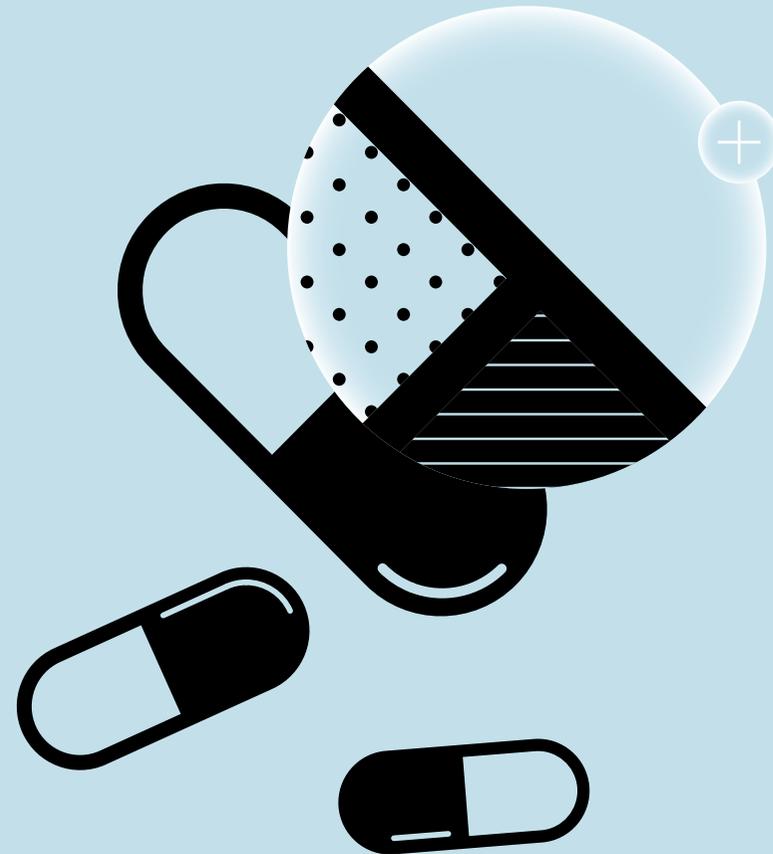

Case Study

Bluepharma

Re-starting-up an approach to innovative business development

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Sandro Mendonça



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Bluepharma: Re-starting-up an approach to innovative business development

Abstract

Bluepharma is a Portuguese pharmaceutical company operating in what would seem the low-end of a high-tech industry. Bluepharma manufactures generic drugs for more than 30 countries. However, it does that for other companies or sells directly under its private label. The company has been committed to innovation from the outset, investing in in-house R&D, university linkages and its own spin-offs. Bluepharma was founded in 2001 through a buy-out of a manufacturing unit of Bayer, the well-known German multinational. Innovation and internationalization have been two basic pillars enabling sustainable growth in a business that is technological and global. It achieved this transition by adopting an entrepreneurial style of leadership and by relying on the available sectoral capabilities of the national system of innovation, which included a smart use of public venture capital for supporting new high-tech initiatives. The company has developed continuously and mastered the ropes of what is a dense regulatory environment and hyper-competitive global arena. Bluepharma combines a rich array of internal innovation processes with an external approach to business development.

Keywords

pharmaceutical industry, generics, buy-out, innovation process

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Management, for *COTEC Portugal*, between May and June 2015.

Personal interviews were held at Bluepharma with the following executives (by alphabetical order): Cláudia Sousa Silva (Chief Scientific Officer), Paulo Barradas Rebelo (Chairman of Bluepharma), Sérgio Paulo Simões (Vice-President, Business and Product Development of Bluepharma, Chairman of Luzitin). Face-to-face interviews were held on June 9th June 2015 with a visit to the headquarters. Selected quotes from those interviews are transcribed in the case. The interviews were in Portuguese language; the quotes were translated into English by the authors.

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Introduction

Origins of the story

“There is a number of ways of telling the story, isn’t it?” So, begins Sérgio Simões, Vice-President at Bluepharma since its foundation in 2001. In his corporate life he is in charge of business and new product development, but he never left the academic world. Since 1991 he has been Professor of pharmaceutical biotechnology at the Faculty of Pharmacy of University of Coimbra, the oldest academic institution in Portugal, founded in 1290. “We can tell it taking advantage of all the data we have today, and we’ll have an interesting story to tell,” he says as he sat down to the interview in mid-2015. He goes on, “How did it happen?”

Paulo Barradas Rebelo, the CEO, is probably the best person there is to supply a persuasive answer. He would agree the way Sérgio put it: “It is a story unlike most stories, but it did happen to us.” Paulo, his long-time friend, was the entrepreneurial force behind the efforts leading to the establishment of the company.

“I was the owner of a pharmacy shop and president of a pharmacy shops cooperative when I learned through the newspaper about the closing of the Bayer plant if nobody bought it. Since I was a kid I dreamed about having my own industrial operation and immediately came to believe it was important to save that factory. And we got together in my pharmacy and we started to discuss the possibility of buying the production unit ... Then we decided to go for negotiation with Bayer. And it wasn’t easy.”

The German-based multinational was active in pharmaceutical production in the country since 1972. A few friends from Coimbra, rallied by a long-time expert in the distribution part of the industry, reacted to the announcement. The factory was engaged in contract manufacturing and that was a very competitive sector. Bayer wanted to leave, shutting disbanding the assets if it had to. From the perspective of those seating in the backroom of Paulo’s pharmacy, Bayer was giving up one of the most sophisticated

BOX 1
The famous four

PAULO BARRADAS REBELO ISOLINA MESQUITA SÉRGIO SIMÕES MIGUEL SILVESTRE

The acquisition of Bayer’s facilities was made by four young and experienced professionals connected to the area. The negotiation process took nine months and involved beating about 100 other applicants (all international). Paulo Barradas Rebelo, a manager of drug distribution business, grandson of a physician and a pharmacist, Sérgio Simões, an academic at Coimbra, Isolina Mesquita, responsible for the operations of the factory of Bayer in Coimbra, and Miguel Silvestre, with a degree in pharmacy and the pharmacist manager in the voluntary sector. According to the own, a fifth “founding partner” was a fund, a Portuguese public concern through a venture capital initiative, SME Capital , which remained from 2001 to 2016, the end of the contract.

Source <http://pwc.to/1rbjStP>, <http://bit.ly/1i5hXuw>, <http://bit.ly/1WVhgny>

business units of the country. People would get unemployed. A depressing impact to the local economy was imminent. A small group of individuals decided against the impending fate (see Box 1).

The knowledge-economy in peril

These developments were also a slap in the face of the *zeitgeist*. This was the time of the New Economy and the Lisbon Agenda, politicians emphasised high-tech industries and commentators hailed the

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knowledge-based society. Paulo Rebelo recollects:

“We were in 2000 and public policy moving in the direction of science and technology, and that was inspiring! Another inspiring thing was that when I returned to Coimbra there was a civic movement with politicians, businessmen and academic researchers and professors looking for a new way to reinvigorate the city and region. Someone said we could choose health as an excellence sector as we had many successful areas like ophthalmology, cardio-thoracic medicine, implant surgery, and so on. This gave some prominence to pharmaceutical sector. The tough standards of admission in the medical degree had the consequence that students who could not get into their first choice went into pharmaceutical sciences instead. This led very good students to this area. Both aspects combined were empowering the pharmaceutical sector.”

A hand-full of highly motivated individuals, connected to the pharma sector from different angles (theory and practice) and steps in the value-chain (from research to commercialisation)

decided something should be done and could be done. High-minded as it was, this represented a high-stakes manoeuvre. Bayer’s shoes were big to fill (Box 2).

Profitability under pressure

There were headwinds: the international competition was getting tougher by the day, as factories from different countries from several continents entered the low-end of the business. There were obstacles in the way: regulation was dense, and becoming more stringent by the day. And it was against the tide: the bet was on maintaining in Portugal a production business intensive in science and technology when the trend was delocalisation to India and China.

The pharmaceutical industry was (and is) technologically and institutionally complex. At the turn of the century prospects for the industry were fuzzy amidst signals of disruption. Debate was ripe. A forward-looking PwC’s 1998 report *Pharma 2005: An Industrial Revolution in R&D*¹,

sounded the alarm. Advice to the young and the unaware: “a climate more hostile than anything it has previously encountered – a climate in which only the smartest managements will survive.” The challenges were driven by soaring R&D costs, sluggish sales growth for prescription medicines, shorter product lifecycles, shifting customer base, fundamentally different life sciences knowledge bases calling for new skills, historically high levels of return demands by shareholders, etc. Big pharma dominated the playing field and search for new drugs scratched the limits of human knowledge. The consultants and commentators, the industry would restructure. Of course, it would do so in ways that are not exactly predicted by then.²

How to find a way in such a sea of moving, indeed qualitatively evolving constraints? The trend was to have lower production prices whereas the costs of new

drugs were on the increase, something had to give. Staying with this business model would be a great risk to any prospect entrepreneur, let alone from a country with no reputation in high-end/large-scale manufacturing. Against this background the general aim was unambiguous: go international, be different and become innovative.

2 · From the early 2000s genomics and big data changed the research practice, emerging economies became demand engines for pharma products, annual output of new drugs flattened, harsher price and promotion controls were implemented by regulatory authorities. See PwC (2012), *From Vision to Decision Pharma 2020*, <http://pwc.to/1rbjStP>.

1 · <http://bit.ly/1En78Oz>

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BOX 2

Bayer, big pharma in a small country

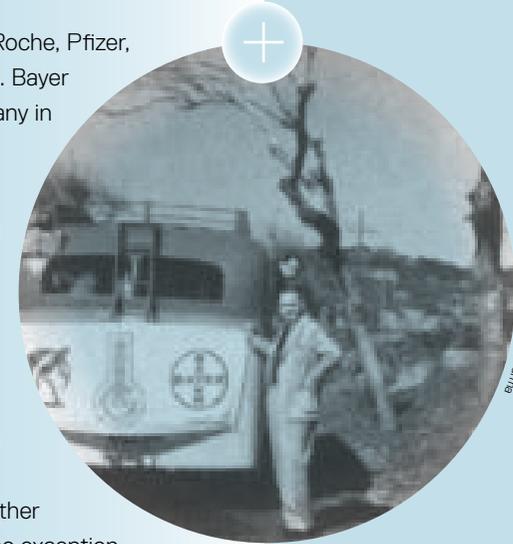
Bayer is one of the traditional big pharma players: Johnson & Johnson, GSK, Novartis, Roche, Pfizer, Sanofi, Merck, AstraZeneca, Lilly, Bristol-Myers Squibb are other well known companies. Bayer was top 100 global company in market capitalization in 2015 and a top 10 pharma company in revenues in 2014.

The partnership giving origin to Bayer was established in 1863, in Barmen, by the dye salesman Friedrich Bayer and master dyer Johann Friedrich Weskott. From 1863 to 1881 the company had a remarkable growth performance in the working force (from 3 to 300 workers). Between 1881 and 1913 the company develops into a fully-blown player into the modern chemical sector as it grows its international operations. An industrial laboratory is developed in the headquarters of the firm (1878-1912), and is credited as being the pioneering in-house formal R&D department. In 1899 Bayer comes up with its greater market hit, the Aspirin. By 1913, less than 20% of revenues came from domestic sales in Germany. Its first great export market was the US, having established there a sales representative early on, but before World War I, Bayer established subsidiaries in other important markets like the United Kingdom, France, Russia and Belgium. Portugal was no exception and Bayer has a long history in the country.

In 1909, Bayer creates “Fed. Bayer & Co.” in Portugal. Eleven years later the company enlarges its activity founding Anilinas Society with subsidiaries in Gouveia, Covilhã and Lisbon. In the early 1930s the medical sales representatives start their activity, approaching doctors and the pharmaceutical industry. Only by 1937, the symbolic representation of Bayer can be seen in the heart of Lisbon, but by that time Bayer already had almost 30 years of work in the country. A big advert was placed downtown Lisbon.

In 1952, Bayer organizes a marketing campaign, announcing “aspirin” all over the country. The next year, chemicals and dyestuffs are concentrated in the same factory, Quimicor. Three years later, Bayer Farma is formed. The 1960s and the 1970s are years of increasing activity and in 1972 a factory is created near Coimbra, in São Martinho do Bispo.

In 1991 Bayer opens new headquarters in Portugal seemingly decided to be deeper involved in the Portuguese market. In spite of this decision, only ten years later, in 2001, Bayer decides to sell Coimbra’s unit. One year later Bayer begins a worldwide reorganization process.



Source Meyer-Thurow (1982), Wimmer (1998)

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An innovator re-borns

Hitting the ground running

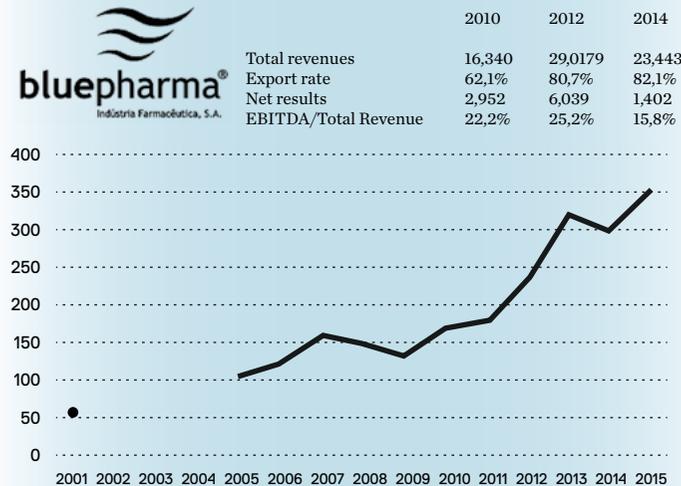
A group of friends joined to take up the greatest challenge of their professional life: Bluepharma (see Box 3, Appendix 1). The hand-over was itself a baptism of fire. There were nine months of negotiations, with about 100 international companies interested in the deal; only one was a Portuguese bid. The Portuguese bidder reached the final stage of selection with two other candidates. And won, just to embark in a tough negotiation process.

Bayer showed a great concern with what the new shareholders wanted to do with the factory. The anxiety was at least partly related with the kind of motives for the buy-out. Real-estate speculation was alive back then and the company feared for the fate of the production unit. It could face demolition and the land for construction. But their project was another. They wanted to invest in knowledge and innovation; to add dynamism to where there was only a centre of

BOX 3

Bluepharma by the numbers

Bluepharma has grown steadily and has kept displaying sound performance figures. (All sources are company sources; euros are in 1000 euros).



industrial production. The new owners-to-be wanted to develop a technological project that could contribute to the region and the country.

This was a risky ambition. At the time, the plant assured 34 different products, primarily for the domestic market with Bayer as monopolist. The agreement was they could rely on legacy buyer for a while. But they had

to gain speed fast for the take-off. It was settled that Bayer would absorb the production for a period of three years. Upon expiration would have to ensure the continuity of production ... by then, Bayer no longer. The new independent company had to be airborne. It also had to set its own course. There was more needed to keep the business going than business as usual.

Getting one's bearings

A number of moves had to be considered, to protect the productive capabilities of the firm and to relaunch it in new directions. The agreement with the incumbent procurer was that it stayed for a while, but the new management was determined chart its own course. The industry was a mature one, but a new phase of globalisation was creeping through. Bluepharma was no start-up, it was a “re-start-up”; its leaders were new to manufacturing, but knew the science and marketing of it. And they were highly motivated. A collective reflection ensued; strategy had to be plotted.

The adopted policy was to maintain all the employees and to do two things: cutting costs and looking for new business and customers during the first year while Bayer was still absorbing all the unit's output. The company could not dismiss anyone as the labour force was already small (58) and their skills were what made the company tick, they personalised the company's know-how. Paulo says: “Starting to cut on personal would have taken us time away from finding

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new business and we would have destroyed the company”. The new management began to negotiate with suppliers to bring down prices of inputs. Some trust was inherited, taking over a Bayer’s plant represented a reputational spillover. On the revenue front Paulo and Sérgio started flying around the world. They began looking for new customers to deleverage the company from past dependences. More than costumer, they were trying to find partners.

Surveying the business models in the field they understood that the market for no-prescription drugs was small and with little value. They also realised that the hospital drugs trade was not remunerative, as buyers were mainly public and bad paymasters. But the generic drugs sector seemed very attractive. Thus, looking at the international environment they knew there were two big segments for pharmaceutical companies: “innovative” companies (Big pharma) and those focused on generic medicines. They went for the second path ... with an eye on the first.

Reading between the trend lines

Generics happen to be no ordinary copies. The market has no ultra-low barriers to entry, especially as far as new generic drugs are concerned. These drugs have to be as safe and as effective as the original version. It is up to the manufacturer to prove this is the case and to demonstrate that the product fits the therapeutically lock. This means that the company vying for such a positioning needs to spend money, time and muster the necessary competencies for the pharmaceutical development and obtain the market authorisation of the new products from the relevant authorities. Meeting the requirements set forth by the regulators, such as the Food and Drug Administration (FDA) is a demanding venture. In other words, developing a new medicine (generic) that is identical (or bioequivalent) to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use it is not an easy task. They call for hard work. For instance, when the first American client appeared and it was

necessary to be inspected by FDA. This federal agency of the United States Department of Health and Human Services is well-known for its high-standards. Bluepharma decided to take on the challenge and prepared the entire process. But, meeting these institutional challenges also becomes a valuable capability on its own as well as a signalling device. Earning certifications for safe standards in highly regulated sectors such as this is a pre-condition for entry in the market.

Displaying a peculiar combination of scientific confidence and entrepreneurial flair Sérgio, both Professor and business co-owner, asserts: “We thought we could innovate in the generic medicines.” Why? “Because this sector was growing at double digits per year. And this happened”, he argues, “because of the public policies on the drug sector.” Indeed, North Europe and the United States were moving towards the path of less budgetary resistance, that is to say, away from branded products. This meant that cheaper generics were not an outlier kind of product and not only for poor countries. They were going mainstream.

Becoming the trend in developed as well as in developing markets, and extending to other markets in between like southern Europe.

Paulo opens his eyes as his lips draw a smile. It was a path worth taking. “Generic drugs make a great contribution to lower the cost of health treatment”. And he adds, as if summarising the outcome of a calculated trajectory: “We are the main Portuguese exporter in this area.” Today the company has more than 60 drugs on the market, exports more than 80% of its production to more than 30 countries, sells products developed internally and has become a basis for creation of other independent companies. Even during the Troika years in Portugal, with austerity imposed by the European Central Bank, the International Monetary Fund and the European Commission during 2011-2013, the company followed counter-cyclical pattern: a turnover of 35 million euros in 2013, corresponding to growth of 20.5% from the previous year. Non stagnation, no decline; rather, growth and upgrading.

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Doing well by delivering well

Demonstrating operational competence, earning trust

Under Bayer the Coimbra unit did not develop any medicine. Plus, no new stimulus would be coming from where no innovative procurement came in the first place. At the beginning Bluepharma was a CMO (Contract Manufacturing Organization). In this business-to-business activity the fit between the contractor and the customer is crucial. The capabilities of the manufacturer have to be matched, quickly and reliably, to users' needs which can be anywhere around the globe.

By the mid-2000s, the year that Bayer left as planned, Bluepharma launched three products. These products were based in a technology transfer process from the costumers; Bluepharma was able to absorb the technologies and carry on with a reliable response. It kicked out "Lamotrigine", an anticonvulsant drug indicated for the treatment of epilepsy. This was done on the same day patent on the molecule expired, and it raced to provide

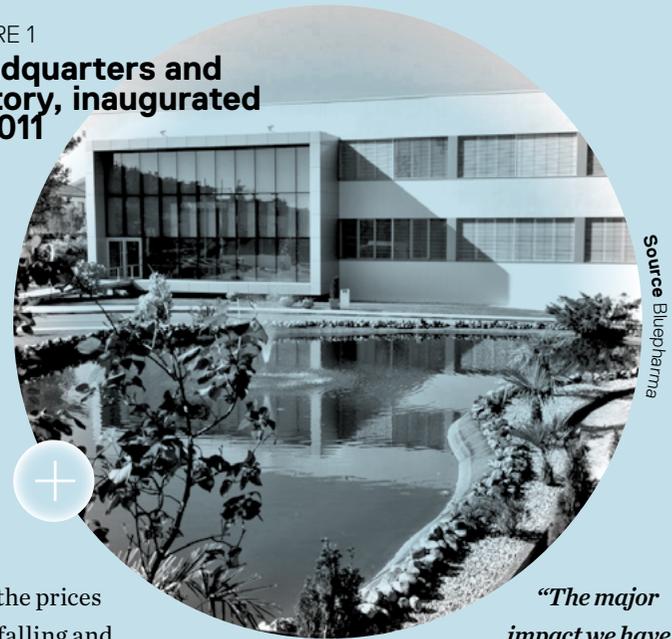
the product to customers from 14 different countries. Then it launched an anti-flu medicine, and in one year produced 60 million tablets for the French market. In September that year it launched "Sertraline", used to treat depression, also dispatched to France. This was a display of operational production expertise as well as practical capability to dispatch quickly.

Bluepharma has been keen to earn as many quality assurances as it can. It has begun a process of quality certification in different areas: ISO 9001:2008 (quality), ISO 14001:2004 (environmental management); OHSAS 18001:2007 (security, hygiene and occupational health); (EC) 761/2001 (eco-management and auditing); NP 4457 (research, development and innovation management).

Fast on their feet

Being ready when the right time came was not automatic. International competition in the generics segment was a problem. The trend was towards ever lowering prices. Bluepharma has to become more efficient faster

FIGURE 1
Headquarters and factory, inaugurated in 2011



than the prices were falling and more flexible faster than the market moved.

But Bluepharma had some assets to complement its technological expertise: "soft skills". A bent to exceed the client's expectations, to go beyond what's the initial plan, to solve problems out of the schedule if needed, to be honest and rigorous with reports, to share the agenda and work in collaboration with the client, to promote forums with them, to invite them to join then in the laboratory. Openness and transparency worked to make clients see Bluepharma as a reliable partner:

"The major impact we have in our clients is the fact we are reliable, they have trust relations with us."

According to the company's records (2013) its generics arm made €6.153 million in EBITDA, a year growth of 24.1%.³ Here the business model is business-to-business, with the exception of the link to the Portuguese pharmacies association. This group of shareholders, representing 400 commercial partners, has 22.2% of the capital of Bluepharma Genéricos. This business strategy is also new and

3 - Annual Report 2013, p. 30.

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unique in Portugal and it creates a stable commercial and financial relation allowing Bluepharma Genéricos to develop a very competitive price discount policy.

From CMO to CDMO

The owner-managers visited potential clients from the start, they felt the urge to know more about the industry itself. They knew if they wanted some kind of stimulus, they felt the need to embrace new challenges. How to do it? They found that only partners could help the company to achieve its goals. They started looking for international companies; they visited pharmaceutical fairs but also looked for agents that could assist in finding potential buyers. The agents started to tell them that the buzzword was Research and Development (R&D) and not Contract Manufacturing Organization (CMO). Usually clients do not change the production place of an old product if there is no problem, rigidity and inertia prevail.

Establishing and maintaining operational competence can be daunting enough. Bluepharma,

notwithstanding, was aiming higher. In order to breakthrough it had to invest in genuine novelty. Outsourcing was low-margin trade, and incumbents hard to displace. If it was to prevail in the generic products market Bluepharma had to differentiate itself. This meant looking for contracts beyond simple production: some degree of product development had to be added.

The solution was to reach a notch above in the value chain: from a CMO to become a CDMO (Contract Development Manufacturing Organization). In this scenario client companies own the medicinal product and try to register it in their target country; when they get this marketing authorisation they get back to order its production (typically from a source that already demonstrated the know-how for the manufacture of that product). If a deal with such a customer is stricken the result is a potential relationship, not just an arms-length/one-off transaction. Such a client can stay approximately 10 years with the supplier by including the research project plus licence for the product plus exclusivity of production

for more five years. At this stage a customer's is no-longer just a customer, it becomes a partner.

Networking to upgrade, upgrading to network

The next step was, thus, to offer not only the ability to produce (i.e. to be CMO) but also the capacity to carry out own development in the generic drug area (to evolve into a CDMO). Not just a one-directional actor in an unbalanced sub-contracting affair, but a co-contracting longer term cooperation.

By offering to their clients these two options customers could do more business with the same supplier and Bluepharma would increase their business portfolio (CMO+R&D). The CDMO's customer registers the new product resulting from the partnership in his target-market, but Bluepharma can also register in home-market or in other markets not in competition with the partner.

From game player to card dealer

So, Bluepharma began developing generic medicines in partnership with others but keeping the ownership of the technology.

In other words, it entered the field of technical services. And it did it without hollowing-out (becoming a virtual company such supplying services) or dumbing-down (keeping in the manufacturing trade only).

Bluepharma showed it was well equipped for this next step, innovation and knowledge-based partnerships. Drug development in the context partnerships means pooling capabilities, share costs and risks and, in the end, also sharing results. Today, as expressed in the annual reports,

“Since its foundation, in February of 2001, Bluepharma has been synonymous of dynamism, competence and innovation, maintaining these pillars in its strategic course. Our values are excellence, ethics and responsibility, making of Bluepharma a leading international company, in which the customer confidence is its most valuable asset.

Throughout its history, the company implemented a business model that resulted in its transformation from a conventional drug manufacturer into a pharmaceutical company that develops and licences technology, promotes innovation, produces and

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registers drugs in the international scene. This is the way Bluepharma is doing, looking for further differentiation throughout the value chain of the medical drug products.”⁴

Bluepharma was a “turn-around”, with an Anglo-Saxon name and eyes set on the global stage. In a first stage Bluepharma was just a producer in an outsourcing-type contract. Then it became a contractor for sophisticated technical services. Now, in a third stage, they are technology owners, they have the rights over innovative technologies and can manage them. The plan was to evolve from selling industrial production and to selling knowledge, that is, build customer loyalty around the efficiency of the plant and then use those linkages to license new technologies.

“Bluepharma offers an integrated approach on the process of drug discovery and development, including innovative research on new chemical and therapeutic entities (based on novel drug delivery platforms) as well as formulation development,

clinical research, manufacturing and commercialization of medicines.”⁵

No firm is an island, an innovative one even less so

The business of socialising *(learning to connect)*

“Yes they could”. The following might have been said by a “community organiser”. Not referring to “civil society” but rather to the economic scene.

“This is also my experience. I believe the economy rules the world, and economy belongs to multinational companies. But I always believed there was an alternative. And that alternative was the association of the little ones with cleverness to organize them and to network. If we achieve that we are unbeatable. When we are associated we can go faster.

But this kind of initiative gave us the possibility to absorb every information and methods that

others were using.”

Paulo Barradas Rebelo shows himself a true believer in distributed approaches to secure market positions and carry out learning as time goes by. The benefits of partnerships are not only found in pooling resources and exchanging ideas. It allows the organisation to access the others’ networks. Indeed, less money is to be earned because it has to be shared; but the organisation always has a part of it. The more partnerships, the more revenue.

And diversification is developing also in terms of partners. Bluepharma is looking for new partners for new purposes. For reinforcing its ability as international and an innovative enterprise.⁶ For instance, the company is engaged in the development of new generic medicines in partnership with European companies. The company is looking for new business areas to increase her competitiveness and trying to generate different offerings for their clients, having a more

diverse product and service portfolio. In the US Bluepharma is now creating a multilateral partnership, with companies from Greece, France, Germany and the US, where each one is a development company in different areas. All firms operate in the business-to-business model and now they are trying to create this partnership to have direct access to the final users.

In Latin America Bluepharma is also starting to have promising business. The most important partners are in Brazil and Colombia. The investments shall involve building new factories and also having a R&D operation there. Bluepharma is investing in human resources there but wants to invest together with locals and create results for all. The company is also establishing offices with their representatives in Mozambique and Angola. China will be important but still in preparation.

Teaming up for new agendas *(connect to learn)*

As Paulo neatly summarises it “In the past a trade secret was at the core of the pharmaceutical

4 · Annual Report 2013, p. 2.

5 · <http://bit.ly/1JB66yr>

6 · Annual Report 2014, p. 28.

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business; now sharing is the core of the business.” He means innovation as a collaborative affair. “Sharing in R&D is very important and in the international area we have partnerships with very different shapes. Partnership and sharing constitute our genetic code.”

From the start Paulo has been a multi-organisation man. He started out serving in a cooperative alongside his own business and still today carries out various duties in the associative sector such as president of the fiscal committee in the national pharmaceutical professional body (ANF). In 2010 he was a force behind the setting up of A2B, SGPS, S.A., a Business Angel focused in high-tech projects. He is also a jury in the João Cordeiro prize for innovation in pharmacy, award by ANF.

Connections can be also explicitly aimed at learning and capability acquisition. From the start Bluepharma integrated a number of business associations. For instance, it is part of the Coimbra Health Cluster, with the Coimbra Hospital Centre it aims to internationalise some

health services of this city. In 2011 Bluepharma joined, as an investor, Biocant Ventures (a framework partnership for promoting young entrepreneurs biotechnology industry dating from 2006 between Biocant Park, a biotech incubator park located in centre region of Portugal and Beta Capital, a private venture capital company). It was accompanied by Portugal Capital Ventures, the Portuguese government-owned venture capital company. Bluepharma joined COTEC Portugal (Portuguese Business Association for Innovation), in 2008, the Portuguese pro-innovation business association.

The academic environment was also important, because academic researchers started to understand that being in research with a company could be something very interesting and as scientific as working for the academy alone. It was also needed for the academic researcher to stay in the deadlines, manage quality and to understand the company research interest as something with its own value.

Another interesting area is connected with a subsidiary that trades generic medicines. This

a partnership with the retailing sector – pharmacies. Pharmacies are associated of the project and benefit the profits the company has. They are around 300 to 400 and they just have to buy an estipulate quantity per year (it doesn't mean exclusivity). It's called Blue Wave.

The public partner

That very special sponsor

The buy-out of the Bayer unit was a visionary, risky, entrepreneurial move. This would not have happened without an unusual suspect. Bluepharma was founded with the state as a shareholder. The Portuguese state took 30% of risk capital in the society, invested through the SME capital mechanism. The company developed a close relation with state representatives, especially with the managers for risk who came for meetings and interacted. This “partner”/“coach” left in 2006 being paid in full.

Three years later Bluepharma needed more capital to invest to enlarge the company. After

consulting the private risk capitals, again the enterprise was supported by public capital, now called INOV Capital. “As the public actor always earned money with us, it's easy to attract them to our projects”, says Paulo.

Now they still have a relation with the state in the start-ups branch of activity of Bluepharma. Public risk investment, through Portugal Ventures, has a stake in Luzitin and Treat U. The benefit of being with public capital was that it was less aggressive, as Paulo Rebelo stated. As for reports they were quite demanding, which pushed the company to improve persistently.

Embedded in a web of state-shaped initiatives

The pharmaceutical sector is well-known for its hyper-regulated environment. Regulators, however, can also be mediators. For Bluepharma, Infarmed (the National Authority of Medicines and Health Products) is its first formal stakeholder: the Portuguese drug agency, which issues guidelines to help them to keep all these areas under control. But, as this is a knowledge-intensive, business, they are



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stakeholders in the innovation arena in their own right. As a regulatory authority, Infarmed can provide the company with pre-competitive information, they may assist companies in fine-tuning problem-solving while being rigorous and impartial at the same time. This institutional hand was valuable. Regulators are not just hurdle managers. In the past two decades there was an important support to R&D by the Portuguese public sector. Government invested massively in research grants and PhD-training policies. Bluepharma acknowledges this. They say that if they compare things in Portugal with other countries the public sector overall is not less competitive than elsewhere.

Investment finance keeps on being helped by the state. Bluepharma has been smart in taking advantage of the means available. For instance, two QREN projects (the national program steering EU funding) have been approved recently: QREN SI Innovation (412 521€) for Blueclinical and QREN IDT Individual (373 072€). In 2012, Luzitin submitted an application to the System of Incentives to Qualification and

Internationalization of SME in the area of industrial property. Project number 30218 was also submitted for application to the System of Incentives QREN, and it was approved, receiving a global public support of €1 365 616.31. Luzitin: project number 5356, financed by QREN and implanted by Luzitin co-working with Bluepharma, had a total investment of €2 312 607.58 (1 387 957.18 are Luzitin's responsibility).⁷

The relationship is intense and goes both ways. For instance, in October 2014 Bluepharma installed an electronic game in the Exploratório Ciência Viva (Life Science Exploratory), named "Jogo da Vida" (life game) on eating behaviours. And Bluepharma is also editing the first number of the collection *Portuguese Pharmacopeia*, in a partnership with the General Library of the University of Coimbra. These are educative activities, public goods.

The link with publically-owned institutions goes further. BSIM² – Biomolecular Simulations: this enterprise is a spin-off resulting

of the scientific activity conducted in the University of Coimbra by two researchers.⁸ In 2013, BSIM² continued the development of products started in 2011, with a QREN application, with a reimbursement rate of 69.1%.

The company has also participated in many official missions to foreign markets. For instance, it went on board in an official state mission to United Arab Emirates (Ministry of Foreign Affairs) and Mission to Saudi Arabia (AICEP).⁹

Standing on the shoulders of human-capital public policy

A big support has been the country's human capital infrastructure. Bluepharma also recruits people through IEFPP (the Portuguese Institute for Employment and Vocational Training). In 2012 they received 108 new workers, including internships, a substantial part arriving through this system. In 2013 new employment contracts were in 60% of the cases for the area of R&D, 19 new professional

internships were through IEFPP.¹⁰ In 2013, there were 8 curricular trainees from universities, 31 professional trainees from IEFPP.

In 2013 there were several PhD projects undergoing at the company. There were also new master projects in a partnership with the Chemical Engineering Department of Coimbra.¹¹ A new PhD project in business model research was started in a partnership with ISCTE - University Institute of Lisbon, an opportunity intermediated by COTEC Portugal.

Innovating yourself out of the maze

Breaking the mould, smashing prejudices

Some years ago, people in general and policy-makers in particular would think it would be impossible to have pharmaceutical industry in Portugal, but experience proved the sceptical were not right.

8 · Annual Report 2013, pp. 31-33.

9 · Annual Report 2014, p. 7.

10 · Annual Report 2013, p. 26; 2014, p. 30.

11 · Annual Report 2014, p. 30.

Bluepharma



So, a great splash is possible in a tough, globalised, high-tech industry. But this was not obvious at all in the beginning. Investment and know-how were the major aspects that made people suspicious about a possible success in this area. But with creative approaches it was possible. As Paulo says:

“People thought I was lyrical believing it was possible to have industry in this area in Portugal, with production and research. Production was seen as a finished sector in Europe and research was seen as impossible in a country with small capacity to invest.”

“The situation today says the contrary: the need for the reindustrialization of Europe is on the table and the small companies are the ones becoming more innovative... so time gave us reason.”

There was purposeful intent from the side of a new generation of willing entrepreneurs. Supporting institutions were there to provide an actionable background. And actual industrial practice also evolved.

Building on national expertise, organically

In 1996 Luís Almeida knew this by heart. He is a recent entry into the enlarging Bluepharma set of concerns but he has been in the industry for a real long time. He did many projects on medicine in Bial where he started to work that year, but most of them never arrived to market. But there was one which succeeded and it was the first Portuguese medicine. He was a researcher at Bial and he was the leader of the project leading to Zebinix (Box 4).

Bial showed it was possible. Bial, founded in 1924 as a small pharmaceutical laboratory, and an early pioneer in branded products, has been the largest Portuguese pharmaceutical company for a long time. The company musters the largest national R&D figures in this sector and is regarded as a key innovative company for the country as a whole (Carvalho, 2007).¹² In 2008, Bial completed the clinical trials of BIA 2-093 (Eslicarbazepine acetate), a

¹² - Surely it also owes a lot to public incentives. It was the second largest receiver of industrial aid for innovation and internationalization between 2007 and 2013 (Expresso, Economia, 14 March 2015).

BOX 4

Vehicles for tacit knowledge build-up

Luís Almeida is today one of the senior experts working in Bluepharma Group. He graduated in 1985 and started working in the pharmaceutical industry as part-time job. In the year Bial creates its R&D department, Almeida joined the research team. It was the first time a Portuguese pharmaceutical company was launching itself in this kind of activity. Almeida was involved in several R&D projects, but he was also one of the responsible for the first Portuguese drug in the market (integrating all the drug process). In 2009, he also founded the Pharmaceutical medicine course at University of Aveiro, three years later awarded as a centre of excellence by Pharmatrain. Some months after the creation of Luzitin, Almeida enters the firm believing in its ability to develop high quality R&D. By 2014 the first Luzitin drug was on clinical trials, being administrated to patients. What seduced Almeida to join Luzitin? He was persuaded by the challenge of a new high quality R&D project in the pharmaceutical area in his country. But maybe the most important question is: what did see Bluepharma Group in Luís Almeida? Certainly they found someone with the same ideals and way of working. Both believe in R&D work in Portugal and are enthusiastic about science developments in the country and the feedback universities are giving in the formation of high skilled researchers.

Source <http://bit.ly/1i0tt3A> , <http://bit.ly/1i7lg4h>

drug used for the treatment of adult epilepsy. Heralded as “the first 100% Portuguese drug”, Zebinix was introduced in the US market in April 2014.¹³ The drug representing 15 years of research and more than 300 million euros

¹³ - <http://bit.ly/1EIQGe> , <http://goo.gl/kCrogV>

of investment is now marketed in more than 50 countries, including Spain, UK, Germany, and France.

He always maintained his own outside projects and was in the University of Aveiro, and he bolsters a unique experience and track-record in the country.

Bluepharma



At a point he was invited to join Luzitin, a result from a spin-off of Coimbra University in collaboration with Bluepharma (see Box 3). In this moment, they already have a project which is in the phase II of clinical trial and already has an International Nonproprietary Names (Each INN is a unique generic name which is globally recognized and is non-proprietary, i.e. public property)¹⁴. It is the first oncological investigational new drug resulting from Portuguese research. It consists of a combination of a new generation photosensitizer with a specific infrared-laser medical device and constitutes a radical innovation. It is a novel approach since the new chemical entity is only activated in the area where the patient has the tumour. Advanced head and neck cancer is the focus of this first clinical trial. The aim is to go through clinical trials, the most expensive of the steps in the drug value chain.

Gearing up for innovation at the global level

Intensively incremental

Throughout its history, the company implemented a strategic path that resulted in its transformation from a conventional drug manufacturer into an innovative pharmaceutical company in its own right. A newcomer that develops and licences technology, produces and registers its own products in the international market (patents, trademarks), a company that dynamically reshuffles more than its product portfolio but also its own innovative of relationships. This is the way Bluepharma is doing, looking for further differentiation through value creation in the drug value chain.¹⁵

Incremental innovation is the backbone of it all as they themselves see it. The company brings to the market a medicine which is bioequivalent to an existing substance. Ultimately, the client of this product is under pressure of the pay-master, mainly the Governments who

design and implement the public health policies. The drive for lower costs in the health sector lowers prospects for the business as whole and has been a regularity (Figure 2). From the point of view of the manufacturer efficiency is an avenue, as well as business diversification. Under this nexus of constraints Bluepharma is pushed for operational productivity but also strategic renewal. How to accomplish this and sustain this drive?

Paulo says, “At Bluepharma we can count our values with one hand: invest to research, innovate

to internationalise.” So, dynamics is the rule.

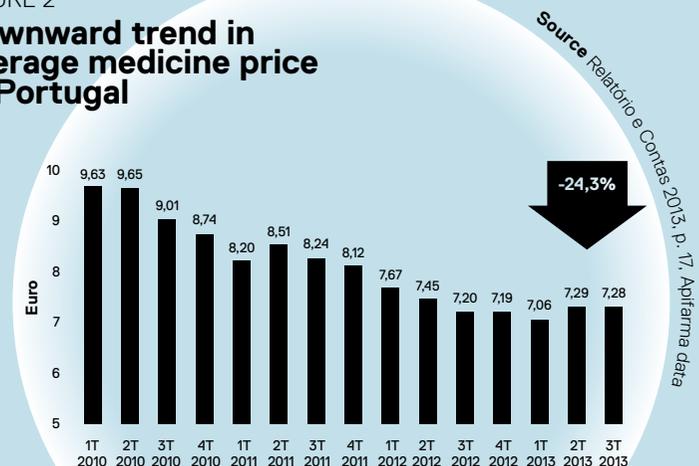
It's Development then Research ... not Research before Development

Paulo Simões refers that the company was innovating from the start.

“We’re doing this without knowing exactly what it was. Only with COTEC Portugal innovation tool we realized what it really meant... but we had no innovation methodology in a protocol, it was something very natural for us to do.”

FIGURE 2

Downward trend in average medicine price in Portugal



14 · For this institution see the World Health Organization, <http://bit.ly/1Kx5Qmy>.

15 · <http://bit.ly/1F2s0oS>

Case Study

Bluepharma



Having to think in terms of alternatives from the outset (new product streams, new customers) the choice was to bring new value to the market and create a research capability. Bluepharma would systematise its innovation approach. In 2003 it founded its first R&D lab, in 2005 it joined COTEC Portugal (Portuguese Business Association for Innovation).

Bluepharma looked for very specialized workers and employed people from the university and began the experience of hosting PhD students in the company. They had the public support via scholarships for these students/researchers and, in this way, they started to develop completely new technologies. The first PhD project was around 2006, but as a strategic perspective this option was established in 2010. Company also reinforced continuous training.

As a university professor Sérgio was used to contact with university world and outside research. This was an easy and convenient interface. “I knew people”, he says, “and was sensitive to their discourse and kind of language.” Today, 59% of the 277

workers have a university degree, 26% have a master and 1% a PhD.¹⁶ The median age is 34. “Today, we have 10 people with PhD and they changed the internal behaviour of the company.”

Even with this model they consider their research area is still incremental, “as the disruptive one is mainly in the university setting” says Paulo. Bluepharma wants to know what is being studied and nurtures mechanisms to keep up with what is new, but they choose not to go further than that.

Nevertheless after having in-company PhD programs they started to have new ideas in a very small part of disruptive research. As a result they created room for more in-depth research; but this was outside the holding company through start-ups, vehicles for projects resulting from their talented associated researchers. In this respect, Bluepharma is shareholder of some start-ups (Luzitin, Treat-U, Biocant Ventures, Blueclinical, Technophage, BSIM2, Blueanalytics) but have other investors and shareholders.

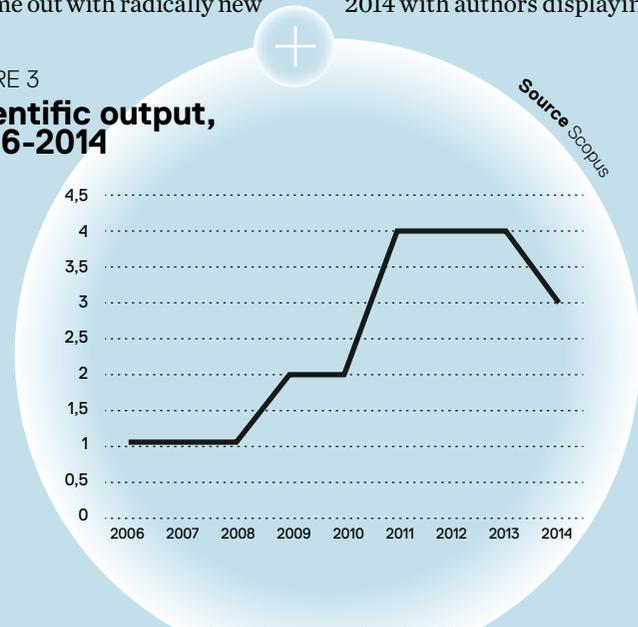
That is to say, Bluepharma had to be good in routine operations (process efficiency). It meant finding schemes to improve productivity in the labour organisation, input acquisition, output dispatch processes (because altering the production process itself meant that all regulatory approvals had to be renewed). Then, in parallel, it thought about adding unfamiliar products to its pipeline (product innovation). To existing products the company developed novel technical solutions around them. Although the managers see shy to admit, the company is now seeking to come out with radically new

products. Hence the deepening of the research dimension as well as the upgrading of the applied component of R&D in recent years. To do that Bluepharma reinforced its partnership mode of conduct. Indeed, new research and new forms of organising (a network governance structure) seem to come hand-in-hand.

Bluepharma's innovation muscle

The company's scientific pedigree can, perhaps, be assessed through its international, peer-reviewed publications (Figure 3). There are 22 papers on record until 2014 with authors displaying

FIGURE 3
Scientific output, 2006-2014



Note: papers are accounted for when at least one authors lists Bluepharma, or its associated ventures like Luzitin, as his or her affiliation.

16 · Annual Report 2014, p. 31.

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Bluepharma as an affiliation. The first article came out five years after the company was founded. After this inauguration there are no years without papers being published. There is a total of 121 authorships, meaning an average of 5.5 authors per paper when a Bluepharma researcher is involved. That track-record places Bluepharma as following the practice of substantially collective authorship; perhaps a little higher than average.¹⁷ Bluepharma mainly publishes with academia as indicated by the structure of author's affiliation in 2006-2014: 39% Bluepharma, 55% university, 6% public laboratories. There are no other company's besides itself in the network of authors. Coimbra University dominates the university affiliations, but researchers from Polish and Spanish institutions also figure (less so Hungary and UK). What is more, from 2010 international co-authorships are continuous. This may be significant. This may indicate that Bluepharma's research agenda is becoming more significant and globalized, i.e. greater in complexity and international scope.

The patenting record also show that after the late-2000's the company was well in its innovative gear (Table 1). Its four patents were submitted in Portugal, Europe, the US and at the international level. The University of Coimbra and a

Hamburg based multi-product trader stand as co-applicants. Inventors range between three and six, almost all Portuguese. Both Bluepharma people and its start-ups are involved. The US is always a special case in the industry ("the market!", says

Paulo), in this case a substantial part of the patenting process carried out in the US, in Boston, where are the firms with more expertise in this area are located.

Surely, Bluepharma is brand-aware. But Bluepharma so far has

TABLE 1
Patent output to 2014

1. ORAL DISPERSIBLE FILMS

Inventor:	Applicant:	CPC:	IPC:	Publication info:	Priority date:
BORGES ANA FILIPA SILVA [PT] SILVA BRANCA MARGARIDA ALMEIDA [PT] (+3)	BLUEPHARMA [PT]	A61K47/14 A61K47/32 A61K47/38 (+3)	A61K47/14 A61K47/32 A61K47/38 (+1)	US2015038594 (A1) 2015-02-05	2013-07-31

2. PROCESS FOR PREPARING CHLORINS AND THEIR PHARMACEUTICAL USES

Inventor:	Applicant:	CPC:	IPC:	Publication info:	Priority date:
PEREIRA MARIA MIGUENS [PT] MOREIRA LUÍS GUILHERME DA SILVA ARNAUT [PT] (+4)	UNIV DE COIMBRA [PT] BLUEPHARMA IND FARMACUTICA S A [PT]	C07D487/22	A61K31/409 A61P35/00 C07D487/22	PT2346874 (E) 2014-03-06	2008-10-24

3. STABLE AND READILY DISSOLVED COMPOSITIONS OF CANDESARTAN CILEXETIL PREPARED WITH WET GRANULATION

Inventor:	Applicant:	CPC:	IPC:	Publication info:	Priority date:
GINDULLIS FRANK DR [DE] SIMOES SERGIO [PT] (+1)	HELM AG [DE] BLUEPHARMA IND FARMACEUTICA S A [PT]	A61K9/1617 A61K9/1623 A61K9/1652 (+4)	A61K31/00 A61K9/00	SI2165702 (T1) 2012-05-31	2008-09-17

4. ENTEROCOCCAL PHAGE PEPTIDES AND METHODS OF USE THEREOF

Inventor:	Applicant:	CPC:	IPC:	Publication info:	Priority date:
DA COSTA GARCIA MIGUEL ANGELO [PT] VILELA PIMENTEL MADALENA MARIA [PT] (+1)	TECHNOPHAGE INVESTIGACAO E DESENVOLVIMENTO EM BIOTECNOLOGIA SA [PT] BLUEPHARMA IND FARMACEUTICA S A [PT] (+3)	A61K38/00 C12N2795/10111 C12N2795/10122 (+2)	A61K38/16	WO2011065854 (A1) 2011-06-03	2009-11-24

Source Espacenet

17 · <http://1.usa.gov/1PWMnKJ>.
See also: <http://bit.ly/1NLwS9a>.

Case Study

Bluepharma



moved to protect with a registered trademark only its corporate identity and a product trademark (BlueOS). It has filled its name with five filings (two in Portugal and Europe and one in the US and Germany) (see Table 2). Following the Nice Classification system, established for classifying goods and services for the purpose of registering trademarks, is Class 5, a “goods” class, and this trademark category covers:

“Pharmaceutical and veterinary preparations; sanitary preparations for medical purposes; dietetic food and substances adapted for medical or veterinary use, food for babies; dietary supplements for humans and animals; plasters, materials for dressings; material for stopping teeth, dental wax; disinfectants; preparations for destroying vermin; fungicides, herbicides.” (see Appendix 5)

It is also telling when data regarding Bluepharma’s start-up trademarks are considered (Table 3). They appear from 2005 onwards, indicating how Bluepharma has been developing as a broader entity. It is also significant that new Nice Classes appear, this time pointing

TABLE 2
Trademark output to 2014

Graphic representation	Trade Mark Name	Office	Application number	Trade Mark Status	Nice Classe	Applicant Name	Application Date	Trade Mark Type
	bluepharma	PT	000003631	Registered	5	Blupharma – Indústria Farmacêutica	24-05-2001	Combined
	BLUEPHARMA	PT	000367417	Registered	5	Blupharma – Indústria Farmacêutica	18-10-2002	Combined
	BLUEPHARMA	EM	003387644 003387644	Registered	5	Blupharma – Indústria Farmacêutica	08-10-2003	Figurative
	BLUEPHARMA	US	77862938 3918586	Registered	5	Blupharma – Indústria Farmacêutica	02-11-2009	Combined
	bluepharma	DE	3020120014828 302012001482	Registered	5	Blupharma – Indústria Farmacêutica	13-01-2012	Combined
—	BLUEPHARMA VET	EM	012299038 012299038	Registered	5	Blupharma – Indústria Farmacêutica	11-11-2013	Word

Source: TM View

TABLE 3
Start-up trademarks output to 2014

Graphic representation	Trade Mark Name	Office	Application number	Trade Mark Status	Nice Classe	Applicant Name	Application Date	Trade Mark Type
—	TECHNOPHAGE	PT	389800	Registered	42	Technophage – Investigação e...	14-04-2005	Word
LUZITIN	Luzitin	US	85807020 4450198	Registered	5, 42	Luzitin, S.A.	21-09-2012	Word
—	Luzitin	EM	011207917 011207917	Registered	5, 42	Luzitin, S.A.	21-09-2012	Word
—	Treat U	PT	20170	Registered		Treat U, Lda.	12/02/10	Word
—	PEGASEMP	—	490845	Registered	5	Treat U, Lda.	04/11/11	Word
TREAT U	Treat U	US	85375300	Ended	35	Treat U, LLC	19-07-2011	Word
BLUECLINICAL	Blueclinical	US	85807045 4591087	Registered	5, 42	Blueclinical – Investigação e Desenvolvimento	21-09-2012	Word
—	Blueclinical	EM	011207974 011207974	Registered	5, 42, 44	Blueclinical – Investigação e Desenvolvimento	21-09-2012	Word

Source: TM View



to “services” categories, due to the star-up’s activities and representing its diversification process:

Class 35 “Advertising; business management; business administration; office functions”;

Class 42 “Scientific and technological services and research and design relating

thereto; industrial analysis and research services; design and development of computer hardware and software”;

Class 44 “Medical services; veterinary services; hygienic and beauty care for human beings or animals; agriculture, horticulture and forestry services.”

Bluepharma’s work quality and product performance has also earned it a number of awards, which has boosted its reputation (Box 4).

Innovation as identity

High-stakes commitment to innovation

Innovation practice may have been ahead of comprehensive planning. Share and quality assurance are the instrumental value. And the money of the company is where their mouth is.

Business and Product Development department activities, trusted with bringing competitiveness and differentiation through its innovative products, are budgeted at 1 972 135€. Total R&D in 2012 reached €5 057 893, roughly about 10% of its annual turnover. This made it the 33rd company in national terms; the 6th company/group in the chemical, pharmaceutical and food processing industries; the 6th SME in terms R&D spending.¹⁸

An increasingly professional approach to innovation

(top-down control)

There is a “System of Integrated Management” based on quality, innovation, continuous improvement and client satisfaction. Sharing knowledge and information, development of improvement actions and monitoring the relevant indicators is continually promoted, according to corporate records.

As Head of Research Cláudia Silva epitomise Bluepharma rational, documented, systematic approach to new-product oriented R&D. “We have two different phases to analyse the risk.” She explains: “The first is when we are evaluating new project ideas and we have a form which is completed since our certification in research, development and innovation.” Risk analysis is progressive and is present in every project phase. As Cláudia states the more innovative projects are, more risk is involved and more need for a systematic R&D practice. She explained the documenting process: **“When we are analysing an idea to develop a new product, the risk is analysed in terms**

BOX 4

Awards and distinctions

- 2003:** Almofariz award as year project.
- 2004:** European Prize for Regional Innovation as a project of the year.
- 2010:** International Quality Trophy in Geneva (prize awarded by the chambers of commerce and embassies).
- 2012:** COTEC-BPI SME innovation award.
- 2012:** SME Excellence prize, awarded by IAPMEI (the Portuguese SME state support agency).
- 2012:** INSEAD Entrepreneurship Award 2011/2012, awarded by the European Institute for Business Administration.
- 2013:** Outstanding Venture of the Year, by Portugal Ventures.
- 2013:** SME Excellence award in 2013, for the third consecutive year.
- 2013:** Bluepharma CEO receives the prize “Entrepreneur of the Year” in the XIII International Conference of Risk Capital and Entrepreneurship.
- 2014:** Best Portuguese exporter, European Business Awards 2014/2015.
- 2014:** Treat U, the start-up, is distinguished as the most promising enterprise in the area of Life Sciences in first International Investors Forum, promoted in Go4Venture and Portugal Ventures.

Source internal documents and publically available information.



Bluepharma



of technical and scientific difficulties, if we have the means and necessary competencies, if there is competition (can mean opportunity or risk). The result is to know if the project can be developed, if it has market and if we have the capacity for doing it.

When we start the project we do a more specific and in-depth risk analysis. We try to detect and preview all the risks of each phase and to design solutions for the possible cases of failure. This kind of prevision is getting more accurate as we have more experience from previous projects. The more innovative projects are, more difficult is to determine risk, but we still try to do it in the best way possible.

Every project has a dossier with the compilation of all information and knowledge generated, including a final report of each project. We have a part dedicated to learned lessons and it is disseminated internally. We also are very concerned with deadlines and budget because it can determine how successful we are.

We also have a documentation management system according

with the pharmaceutical industry highest standards. In the form the project is codified, with the identification of the team, date of beginning, date of ending, evaluation of the project and milestones, global evaluation, when there are delays we must know if they are due to internal or external factors.”

Pedestrian, bottom-up creativity *(change is everywhere)*

The pharmaceutical industry is a high-tech industry and has played its parts in pushing life expectation to move above than 81 years. Interestingly enough it remains deeply conservative and with little appetite for risk and innovation. Risks are high, backlash from malfunctioning products may be tremendous.

Bluepharma can be said to have slowly built up an all-round corporate innovation system. It has become a culture. To start with, information circulates internally.

Bluepharma holds the forum for employees called FIQ – Forum for Innovation and Quality, where

someone presents a subject during 30 minutes, fortnightly. Human resources department organizes it and it can be about R&D or about quality. They also introduced another organisational innovation with seminars on transversal themes with interest for different departments. The participation in FIQ is decided by the worker, but the participation in seminars is broader and people are invited to be present. It takes one hour.

In 2011 the managers thought they needed to have more staff with knowledge in the strategy area. So they did an agreement with Porto Business School and did a course with a tutor who visited the company and developed a close relation with the students/workers. By that time they decided to extend the annual management meetings to workers representing the main departments.

Then, through the certification under NP 4457:2007, a Portuguese standard developed under COTEC Portugal aiming to reinforce business innovation competences, Bluepharma got a little further. It gave the possibility of any worker to pitch a business idea and present it during five

minutes in the annual meeting dedicated to discuss the strategy of the company. For this strategy meeting they should present a more formal idea for business. They have to fill a form and to have an internal “sponsor” who helps them do develop the idea. Then they present it doing a pitch. Good ideas have been acknowledged to have been submitted and this organisational device is also useful to screen talent, according to the Administration statements about this initiative.

Bluepharma also has other ways to stimulate creativity. They have an “Ideas Management System” by which any worker can apply with his idea in a digital platform. In 2015 it was about human resources and how to improve conditions for workers in the company. It is announced in the Christmas dinner and in the summer lunch.

Regarding process innovation there was “Rationalization Plan” for energy consumption approved for 2013-2020, including fuel substitution.¹⁹



The company as incubator

Harbouring outside innovation

Luzitin is the prototype of an answer to a new environment in the pharmaceutical area. This is actually a trend. Big pharma themselves become too big and complex with the headquarters and centres of decision far away from the research area. Spaces open for new entrants to develop their own niches.²⁰ So they have high cost for researching as they have to sustain a bureaucratic organization in every department. Getting higher cost, they started to look for new talents and projects outside their companies, buying the results of their research.²¹ Luzitin is inscribed in this kind of logic.

And the big pharma enter when there is already a technology to be tested in clinical essays. With this business model the risks are

20 · <http://pwc.to/1loXA0i>

21 · See Ismael Rafols, Michael M. Hopkins, Jarno Hoekman, Josh Siepel, Alice O'Hare, Antonio Perianes-Rodríguez, Paul Nightingale (2014), "Big Pharma, little science?: A bibliometric perspective on Big Pharma's R&D decline", Technological Forecasting and Social Change, Vol. 81, pp. 22-38.

small for the big company, and all the shareholders accept to invest in a final phase of research. Their problem is not the volume of investment but the question if it will generate revenues or fail. Even big pharma are creating spin-offs as Lilly created Chorus. Outsourcing R&D and production became more attractive and safe for those big pharma who operate in the global market.²²

The challenge today is to do research small groups, target with some specifications, so small companies with more adaptive skills are better doing this. Now the trend is that research should be patient-oriented.²³ As a result of this trend operators are having more feedback from the patients and focus on them instead of the usual and previous concentration on the doctor's opinion. The actual trend for medicine is the personalized medicine, adapted to each patient and pathology. This now is possible because there are biomarkers and technologies that can be applied to each patient. Even Luzitin's slogan is oriented for this new approach in the

22 · <http://pwc.to/1KSdHW4>

23 · <http://pwc.to/1APVvwx>

relation medicine/patient. That is why "Your wellness matters".

BlueClinical is a CRO (Clinic Research Organization). Bluepharma knew there was an expert in this area, Luís Almeida, who got out of Bial open to new collaborations and that this kind of enterprise was needed in Portugal. This company can work for Bluepharma and for other clients. BlueClinical R&D activities are involved in evaluation of projects resulting of spin-offs of Universities (University do Minho, Oporto, Beira Interior, Coimbra and Lisbon).²⁴ It also participated in two Horizon 2020 projects, forming part of an international consortium. With an Israeli company as client, started a clinical study in four public Portuguese hospitals. BlueClinical changed the name of its business unit from SMO (Site Management Organization) to CRP (Clinical Research Partnership), in order to better convey the type of cooperation established with the different unities forming part of the health national system.

24 · Annual Report 2013, pp. 31-32.

A firms of firms?

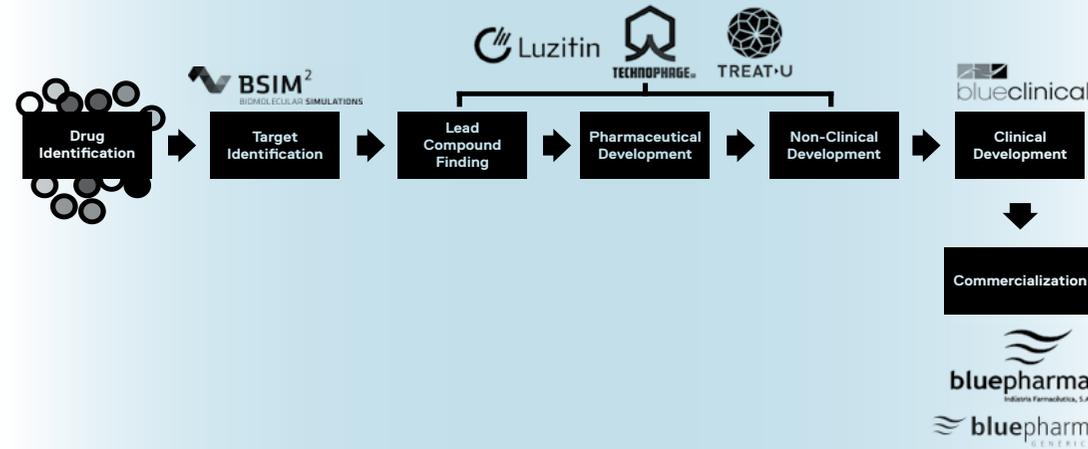
What new directions in innovation governance?

In this moment Bluepharma is connected to Luzitin, Treat U, BSIM2, Blueanalytics and BlueClinical. In Bluepharma group, Bluepharma Industry the CDMO (Contract Development and Manufacturing Organization) is still the most important operation in terms of revenue, but it is reinforced by the new product development area. There is a complementary dynamics to this approach.

"The model is simple and intuitive: Bluepharma 'lends' the new company its valences in the quality management area, regulatory affairs, pharmaceutical development, human resource management, accounting and finance and management experience and international network, while promoters 'scientists' contribute with talent, scientific expertise and international network of scientific contacts. This is a complex and costly process, with a strong risk component and with some particular challenges. These challenges include the need to align R&D procedures



FIGURE 4
The drug value chain and Bluepharma's group strategy



Source: "Apresentação Bluepharma", 14-05-2015, p. 23.

between teams of companies and university research centres, and alignment strategy, the specific objectives of the projects, and the management of time and resources. Difficult but fundamental is the establishment of effective communication between teams, which facilitates the management of generated knowledge and different expectations, particularly in terms of the protection of intellectual property generated and disclosure.

*Bluepharma is in some ways a pioneer in this type of cooperation. We think that the results the next 5 years with these two companies (Luzitin and Treat-U) will determine the future of this type of partnership in Portugal.*²⁵

Will the next step be the incorporation of the start-ups in Bluepharma? Solving the problem would certainly be of interest to the broader community of

global-oriented mid-sized up-and-coming firms.

In this moment within the Bluepharma universe there is already production, development, research and a company for clinical studies. They are completing the value chain. They can offer their clients different phases of medicine R&D and production, but do not have the active substances. So, they would like to have some in-sourced core raw materials for production, i.e. generating themselves some

of these basic inputs such as the active substances. If it cheaper to buy the raw materials it is out of question to own them, but if it is not, it's very attractive they say. In big pharma full vertical integration ran out of favour.²⁶ However, Bluepharma is pushing to be present in all phases of drug development.

As the company grows they become interested in what how others did it, so they look for references that might inspire them in the future. When they gaze around they do research on technology roadmapping tools, bibliometric trends, and case studies. They find other insurgent companies as the best examples, for instance Teva from Israel, an innovative generics company basing strategy on knowledge and patenting and which is now itself a company emulated by catching-up firms which emulate its approaches and challenge it with a taste of its on medicine. A shape of this to come?

25 · <http://bit.ly/1i5T5CG>

26 · <http://pwc.to/1KSdHW4>,
<http://bit.ly/1Uhec2B>

Bluepharma



From the pharmacy shop to science-based pharmaceuticals

“In professional terms,” says Paulo, “I did the entire drug circle: from the standing pharmacy shop to wholesale distribution to industry to research and venturing.” And provides reminder of the industry level pattern: “All multinational drug producers started out in the same way.” Indeed, this was the way itself Friedrich Bayer started in the 19th century. The paths taken in the 21st century can be very different.

Bluepharma’s path has been a little treaded one. But what ways forward now? As the pharmaceutical industry is turned on its head the lessons Bluepharma learns are of relevance for the overall sector.

Globalisation is hitting a new phase of turbulence. Markets exhibit permanent mix signals, sharp falls are followed by rapid recoveries and vice-versa. Demography in the west and east point to ageing but the business landscape in

pharma is characterised by complex regulatory pressures by government willingness to cut costs in healthcare. What strategies should Bluepharma pursue? What markets can it target successfully?

Bluepharma has mastered the art of diversification and differentiation. But there are trade-offs. Should it keep increasing the number of products it is able to generate? What parts of its product portfolio should it sacrifice?

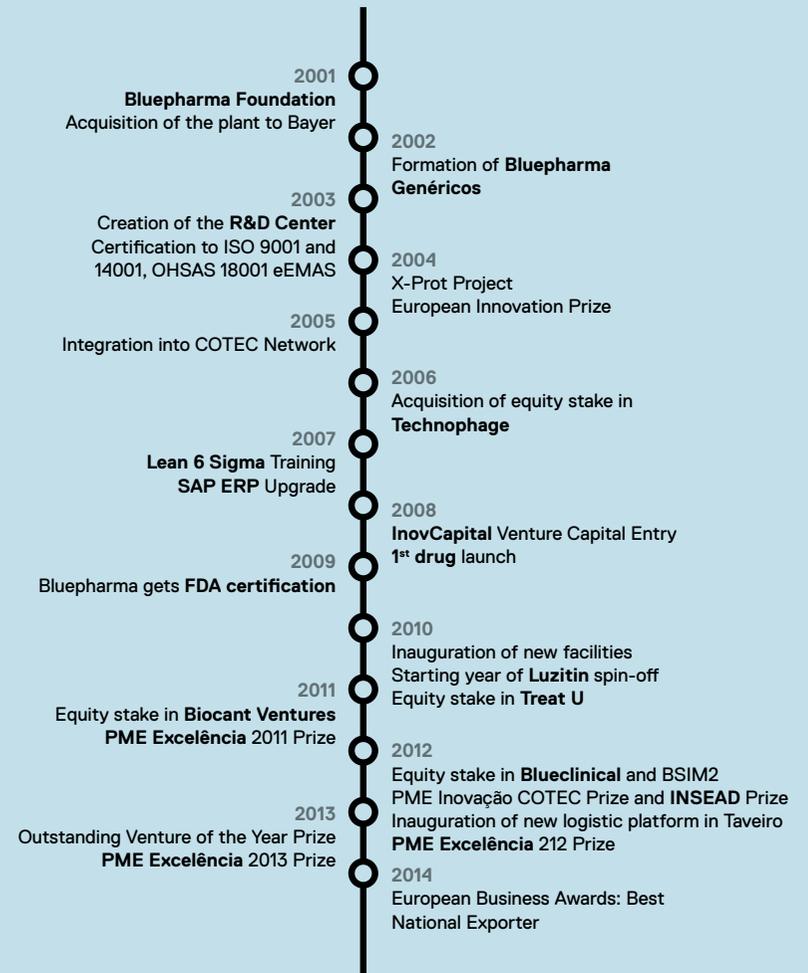
Vertical integrations seems to be order of the day. To what extent should this organisational drive be pursued? What are the costs and advantages? What decisions regarding scale and scope are there?

Bluepharma is becoming a fleet of firms. To what governance form should it adhere in the future?

And what happens if one day a Big Pharma presents them with an offer they can’t refuse? Is the rest of the industry ready to do full circle too?

APPENDIXES

Appendix 1.



Source: Translated from Annual Report 2014, p. 8

Bluepharma



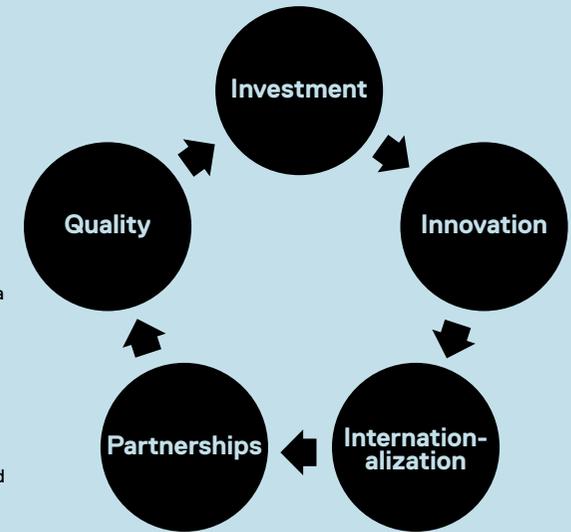
APPENDIX 2. Bluepharma's mission (translated statement)

The Bluepharma's MISSION is based on providing pharmaceutical products of the highest quality and competitive prices, thus contributing to the rationalization of expenditure in the health sector while, simultaneously, improving the quality of living of people.

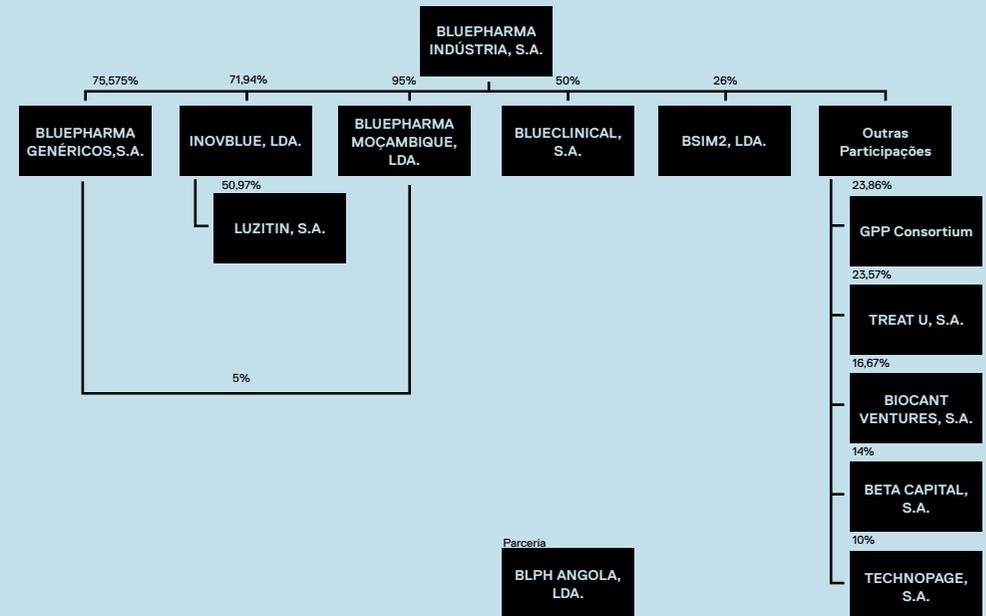
The excellence is the key success factor of the Bluepharma activity. The VISION of the company is based on the continued focus on **Investment** - in people, in facilities and new equipments - in order to **Innovate** and **Internationalize**. Thus, it was made a bet on **Partnerships** (national and international) and, in addition, the focus on **Quality** (know-how of Bayer, dynamics and innovation Bluepharma, the necessary professionals and the ability to "look out").

Source: Translated from Annual Report 2014, p. 9

- **Investment**
 - Carried out continuously, in people, in new facilities and in the acquisition of new equipments.
- **Innovation and R&D**
 - Own R&D Center
- **Internationalisation**
 - Export represent more than 80% of turnover (Europe, USA, Asia, Latin America and Australia)
- **Partnerships**
 - National and international partnerships with research centers of Excellence
- **Quality**
 - 1st pharmaceutical industry with integrated and FDA certification



APPENDIX 3. Bluepharma's organisation structure



Source: Annual Report 2014, p. 10

Bluepharma



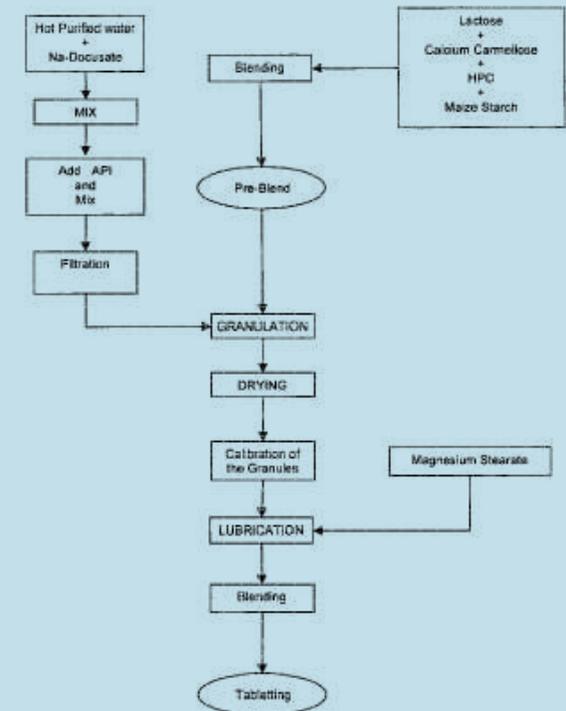
APPENDIX 4. Bluepharma's patent, example

Inventor(s):	GINDULLIS FRANK DR [DE]; SIMOES SERGIO [PT]; LEITAO DA SILVA ALBERTO GABRIEL [PT]
Applicant(s):	HELM AG [DE]; BLUEPHARMA IND FARMACEUTICA S A [PT]
Classification:	
- international:	A61K31/00; A61K9/00
- cooperative:	A61K9/1694; A61K9/2013; A61K9/2018; A61K9/2054; A61K9/1617; A61K9/1623; A61K9/1652
Application number:	SI20080030536T 20080917
Priority number(s):	EP20080016396 20080917

Abstract of corresponding document: EP2165702 (A1)

The present invention relates to new pharmaceutical compositions in which Candesartan cilexetil is contained in a stabilized form with enhanced solubility and from which it is readily bioavailable when applied in conventional pharmaceutical dosage forms, and a process for the preparation of the same as well as of kits containing such compositions. The pharmaceutical compositions of Candesartan cilexetil or of its combinations with other active ingredients can be used in methods to treat subjects suffering from cardiovascular diseases.

Source: Espacenet



APPENDIX 5. Bluepharma's US trademark



Word Mark	BLUEPHARMA
Goods and Services	IC 005, US 006 018 044 046 051 052, G & S: Pharmaceutical products for the treatment of gastrointestinal acid related disorders, cardiovascular system diseases, inflammatory diseases and rheumatic disorders, alimentary tract and metabolism disorders, thrombotic disorders, cholesterol, bone diseases, genito-urinary system diseases, fungal infections, nervous system disorders, allergic reactions
Mark Drawing Code	(3) DESIGN PLUS WORDS, LETTERS, AND/OR NUMBERS
Design Search Code	26.17.02 - Bands, wavy; Bars, wavy; Lines, wavy; Wavy line(s), band(s) or bar(s)
Serial Number	77862938
Filing Date	November 2, 2009
Owner	(REGISTRANT) Bluepharma - Indústria Farmacéutica, S.A. CORPORATION PORTUGAL Sao Martinho do Bispo 3040-086 Coimbra PORTUGAL
Registration Date	February 15, 2011

Source: USPTO



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Case Study

Bluepharma



Bluepharma:
Re-starting-up
an approach to
innovative business
development

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