopment. "There is still very modest entrepreneurship in the biotech sector and not many structured and savvy intermediaries. Deal flow is not significant compared to other EU countries of similar size," says Joël Besse, senior partner with Atlas Venture in London, who participated in investments in two Italian biotech: Milan-based Novuspharma and Bresso-headquartered Newron Pharmaceuticals. These two firms, along with BioSearch Italia and Milan-based BioXell were all established as either spin-outs from or management buy-outs of international pharma R&D centers that had been located in the country. Only BioXell and Newron Pharmaceuticals remain independent. BioSearch Italia merged with Versicor, to form Vicuron Pharmaceuticals, an



Francesco Sinigaglia, BioXell's CEO, is at the helm of one of Italian biotech's success stories.

anti-infectives specialist located in King of Prussia, Pennsylvania. Pfizer then acquired Vicuron for ~\$1.9 billion in cash in September 2005. Novuspharma was acquired in January 2004 by Cell Therapeutics, of Seattle, in a stock-based deal initially valued at \$236 million.

It is difficult to predict whether other biotechs would follow the example of the likes of BioXell. The gap between these companies, all of which were established with relatively broad clinical development pipelines, seasoned management and access to international venture capital finance, and the rest of Italy's fragmented and, for the most part, undercapitalized biotech industry has been considerable. The great challenge for the sector has been how to close that gap. Regional authorities, notably in Lombardy and Piedmont, where the bulk of Italy's 160 biopharmaceutical firms are based, are actively involved in promoting biotech, through funding technology transfer agencies, incubators and seed funds (**Box 1**). Newer initiatives have sprung up in Tuscany and in Sardinia too.

"Clearly the lack of Italian specialist venture capital funds is a problem," says Sinigaglia. However, individual companies are pursuing alternative funding models. Some, most notably MolMed, have managed to raise cash directly from financial institutions and private investors. MolMed, located in the San Raffaele Science Park, adjacent to the San Raffaele University Hospital and the eponymous Scientific Institute, the country's largest private clinical research center, has so far secured some €60 (\$77) million by this route and may undertake an IPO during the first half of 2007. "We have a broad pipeline and we think we would be ready in the near future," says Marina Del Bue, general manager at Milan-based MolMed, which is developing cell-based therapies and biotech drugs for cancer.

Elsewhere, investors in Genextra, a holding company with a controlling interest in four companies, agreed to double their commitment, to €60 (\$77) million, this summer, following their participation in a \$41-million investment round in Intercept

Pharmaceuticals, a company headquartered in New York City but based on research into the bile acid-activated nuclear receptor farnesoid X performed at the University of Perugia. "Although it is supplying mentoring and administrative support, Genextra is neither an incubator nor an investor. We are not an investment fund. We are a biotechnology group," says Paolo Fundaro, Genextra chief financial officer.

Milan-based Genextra has high visibility in Italy because its backers include leading entrepreneurs and industrialists, such as its founder, telecoms entrepreneur Francesco Micheli, Marco Tronchetti Provera, chairman of Pirelli & Telecom Italia, FIAT chairman Luca Cordero di Montezemolo and Diego Della Valle, CEO and chairman of the luxury shoemaker Tod's. The model is borrowed directly from that of another Micheli-led enterprise, the internet and telecoms group eBiscom, now FastWeb, which raised \$1.5 billion at the beginning of the decade. Its progress, along with that of BioXell—now the country's flagship biotech firm—could help to shape investor sentiment toward the sector.

Assobiotech, in Milan, which represents the industry, thinks the country's new national government can help as well. One measure, says Assobiotech president Roberto Gradnik, would be to create a national agency for innovation that would support technology transfer and partnering. "At the moment, if anybody, such as a private investor, is interested in investing in biotechnology, they don't know where to go," he says. Risk-averse Italian investment funds might engage with the sector if a 'guarantee fund' were put in place—a sort of voluntary insurance scheme that would allow venture capital funds to offset their investment losses against profits on more successful ventures.

Assobiotech is also trying to persuade the government to adapt the 'Young Innovative Company' concept, originally developed in France to provide tax breaks and other fiscal supports to research-intensive startup companies, to the Italian tax code. Italy had a change of government in May. In its new cabinet, led by Prime Minister Romano Prodi, responsibility for innovation policy was transferred from the research ministry to the industry ministry, headed by Pier Luigi Bersani. Gradnik interprets this as a positive move. But, says Sinigaglia, a real shift away from manufacturing and towards a knowledge-based economy still needs to happen. "We need to see government to commit to that switch."

Cormac Sheridan, Dublin

Box 1 Italian biotech park taps into traditional industries

Italians are often praised for making up for the deficiencies of their country—burdened by bureaucracy and lack of flexibility—with individual creativity. The Canavese Bioindustry Park may be a proof that there is some truth in this cliché. The park is located near the northern city of Turin and its creation was supported in the 1990s by the Piedmont region with the aim of reinforcing the high-tech dimension of the local economy after a major crisis. As a result the park shareholders are 70% public and 30% private.

Since 2004, seed capital for startups has been available thanks to a model of financing based on the business angel concept devised to bypass the lack of interest from venture capital investors for early stage projects. "We collect money from wealthy people with no experience in biotech, such as local small entrepreneurs in the textile or mechanical sector, lawyers or accountants. Before meeting us they never thought of becoming business angels," says Silvano Fumero, who conceived the park when he was still head of R&D at Serono.

Thirty people gave a total of €3 (\$3.8) million, each contributing a small sum and becoming founding members of a seed capital society called Eporgen Venture. "We are hopeful in a couple of years the most promising newborn companies may attract investments from [the] biggest players, maybe one [of] the international venture capitalists we have involved in the selection of projects," explains the park project manager Fabrizio Conicella. Birth rate is unusually high by Italian standards with five new startups born last year and the intention of starting another five companies by mid 2007.

The initial success of the project is already a blow against the cultural and political foot-dragging of the country, but is it replicable? "We are actually examining the way to implement a similar model in the Rhône-Alps region [of France] but it's not so easy," says Valérie Ayache, managing director of the biotech association near Grenoble, Adebag. She points out that the motivations of people investing in Eporgen are very much related to the history of the territory, the charisma and experience of the project fathers, and the very integrated model they have created between the park and Eporgen. Other Italian regions are trying to learn a lesson from the Canavese experience, too: until now biotech has played a minor role in the national business angels network (Iban) but its secretary general Tomaso Marzotto Caotorta thinks it's time to create a club of senior managers scouting Italian life sciences institutes for innovative ideas.

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