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Dear Readers,

Our team at Global Business Reports is delighted to present the following overview of Spain's pharmaceutical and biotechnology industries. After nine weeks of research on the ground in Madrid and Barcelona, we have come to learn from some of the sector's most prominent executives and thought leaders across the value chain.

As one of the world's most mature pharmaceutical markets, Spain is scientifically equipped to be an innovative economy. While it has experienced a severe economic crisis—resulting in a decline of the country's pharmaceutical and biotechnology industries—Spain continues to harbor unique potential in terms of its research capabilities and talented pool of human capital. A glimmer of optimism pervades the sector in light of the positive 0.9% growth it experienced in 2014, after four consecutive years of industry-wide contraction.

With upcoming elections later this year, accompanied by the potential rise of new political parties, an air of uncertainty continues to characterize the sector. Nevertheless, all players recognize the need for increased research and development, production and export of value-added products, and adoption of novel investment vehicles, and are taking steps to realize these changes. The biopharmaceutical landscape is evolving in this Mediterranean nation, slowly but surely.

We would like to heartily thank the National Trade Association of the Spanish-based pharmaceutical industry (Farmaindustria), the Spanish Bioindustry Association (ASEBIO), the Spanish Generic Medicines Association (AESEG), the Catalan Association of Biotechnology Companies (CataloniaBio) and key companies for their support and insights, without which this book would not have been possible.

Sincerely,

Vanessa Benz
Senior Project Director

Neha Ghanshamdas
Journalist

JP Stevenson
Journalist

Introducing Spain and its Pharmaceuticals Industry

Internationalize and Diversify: Manufacturing Pharmaceuticals in Spain

The Search for Growth: Supply Chain Dynamics

Spain's Strategic Sector: Biotechnology

Into the Future

This research has been conducted by Vanessa Benz, Neha Ghanshamdas, and JP Stevenson.

Edited by John V. Bowlus
Graphic design by Gonzalo Da Cunha

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Exclusive Interviews

Leaders of large and small companies alike as well as associations discuss market trends and opportunities, as well as pitfalls and current business strategies.

10, 19, 21, 23, 25, and many more

Editorial Content

Global Business Reports' journalists provide unique insights into all aspects of the sector by working on the ground for weeks and meeting face to face with industry leaders.

8, 11, 16, 31, 38, 48

Quantitative Data and Maps

Maps and quantitative data highlight and clarify the key trends across all levels of the value chain in Spain's pharmaceutical industry.

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Biotechnology

Spain has a decades-long commitment to the biotech sector, and GBR highlights several companies at the forefront of it.

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Future Outlook

The future is being built today. Companies share their visions for products to be developed and for the future of Spain's pharmaceuticals industry.

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FARMACIA
PLANA
DE L'OM
4
DR. A. ESTEVE

Introducing Spain and its Pharmaceutical Industry

"In Spain, we have important manufacturing capabilities that have developed over decades. We have talented people and reasonable labor costs. We are also a politically stable country, and represent an important society for international companies. Our people have been in the manufacturing business for years, which has helped us establish our presence within the global playing field."

- Antoni Esteve, Ph.D.,
Director,
Esteve

Image: Esteve

Skeptical Spain

A Brief Political and Economic Overview

While all eyes were on Greece during the summer of 2015, Spain may be a more suitable barometer for measuring the political and economic health of the European Union. Of the EU's larger members, Spain experienced the most acute economic downturn in 2008, as a result of a housing bubble, unsustainable growth levels, and the headwinds of the global financial crisis emanating from the United States. Though the Spanish economy started to gain strength in 2011, it dipped back into recession in 2012, prompting a new round of €100 billion in rescue loans and other relief measures from the EU's fiscal authorities. These measures calmed fears about speculative runs on Spain's sovereign debt and stabilized the euro. Yet continued austerity and endemic unemployment have made Spain's citizens restless and spawned high levels of emigration. Unsurprisingly, political support for parties and movements that are skeptical of austerity has grown.

This fall, Spain enters a critical round of national elections. Two political parties—the People's Party (PP) and the Spanish Socialist Workers' Party (PSOE)—have dominated Spanish politics since the 1990s. Prime Minister Mariano Rajoy leads the ruling PP, which is on precarious footing after a massive electoral setback in the May 2015 local and regional elections. The left-leaning Podemos and center-right Cuidadanos, both of which are anti-austerity, collectively garnered 18% of the vote and dented the dominance of the PP and PSOE. It remains to be seen how effectively these new parties can influence the overall direction of the country, let alone their respective municipalities and regions. Still, few doubt that the Spanish left is rising and shaping local politics. This political current could either transform Madrid from the bottom-up or simply splinter the electorate, as the Spanish voter will have four choices at the ballot box instead of two.

The rise of political opposition to the PP and PSOE is somewhat unfair when considering the PP's recent management of the economy. Unemployment has declined from 26.3% in early 2013 to 22.5% in June 2015, whereas GDP growth rates have risen since early 2014 to grow by 0.9% in the first quarter of 2015 and 1% in the second quarter. This growth has exceeded that of the EU as whole, which has grown by only 0.4% in 2015. Rajoy trumpets the numerous reforms that the PP has passed for increasing efficiency across numerous sectors and regions and fostering entrepreneurship, but some of the upturn must be attributed to larger factors, including lower oil prices and the European Central Bank's policy of quantitative easing.

Others, however, maintain that the improving economy is due to efficiencies and cost improvements that Spanish businesses naturally undertook to weather the crisis. Moreover, the EU's structural reforms instituted in 2012

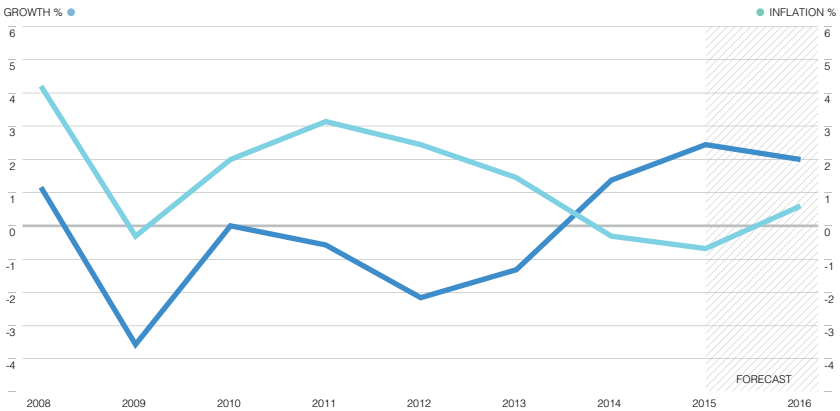
SPAIN AT A GLANCE

Source: CIA World Factbook

Population: 48,146,134 (July 2015 est.)
Land Area: 505,370 sq km
Official Language: Castilian Spanish
Capital: Madrid
Chief of State: King Felipe VI (since June 2014)
Head of Government: President of the Government Mariano Rajoy (since December 2011)
GDP (PPP): $1.534 trillion (2014 est.)
Growth Rate: 1.3% (2014 est.)
GDP per Capita: $33,000 (2014 est.)
GDP Composition by Sector: 3.2% agriculture, 25.4% industry, 71.4% services (2014 est.)
Exports: $317.3 billion (2014 est.): machinery, motor vehicles; foodstuffs, pharmaceuticals, medicines, other consumer goods
Imports: $337.9 billion (2014 est.): machinery and equipment, fuels, chemicals, semi-finished goods, foodstuffs, consumer goods, measuring and medical control instruments
Major Trade Partners: France, Germany, Italy, Portugal, UK, China

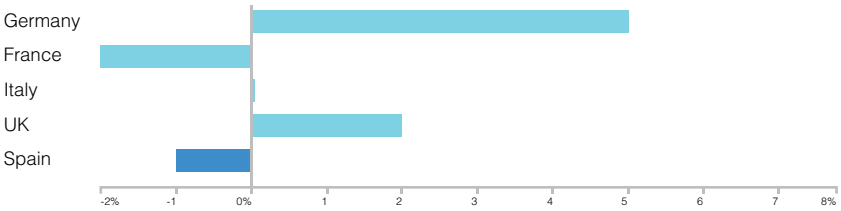
SPAIN GROWTH VS. INFLATION (2008 TO 2013)

Source: International Monetary Fund



PHARMA GROWTH IN TOP 5 EUROPEAN MARKETS (2012-2013)

Source: Farmaindustria, IMS



% OF PHARMA SALES IN TOP 5 EUROPEAN MARKETS (2012-2013)

Source: Farmaindustria, IMS

Germany	37%
France	25.2%
Italy	13.9%
UK	12.4%
Spain	11.5%

7.3% 2002

8.9% 2013

TOTAL HEALTHCARE EXPENDITURE AS % OF GDP, SPAIN

Source: WHO

21.6% 2002

23.1% 2013

% OF POPULATION OVER 60, SPAIN

Source: WHO

gave a clean bill of health to the country's banks, which was far more important to sparking growth than reforms from the federal level. As difficult as it is to assign credit for the upturn, the truth remains that the Spanish economy was so devastated by recent events that it will take years before it recovers what it lost and wider confidence returns.

Amidst these EU-wide struggles, a new round of geopolitical tensions with Russia adds uncertainty to the continent and its energy supplies. Fortunately, Spain is not dependent on Russian gas, as it imports liquefied natural gas, is not connected into Russian gas pipelines, and receives 39% of its gas from Algeria through the Maghreb-Europe Gas Pipeline under the Mediterranean Sea. The proposed free trade agreement between the European Union and the United States, the Transatlantic Trade and Investment Partnership (TTIP), could be a shot in the arm for the continent's economies, including Spain's, but, if ratified, the agreement will likely come under political attack if Spain's autonomous governments lose the ability to regulate their respective markets. Though these types of concerns are associated with any trade deal, they seem particularly vexing in light of the challenges faced by the EU.

The following report on the Spanish pharmaceuticals industry provides a window into one of Europe's most dynamic and innovative economies and helps to elucidate some of the emerging trends on the continent and across the global pharmaceuticals industry. •

Humberto Arnés

Director General
FARMAINDUSTRIA

Farmaindustria is the national association for the pharmaceutical industry, whose reach encompasses the entirety of the prescription drug market in Spain through its members. What is the mission of Farmaindustria and what separates it from the other associations?

We are an association of research-based companies that have proprietary products. Our members are all companies that compete with those that have innovative technology and products. We have three very important fields of action: to generate a circle of understanding and trust with our regulators so that the relationship with pharmaceutical companies is conducive to better develop their business; to provide services and information to our associates that are valuable for their performance and encourage an active participation in our association; and to create alliances to defend common interests. Our vision is that our industry continues to contribute to society by providing the best medications and treatments to its citizens and improving their quality of life.

What are some of the largest projects that Farmaindustria has been involved with thus far in 2015 and what will you work in 2016?

Before speaking about our projects and actions, it is important to recognize why we are engaged in them. We are facing a series of threats as well as opportunities that we are meeting through a strategy developed by the association and approved by our governing bodies. We are living in a volatile political situation. There is uncertainty surrounding a potential fragmentation of the market. Our main threat is that political instability may generate regulatory uncertainty, which could weaken our sector and fragment our market. Another threat we face is that Spain still needs to follow through on select European requirements in order to reduce its public deficit. As a consequence, there are autonomous communities facing economic hardship as far as public expenditure is concerned in certain sectors such as healthcare and pharmaceuticals. Yet there are positive circumstances, such as Spain's exit from the economic crisis. Our risk premium has decreased, our growth rate forecasts currently reach 2.8%, and we have made great efforts to reduce our public deficit. Additionally, we have preserved a relationship with the government based on dialogue and mutual trust, which allows us to build credibility and face. A third strength we have is a dynamic corporate network that contributes greatly to the economy, making our sector a prototype from which Spain is developing a new economic model.

Farmaindustria continues to work on constructing a predictable regulatory and economic framework. We have developed a Protocol of Collaboration that links the growth in pharmaceutical spending with the growth of our economy. At the same time, we have been searching for means to allow citizens access to the best treatments that are in line with sustainable public spending. We are introducing new commitments to improve the transparency in our relationship with healthcare professionals. We have approved a new deontological code aimed at making all economic transactions between the industry and healthcare professionals transparent.

The pharmaceutical industry is a very important contributor to research and development (R&D) for the Spanish economy, constituting about 20% of the total investment of the industry in Spain. What will be the focal point of manufacturers' R&D strategies?

Our principal objective as an industry is to increase the resources that our sector dedicates to research. This industry is only able to survive if it is capable of producing new medicines, which is why it is fundamental to have a predictable regulatory and economic framework. Additionally, it is also crucial to have a system of intellectual property rights that protects innovation. There must always be a balance between the savings that a generic drug may produce once a patent expires with the rights of an innovator to benefit from their research. The concept of open innovation is also as important as ever, as we are seeing about one third of the resources dedicated to research directed at collaboration with other research centers.

Emerging markets are expected to provide 50% of the growth in pharmaceuticals globally in the next few years. What trade partners are most important for Spain?

Spain is home to both national and multinational companies. Our national companies are related in terms of their geographical reach—Europe being the most important—and there is still much work to do in terms of internationalizing them. At the same time, the industry needs to generate trust from foreign investors to build a predictable Spanish market and export platform. Spain is well positioned to grow, as we have well-trained personnel, accessible labor, and well-developed infrastructure. Farmaindustria tries to promote ways in which its members can collaborate to penetrate new markets all over the world, fostering trade and internationalization with a special focus on bilateral and multilateral agreements. •

Looking Beyond the Crisis

An Introduction to Spain's Pharmaceutical and Biotechnology Sectors

Spain is home to well-established and heavily regulated pharmaceutical and biotechnological industries, concentrated primarily in the capital city of Madrid and the northeastern autonomous community of Catalonia. While Madrid has hosted many of the world's multinational pharmaceutical giants for years—including Novartis, GlaxoSmithKline, Roche, Sanofi, and AstraZeneca—the country's northeastern region has fostered the development of Spanish multinational players such as Esteve, Almirall, Ferrer, and Grifols. Today, Spain is the fifth largest European pharmaceutical market, with the sector accounting for 1.4% of the country's total GDP.

The industry's longstanding relevance parallels the country's world renowned National Health System, which consistently ranks highly among its peers. In 2014, Bloomberg ranked Spain as the world's 14th most efficient health care system, far ahead of the United States and Canada. The Spanish National Health System provides universal coverage to its citizens and foreign residents, stemming from a constitutional mandate written in 1978 to ensure health protection and care to all. Years later in 2002, the administration of healthcare was devolved to the country's 17 autonomous regions, resulting in the establishment of 17 regional ministries. Today, each autonomous region exercises control over the coordination and delivery of health services in their respective territory.

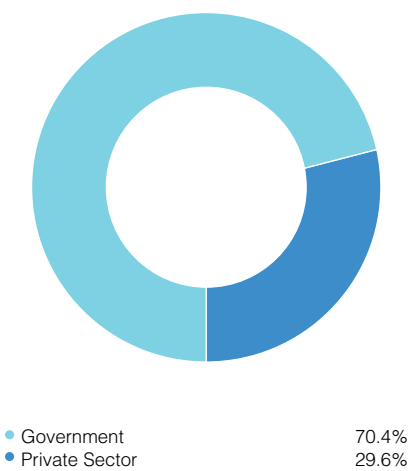
Since the economic crisis of 2008, however, Spain's expenditure on healthcare has progressively declined, placing the nation well behind its fellow OECD countries. According to the Economy and Health Foundation, in 2013 public healthcare expenditure was only 7% of Spain's GDP, compared with 8.4% in Germany and 9% in France. Prior to the economic crisis, Spain was a leader in healthcare investment, spending up to €64.3 billion in the sector in 2009, compared with €53.5 billion in 2014. Furthermore, spending cuts have not been consistent across the country, creating causes for concern over the rise of regional inequities.

"Currently, investment per capita in healthcare is not consistent across Spain, which if sustained will give rise to discrepancies in standards of care," said President Director General of MSD Ángel Fernandez.

The Spanish government has implemented a series of cost-saving measures, presenting financial concerns to the industry at large. According to IMS

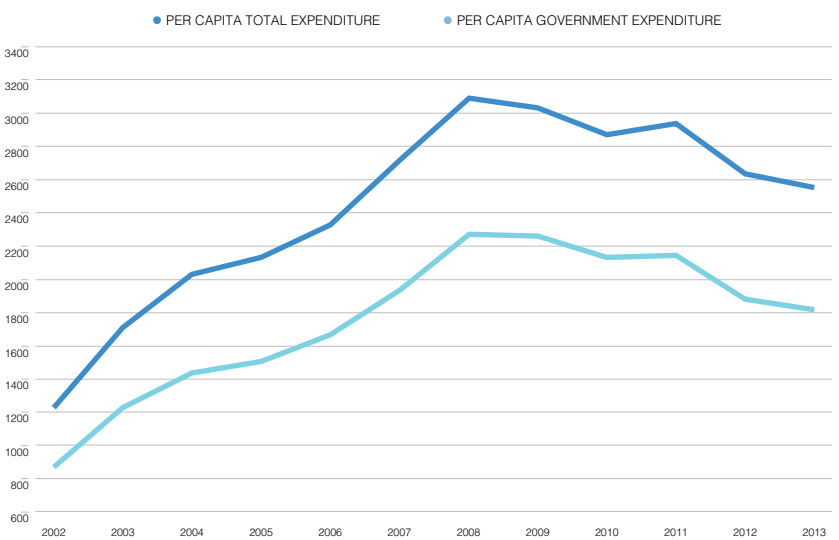
PUBLIC-PRIVATE EXPENDITURE ON HEALTHCARE AS % OF TOTAL (2013)

Source: WHO



PER CAPITA HEALTH EXPENDITURE, 2002-2013 ($ MILLION)

Source: WHO



PHARMACEUTICAL SPENDING PER CAPITA PER AUTONMOUS REGION (2013)

Source: Farmaindustria

	%	% Change	Value (€ million)
Extremadura	13	-3.8	251.9
Galicia	7.5	-1.9	250.5
Asturias	2.7	-7.4	230.6
Community of Valencia	12	-7.5	216.3
Aragon	3.1	-6.9	213.2
Basque Country	5.1	-4.8	213.1
Murcia	3.4	-6	213
Castile-La Mancha	4.8	-8.1	211.5
Castile and Leon	5.7	-5.2	209.2
Cantabria	1.3	-5.7	202.5
La Rioja	0.7	-6	197.2
Canaries	4.4	-3.3	192.4
Andalusia	17.4	-4	189.2
Navarre	1.3	-7.4	184.4
Catalonia	14.3	-8.7	174.1
Balearics	1.9	-4.1	155.3
Madrid	10.9	-5.1	154.5

Health, between 2010 and 2014, the country's pharmaceutical industry contracted by 13.7% in value. "The pharmaceutical sector in Spain has changed dramatically within the last six to seven years. The reduction of government expenditure in healthcare has affected all companies. 90% of Spain's pharmaceutical market is covered by the National Health System, which means that the prices are fixed by the authorities. Reductions in margins have caused us to adapt very quickly and institute new strategies," said President of Grupo Juste, Inés Juste.

Pharmaceutical companies have had to remain flexible in the context of a new regulatory environment. One strategy many players are adopting is diversification, most notably through the production of consumer health products. To avoid price and reimbursement related hurdles, many firms have entered the segment, or ramped up their existing production of these goods. According to IMS Health, between 2012 and 2014, the consumer health market grew by 5% in value, while the prescription drug market contracted by 3.7%.

Additionally, after a decade of growth, according to Farmaindustria, investment in research and development (R&D) has fallen from 1.38% to 1.30% of GDP between 2009 and 2012. This number remains far from the European Commission's target of 3%. And while the country is home to world-renowned academic institutions and research

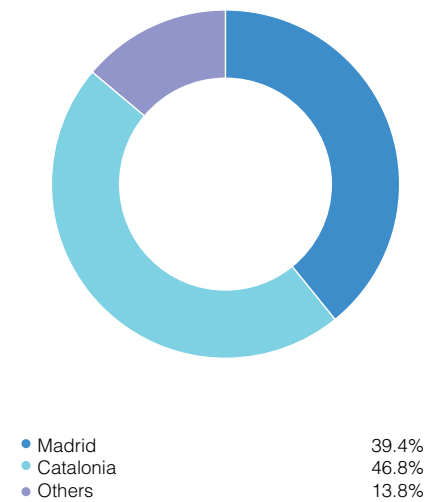
> "Spain is ranked tenth in the world for its scientific capabilities, and fifth in Europe."
>
> - Regina Revilla, President, Spanish Bioindustry Association (ASEBIO)

SPANISH R&D (2012)

Source: Farmaindustria

GEOGRAPHIC DISTRIBUTION OF R&D (2013)

Source: Farmaindustria



> Currently, investment per capita in healthcare is not consistent across Spain, which if sustained will give rise to discrepancies in standards of care.
>
> - Ángel Fernandez, President-Director General, MSD Spain

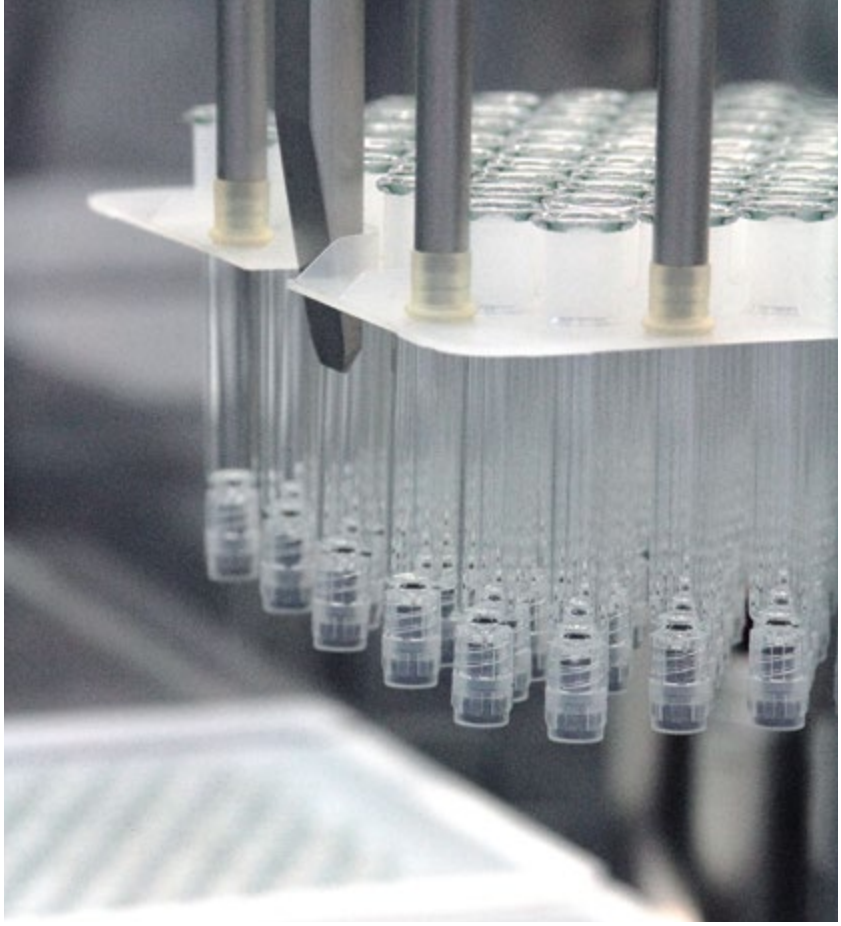


Image: TEDEC-MEIJI FARMA

centers forming a strong foundation for basic research capabilities, Spain lacks an ecosystem—existent in many other countries—to translate basic research into commercialized products. Such a framework is crucial to promote competitiveness and drive new products to the market. While research grants are commonly approved, the resources needed for product development and production of proofs of concept are lacking. This gap impedes the development, marketing, and sale of commercialized products. While other governments and countries utilize incubators and additional tools to attract public and private investment, Spain has yet to implement this framework, and thus many innovations are not making it to the market. "At present, there is a tremendous amount of knowledge that is lost in Spain. This includes knowledge stored within the projects of our academic institutions, and the work of researchers that could be used to create innovative products and improve the quality of life. Spain is capable of better capitalizing on its strengths in basic research, however first an environment must be created that will enable research and innovation to be more easily transferred into the market," said president of SUANFARMA, Héctor Ara Sanz.

This issue is most pressing within the biotechnology sector in Spain. The country was an early adapter, with its roots in biotech dating to the 1980s, and has experienced tremendous expansion since. Yet today "[the sector] is at a delicate moment. Despite the good news from companies like Oryzon or PharmaMar, shortage of capital, lack of liquidity and shrinking government budgets have weighed on the sector, right in its prime," explained President of Spanish Bioindustry Association, ASEBIO, Regina Revilla.

The sector is currently comprised of small firms, many of which are in infant stages of development. Revilla stressed the need to promote mergers and acquisitions, increase access to capital markets, reduce dependence on public funds and develop specialized communication programs, in order to spur growth within the sector.

But there are glimmers of economic recovery in sight, and Spain is cautiously moving to reclaim its position in the healthcare market. There is sector-wide consensus on the need for increased investment, especially in R&D, to meet the European Commission's target. But companies and administrators are proceeding with caution. Due to heavy price competition from Asian production powerhouses such as India and China, Spanish firms recognize the need to grow strategically, in areas such as innovation and quality. At present, Spain is well positioned to excel on both fronts, due to its extensive capacities for basic research. In fact, according to Farmaindustria, pharmaceutical R&D accounts for approximately 20% of the country's total R&D expenditure. Additionally, policies have recently been instituted by the administration to provide fiscal incentives for R&D and further capitalize on Spain's burgeoning medical research potential.

Given the challenges facing the pharmaceutical and biotechnology sectors in Spain, especially in the aftermath of the economic crisis, the country is still poised for future growth. "Spain is ranked tenth in the world for its scientific capabilities, and fifth in Europe," said Revilla.

As a leader in medical research, the country boasts excellent academic infrastructure and ranks second after the United States for the number of biotechnology firms in the country, which totals 6,860. With increased public investment and targeted private capital, Spain's biopharmaceutical sector has the potential to steer the country forward. Through strategic investments in health, Spain can preserve its stature in the world, promote innovation and ensure the long-term success of its pharmaceutical and biotechnology industries. •

Internationalize and Diversify Manufacturing Pharmaceuticals in Spain

"As of today, 40% of our business comes from the Spanish market, 50% from the rest of Europe, and the remaining 10% from the rest of the world. For us, the most promising area of growth is the rest of the world, where we perceive the most opportunities for future expansion. We are working hard to penetrate both the United States and Asia. Additionally, there are some countries that may not be considered very developed from a pharmaceutical perspective, that pose many opportunities. Essentially, we would like to focus the bulk of our attention outside of Spain and Europe, but without undermining our local market position."

- Ignasi Biosca Reig,
CEO,
Reig Jofre

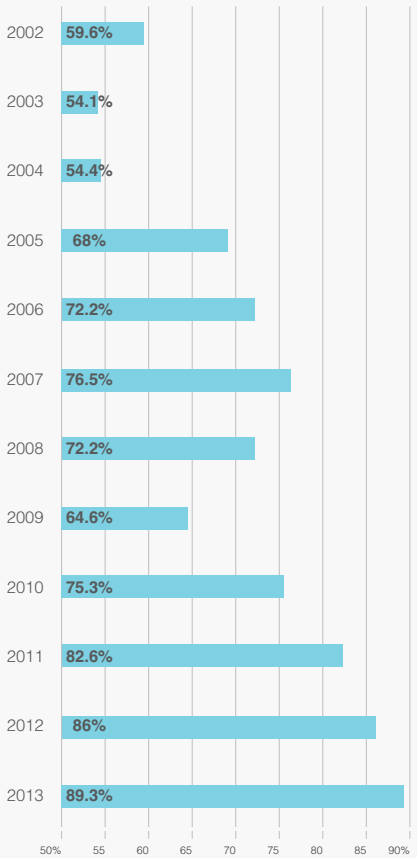
Image:

The Spanish Government and Domestic Pharmaceutical Manufacturing

Challenges to Growth and Strategic Vision

SPAIN PHARMA COVERAGE RATIO EXPORTS/IMPORTS

Source: Farmaindustria



Having maintained its relevance as a manufacturing hub for years, Spain has evolved into one of the most mature pharmaceutical markets in the world today. National laboratories that once began as small pharmacies in Barcelona have grown into international powerhouses, exemplifying Spain's scientific competitive advantage. "In Spain we have important manufacturing capabilities that have developed over decades. We have talented people and reasonable labor costs. We are also a politically stable country and represent an important society for international companies. Our people have been in the manufacturing business for years, which has helped us establish our presence within the global playing field," said Director of Esteve, Antoni Esteve.

The economic crisis of 2008, however, forced many local companies to rethink their strategies. Budget cuts on the part of the Spanish government have led to a contraction in public healthcare expenditure. As in other European countries, reimbursed products are being delisted, and margins have narrowed for many producers. Both public and private investment in R&D has declined, calling into question the industry's long-term sustainability. "The main threats faced by the pharmaceutical market are regulation, specifically with regards to pricing; market access; and cuts in healthcare spending. In the last six to seven years, the pharmaceutical market has contracted by one third. New innovations (such the latest portfolio in Hepatitis C and Oncology for example) have yet to be financed. The debate today is about which healthcare system we can afford to finance," explained President of Grupo Juste, Inés Juste.

As a result of these challenges, manufacturers have had to think outside the box to remain competitive. Spain's biopharmaceutical landscape has evolved significantly to become dominated by large multinationals and generics manufacturers. According to IMS Health, the top ten generics manufacturers occupy 81% of the total market share. These new dynamics have forced other players to diversify, internationalize, specialize, or ramp up their R&D efforts in order to stay afloat. "One strategy that we have adopted is diversification into other product ranges, hence the decision to merge with Forte Pharma," said CEO, Ignasi Biosca Reig of Reig Jofre.

A strategic merger with Swedish company Forte Pharma in 2014 allowed Reig Jofre to penetrate the consumer health market. By selling products within this segment—food supplements in this case—companies can avoid price hurdles. According to IMS Health, between 2013 and 2014, the consumer health market has expanded by 0.7% in volume, and 4.1% in value. This is in contrast to the prescription drug market, which has contracted by 1.2% in volume, and 1.8% in volume, in the same time frame.

Other smaller firms are seeking to penetrate therapeutic areas in which they can specialize and add value. Seid Lab, for example, has found success within the Women's Health segment. "Women's health is a strategic sector, as it is a non-generic market. Most products are branded, making it difficult to find many generics in this area, which is beneficial for companies like us," said director general of Seid Lab, Joaquin Vila.

Seid Lab has been able to specialize in the area of fertility, notably through the development of a specialized over-the-counter (OTC) product in response to a new discovery made about men's nutritional needs. This put Seid Lab on the map and allowed the firm to compete with a renowned international player in women's health. "As a medium sized enterprise, we do not have the capabilities to develop new molecules. Hence, we are targeting the OTC market. This

FARMAINDUSTRIA MEMBER COMPANIES BY AUTONOMOUS COMMUNITIES (DECEMBER 2014)

is the case in most countries in Europe, especially given recent budget constraints. Many governments are delisting reimbursed drugs across Europe.

> The main threats faced by the pharmaceutical market are regulation, specifically with regards to pricing; market access; and cuts in healthcare spending…The debate today is about which healthcare system we can afford to finance.
>
> - Inés Juste, President, Grupo Juste

In this regard, while the rate of OTC penetration has been relatively low in Spain, we are developing products that fit within this category. They can be publicly advertised, do not require a prescription and are sold in pharmacies," explained Vila.

Aside from expanding and targeting their product offerings, many Spanish manufacturers are turning towards export markets to drive growth. Latin American markets have long been key markets for Spanish products due to historical and cultural affiliations, and this is still the case today for players of all sizes. "It is clear that for any Spanish company, Latin America remains a key driver for future growth," said executive vice-president of Grupo Indukern, Raúl Díaz-Varela.

The fifth largest generics player in the Spanish market has partial roots in Venezuela, and continues to conduct a large portion of its business in South America. Smaller players such as Laboratorios VIR also want to strengthen their presence in the region. "At present, 15% of our products are exported, and we will continue to look outside Spain to expand our market. We are making concerted efforts to establish a presence in the Dominican Republic, Chile, Venezuela and Panama," said Business Development Manager at Laboratorios VIR, Enrique Ruiz Rueda.

The United States is also becoming progressively more important for Spanish pharmaceutical manufacturers and will potentially serve as the next prime market for Spanish products. While larger players such as Grifols and Esteve have long since been established in the United States, many other Spanish players are currently seeking to enter or increase their presence in the world's largest biopharmaceutical market. •

Esteve

ORIGINS AND FOUNDER

ESTEVE is a leading pharmaceutical chemical Group in Spain with a significant presence worldwide. Laboratorios Dr. Esteve S.A., the company founded by Dr. Antoni Esteve i Subirana in 1929, was the first in the Group. Since then, and thanks to its research vocation, its desire to expand internationally and an active policy of strategic alliances with other pharmaceutical firms, ESTEVE has established a strong position as a leading business Group in Europe.

ESTEVE operates in the pharmaceutical sector by researching and developing new drugs, marketing a wide range of ethical and OTC products, generics and active pharmaceutical ingredients (APIs), thus providing a comprehensive solution in the area of health.

A LEADER IN SPAIN - COMPETITIVE IN THE WORLD

At an international level, ESTEVE has production plants in Spain, Mexico and China, subsidiaries in USA, Portugal, Italy, Germany, Turkey and Sweden and a commercial office in Japan. ESTEVE products enjoy a strong presence the world over.

The drug specialties manufacturing plant in Martorelles (Barcelona) is one of the most modern facilities in Europe and its annual production, for both the Spanish and international market, exceeds 100 million units.

In pharmaceutical fine chemicals, ESTEVE channels the production and marketing of APIs through Esteve Química, an exemplary company in the international market. A key factor to this business unit's success lies in the innovation applied to producing high added value active pharmaceutical ingredients and in spreading its production facilities on three continents.

The high technology of all its production centres and their strict compliance with GMPs allow ESTEVE to provide third parties with services to develop new manufacturing process for NCE and produce drugs.

With a staff of 2,300 people, ESTEVE's turnover in 2014 totalled 838 million euros, of which 438 million (52%) came from international operations as active ingredients and finished dosage forms.

A COMPANY DRIVEN BY R&D

The R&D portfolio of ESTEVE encompasses projects of different natures spanning new chemical entities (NCE), new biological entities (NBE), life cycle management strategies (LCM) and generic medications leveraging different R&D partnership architectures, diversified across different therapeutic areas and at different stages of development.

Today our portfolio comprises:

- New Chemical Entities in Analgesia
- New Biological Entities / Advanced Therapies in different Therapeutic Areas
- New Formulations for Innovating Concepts in several Therapeutic Areas
- Projects involving Generics of High Added Value in several Therapeutic Areas
- Life Cycle Management Projects to enhance the positioning of our marketed products

ESTEVE's pain programs are designed to understand pain mechanisms and their impact on physical and emotional well-being. Our research is closely connected to patient unmet needs. We are currently developing innovative treatments for pain which form a key component of ESTEVE's R&D portfolio. Formulation technology, an innovative co-crystal approach and proprietary tools are also amongst our key assets.

As part of an R&D portfolio diversification strategy into other therapeutic areas besides analgesia, ESTEVE has in place different types of R&D collaborations to have access to external projects that are developing novel medicines that would represent a real added value for patients.

Examples of this strategy are the projects HIVACAT and Sanfilippo. The HIVACAT research and development project is a joint Public and Private Partnership (PPP) with a unique architecture at the forefront of international HIV and AIDS research for the development of AIDS prophylactic and therapeutic vaccines. The Sanfilippo programme is also a PPP between ESTEVE and the UAB (Universitat Autònoma de Barcelona) for development of gene therapies for the treatment of mucopolysaccharidoses, a rare disease. The lead program has been designated as an Orphan Drug by both the European Medicines Agency (EMA) and the US FDA.

RECENT PRODUCT LAUNCHES

In 2014, ESTEVE launched through its three main business units a wide range of different products, for example four innovative drugs in Spain, 50 generic drugs, and seven new manufacturing processes for active pharmaceutical ingredients. These new products come from different sources, some are due to strategic alliances and other come from our own internal R&D.

CORPORATE SOCIAL RESPONSIBILITY

Beyond our chemical-pharmaceutical activities, ESTEVE's commitment to society is evidenced by a wide range of collaborations with persons and institutions on an entrepreneurial, public, non-profit basis.

This social activity is reported every year though our Sustainability Report. This report summarizes all our activities from the triple bottom line. That means that we report activities from the economic, social and environmental point of view.

For more information please visit www.esteve.com

Antoni Esteve

Ph.D., Director
ESTEVE

Esteve was founded in 1929 and is an international pharmaceutical pillar today. Please tell us about some accomplishments that as member of the Esteve family you are most proud of.

Esteve was founded in 1929 by my grandfather, who dedicated his life to research. To date, we remain a family-run enterprise that embodies his philosophies. We have built our business over the past 85 years and maintain the same philosophies of great talent, good people, and an entrepreneurial spirit. We are ambitious not only with regards to our goals as a company, but also to improve society and resolve the world's problems.

Esteve is primarily active within three areas: pharmaceuticals, chemicals, and generics. Which area constitutes the greatest revenue stream for Esteve, and which poses the most opportunity for growth?

Esteve has three main lines of business that are all interrelated. We research, produce, and market new pharmaceuticals, which has been our core business since the company's founding. Over the course of time, we have developed the business and diversified our portfolio. Esteve entered into the generics business, as well as the manufacture of APIs, and has since grown to become one of the primary suppliers in this field. Currently the company relies on all three of its pillars equally as they are comparable in size. We dedicate resources and efforts to remain prominent competitors in all sectors, and there is equal potential for growth in each of the three sectors. Within pharmaceuticals, we are investing heavily in research and development (R&D) to develop first-in-class compounds. In this field, it is worthwhile to be ambitious, and we currently have some drugs in phase II clinical trials that address pressing medical needs. Within the field of generics, significant efforts are required to ensure low cost and high quality. Esteve has established a presence in Europe and the United States for these products. Lastly, for the production of APIs Esteve has four top-notch GMP certified chemical plants in Spain, China, and Mexico. These facilities fulfill international quality requirements and are regulated by authorities such as the FDA.

Esteve has historically had a strong focus on the Far East, establishing a plant in China and strategically aligning itself with ZHP. In what way has Esteve seen Asia transform as a supply base for raw materials?

Esteve's presence in China began as a pure commercial relationship with a local player. We later entered into a joint venture that helped form a synergy between the two parties. This relationship began in the 1990s and has survived up until today, serving as a strong channel for Esteve's presence in Asia. Today, China has become an international hub for raw materials. With increased accessibility and translation options, China has attracted businesses from all over the world to source their raw materials.

Why do you think Spain has remained a relevant manufacturing location for pharmaceuticals?

In Spain, we have important manufacturing capabilities that have developed over decades. We have talented people and reasonable labor costs. We are also a politically stable country, and represent an important society for international companies. Our people have been in the manufacturing business for years, which has helped us establish our presence within the global playing field.

How fluid is the relationship in Spain between companies that are innovating and local universities and research centers?

This relationship is in its early stages, but we do acknowledge the importance of maintaining alliances with third party organizations and academic institutions. Esteve is a cornerstone company in this respect, employing 245 researchers in laboratories located in our facilities and within university campuses. In fact, we closed our in-house discovery and preclinical labs and moved our researchers and equipment to the Parc Cientific de la Universitat de Barcelona (University Park).

More Spanish companies are looking to export markets for growth, and more than half of Esteve's revenues are generated from international sales. Is this the future for Spanish firms?

Growth in Spain is difficult, as it is expensive and tough to grow in a mature market. We expect to maintain our position in the Spanish market, but we must export globally in order to expand our business. In terms of markets, Europe and the United States have the highest potential.

Esteve has grown tremendously, both organically and inorganically. Are there any further plans for growth by acquisition?

Esteve remains open to opportunities for growth. We believe in both organic and inorganic growth, as some acquisition opportunities present value for Esteve. Yet we are continuing to grow Esteve organically, investing about 10% of our revenues in R&D alone. We expect to improve our global presence with sustainable growth. We want to maintain our efforts in R&D for the next five years.

What is your final message to the readers of this publication?

At Esteve we believe in collaborating with third parties. We are a unique company in our ability to ally to create value and aim to continue creating value for generations to come. •

Grupo Indukern

FOUNDER

The Indukern Group was created in 1962 as a small, family-run business. Its founder José Luis Díaz-Varela, an entrepreneur with an international vision, chose to base the company in Barcelona, a port city, with a considerable industrial infrastructure. The business originally focused on the distribution of chemical products with a clear mission to become a leading company thanks to its excellent production processes and prime quality products. The Indukern Group currently comprises three main companies: Indukern, Calier and Kern Pharma and it has more than 1,600 employees worldwide.

LEADERSHIP

The three main companies of the Indukern Group are key players in its areas. Indukern acts in the area of fine chemistry marketing and distribution and associated services, and it is leader in Brazilian and Mexican markets. Calier specializes in the research, development, registration and marketing of products for veterinary use and it is currently in 2nd place of the Veterindustria ranking for family-owned laboratories. Kern Pharma is a diversified laboratory providing solutions for patients, to improve their health and quality of life. It is a key player in the development, manufacturing and marketing of generic drugs and it produces in excess of 100,000,000 units per year, which places the company in 3rd position in the ranking of manufacturing laboratories of generics in Spain per volume of units. Today, its activity also involves self-care products, biosimilars and production for other companies.

REVENUE AND GROWTH

The Indukern Group's turnover currently reaches €692million. International operations account for 59% of the business, and 41% are from national market. Per companies, Indukern's turnover reaches €444 million. International operations make up 66%, mainly from European countries and Latin America. Calier's annual turnover reaches €96 million. Some 84% of sales correspond to international markets, especially Latin Amercia, which represents 60% of its business. Kern Pharma turnover reaches €171 million, being Spain its main market with a 77% of the sales.

EXPORT MARKETS

The Indukern Group has twenty subsidiaries—Germany, Argentina, Brazil, China, Colombia, Spain, EE.UU, Guatemala, India, Italy, Morocco, Mexico, Poland, Portugal, Dominican Republic, Switzerland, Russia, Turkey, Uruguay and Venezuela—and products marketed in over 70 countries. The diversification of its three lines—chemical distribution, animal health and pharmaceuticals—and the detection of market opportunities in which it operates have been very important in its internationalization.

RECENTLY LAUNCHED PRODUCTS

Kern Pharma, the pharma company of the Indukern Group, launches 25 news products per year. In 2015, it has been the first Spanish laboratory in commercializing the first biosimilar monoclonal antibody approved by the European Medicines Agency (EMA) –Remsima. Calier, the veterinary laboratory, has comercialized the first avian vaccine against *Salmonella Enteritidis* developed and produced completely in Spain.

Finally, Indukern, the chemical company, has changed the focus of its business and its activity currently revolves around three lines: as intermediary between suppliers of raw materials and manufacturers of finished products in sectors such as human food, flavourings and fragences, pharmacy, veterinary and animal nutrition, and industrial chemical products; as a representative of some of the leading global manufacturers in the sectors in which operates; and as a developer of its own products, which are adapted to meet its clients' needs thanks to a deep knowledge of the market and its techinal services.

Image: Facilities for Kern Pharma pharmaceutical company in Terrassa (Barcelona)

Raúl Díaz-Varela

Executive Vice-president
GRUPO INDUKERN

Please walk us through some historical milestones that have shaped Grupo Indukern's strong position in the market today.

My father José Luis Díaz-Varela founded Grupo Indukern in 1962, after he returned to Spain from Venezuela, where he had worked with an Austrian man named Mr. Kern. Today, Indukern performs licensing, business development, and manufacturing of APIs, is present in 19 countries, and commercializes products in more than 70 countries. In 1968, Calier was founded to produce veterinary products. The newest company within Grupo Indukern is Kern Pharma, which was founded in 1999 to propel Grupo Indukern into the generics market. Grupo Indukern's three business lines equip us with capabilities to generate business in both the pharmaceutical and veterinary industries. Having these three business lines differentiates us from other groups, as we are able to cooperate with customers worldwide on various fronts.

Kern Pharma engages in third-party manufacturing as well as the manufacturing and development of its own products. Can you walk us through these two business lines?

Kern Pharma was founded when Grupo Indukern purchased a plant from Roche to perform contract manufacturing. Kern Pharma launched its generics business roughly 16 months after the acquisition in 2000. At the time, the plant only supplied Roche, and we refocused our attention to build our sales and development teams and expand our business. We have since developed our third-party manufacturing business, and today have agreements with important multinationals, as well as licensing contracts for businesses focused on generics.

As the Kern Pharma brand, we were the first company to launch select products such as Azithromycin, which helped us build a reputation for bringing new products to the market. Today, Kern Pharma has a large portfolio of products.

Both business activities were developed in parallel, anticipating that generics and branded pharmaceutical companies were going to launch progressively fewer new products in the future. Hence, we prepared for this well in advance and today can focus on expanding into other business lines. In February 2015, for example, we began commercializing and selling biosimilars and launched the first infliximab into the Spanish market under the brand Remsima®. We did this in collaboration with Celltrion, a Korean company. Additionally, we launched Kern Pharma Consumer, along with a new sales team and approach.

Does Spain have the potential to be the next hub for biosimilar production?

Having visited biosimilar plants in South Korea and some Eastern European countries, I understand that these drugs require a large amount of investment, making domestic success on this front unlikely. I am not certain that Spain can become a true hub in this regard. We have formed a few companies to develop biosimilar production in Spain, but the reality today is that few biosimilars have been approved relative to the large amount of investments being made worldwide.

As President of the official representative body of the generic and biosimilar pharmaceutical industry in Spain, AESEG, what is your opinion about the generics market in Spain. Now that branded products are priced 40% lower to match those of generics, where is the market headed?

There are still a host of products whose patents are set to expire shortly, but due to the fact that brands are obliged to reduce their prices, the generics market is indeed suffering. AESEG is working with the government on ways to differentiate generics from their branded equivalents. Any generic market in the world requires certain measures of support stemming from clear pricing rules that make it easier for products to remain differentiated. Recently AESEG signed a sustainability agreement with the government. While it has not been formally finalized, both parties have demonstrated their commitment to finding a solution.

Kern Pharma experienced 5% growth in revenue last year. How do you account for both Kern Pharma and Grupo Indukern's continued success?

Firstly, we have a team of hard-working, capable people. Today, it is not enough for a generics company to produce only one product type, such as tablets or pills. It is necessary for us to have vast production capabilities and a diversified product line. These factors have helped us reach agreements to develop more new products. Grupo Indukern is investing heavily in building a large portfolio along with the technologies needed to develop new product ideas. This type of flexibility and dynamism has enabled us to grow continually.

Internationalization is a key growth objective for Kern Pharma. Which markets are most important to you and how do you see this playing out in the future?

Grupo Indukern has been quite successful in Portugal, Venezuela, and Colombia. We recently established a business in Russia where we have registered products, and plan to grow it in parallel to our licensing business there. We have introduced products in all European markets on a product-by-product basis and plan to continue utilizing this approach. Today, we are of a size that allows us the ability to grow by acquisitions, and we are searching for opportunities. Additionally, it is clear that for any Spanish company, Latin America remains a key driver for future growth. •

Grifols

75 ANNIVERSARY OF IMPROVING PEOPLE'S HEALTH

Grifols is a global healthcare company founded in 1940. In 2015, Grifols celebrates its 75th Anniversary of improving people's health and well being through the development of life-saving plasma medicines, diagnostics systems, and hospital pharmacy products.

The company is present in more than 100 countries worldwide and is headquartered in Barcelona. Grifols is a leader in plasma collection with a network of 150 plasma donor centers in the U.S., and a leading producer of plasma-derived biological medicines. The company also provides a comprehensive range of transfusion medicine, hemostasis, and immunoassay solutions for clinical laboratories, blood banks and transfusion centers, and is a recognized leader in transfusion medicine.

In 2014, sales exceeded €3,350 million with a headcount close to 14,000 employees in 30 countries. Approximately 80% of sales are concentrated in Europe and the United States, although other emerging areas such as Latin America and the Asia-Pacific region are gradually gaining in importance.

The company's class A shares are listed on the Spanish Stock Exchange, where they are part of the Ibex-35 (MCE:GRF). Its non-voting class B shares are listed on the Mercado Continuo (MCE:GRF.P) and on the U.S. NASDAQ via ADRs (NASDAQ: GRFS).

THREE DIVISIONS TO MEET THE NEEDS OF PATIENTS AND HEALTHCARE PROFESSIONALS

Grifols is one of the leading companies in the world in the production of plasma proteins, with a global market share of approximately 19% . Following the acquisition of the Novartis diagnostics unit in January 2014, Grifols completed its range of immunological diagnostics and is a world-leading company in transfusion medicine. In Spain it maintains its leadership in intravenous solutions.

Grifols business model is one of vertical integration, enabling it to control the entire production cycle, starting with the collection of raw material in the form of plasma through an extensive network of donor centers in the United States, and ending with the finished product. In the area of diagnostics Grifols offers comprehensive solutions that contribute to transfusion safety for clinical laboratories, blood banks and transfusion services.

The Bioscience division is Grifols' principal line of business, accounted for approximately 75% of income in 2014; it draws on the legacy of over 75 years of delivering human plasma proteins that improve the quality of life for patients with potentially life-threatening diseases. The main plasma derivatives are: intravenous immunoglobulin (IVIG), to treat immunological disorders; factor VIII, for the treatment and prophylaxis of haemophilia; albumin, to re-establish and maintain blood volume; alpha-1-antitrypsin (A1-AT), to protect against the deterioration of lung tissues (pulmonary emphysema); and other hyperimmune immunoglobulins.

In addition, Grifols is world leader in plasma collection capacity. The company owns and operates a network of 150 plasma donor centers in the United States, which daily receive more than 25,000 plasma donations, to obtain more than 7.5 million liters of plasma per year. This plasma collection capacity underpins Grifols' leadership position by ensuring a constant and reliable supply of raw material to meet the growing demand for plasma protein treatments.

For the fractionation process, plasma protein separation and purification, and the dispensing of the final product Grifols uses manufacturing sites in the United States (Clayton-North Carolina, and Los Angeles) and one in Spain (Parets del Vallés-Barcelona). Adding the three manufacturing sites Grifols' overall fractionation capacity currently stands at 12.5 million liters of plasma per year.

Diagnostics also contribute to healthcare by helping medical practitioners in the decision making process. Grifols' Diagnostic division, accounting for 18.5% of income in 2014, focuses on two key areas of specialization: transfusion medicine and clinical analysis. For development and manufacturing diagnostic products, Grifols uses manufacturing sites in Parets del Vallés, Düdingen (Switzerland), Melbourne (Australia), and San Francisco (California).

Grifols is a leader in transfusion medicine with its blood typing and NAT technology products and the manufacture of antigens for immunoassay reagents. It has become the only company to offer integrated solutions for blood and plasma donor centers, controlling the entire process, from donation through to transfusion.

Hospital Division, accounting approximately 2.8% of income in 2014, is specialized in non-biological pharmaceutical products and health supplies for hospital pharmacy. The division's main products include parenteral solutions (fluid therapy), enteral and parenteral clinical nutrition products, and hospital logistics systems.

Since 2005, the division's plants in Barcelona and Murcia (Spain) have offered third-party manufacturing services, an area where there is significant growth potential.

R&D: A PRIORITY

Grifols is listed in the top 100 most innovative companies in the world and promotes innovation through research into new therapeutic plasma proteins and the investigation of new indications for existing proteins. In 2014, Grifols invested approximately €181 million in R&D and funded research projects in its portfolio companies.

One of the principal research lines is an integrated Alzheimer's research strategy. The company's strategy for conducting research into Alzheimer's disease follows two pathways: one is directly handled through the company and the other is through Araclon Biotech. This means that a comprehensive approach is taken in the three main areas of activity: new treatments aimed at slowing the progress of the disease, an early diagnosis and the development of a preventive vaccine.

Other research lines are: Albumin in hepatology, Anti-thrombin in cardiac surgery, Fibrin biological glue and research in the field of personalized medicine. •

Nuria Pascual

Director of Finance and Corporate Investor Relations
GRIFOLS

Grifols is celebrating its 75th anniversary this year. Please tell us about the company's most impressive milestones.

Grifols' international expansion and worldwide presence originate from its early days. At the time of its founding, Spain was emerging from the war, and there were few corporations in existence. When Dr. Grifols, the grandfather of our current CEO, founded the company, he quickly formed international connections with doctors and industrialists. In fact, Grifols was one of the first companies to be annually audited, as we had international partners. (This was also a way to attract new technology.) The company consolidated the research and discoveries of Dr. Grifols along with manufacturing capabilities of international players in the plasma derivative field. This marked the initial stage of our international presence.

In the early 1950s, Dr. Grifols Jr. discovered the plasmapheresis technique, which formed the basis of the plasma industry. Currently, we receive 26,000 donations per day in the United States and almost eight million liters of plasma are processed in our facilities. The opening of our subsidiaries in Latin America was another milestone for our organization. In 2002, we began a vertical integration process and later, in 2003, we acquired our first assets in California, serving as our primary manufacturing facility in the United States. At this point, we were not only a multinational company but also a global manufacturer. Currently, we have three manufacturing facilities and source all of our raw materials from the United States. Our products are sold in over 100 countries. Since 2006, Grifols has been listed on the Spanish and American stock exchanges.

What do you attribute to Grifols' astounding success?

Prioritizing patients has enabled Grifols to experience our present-day success. We always ensure a high level of quality. Our employees are aware of the importance of doing their jobs in an accurate and safe manner. We also value our donors, as they serve as the suppliers of our raw material. Therefore, we not only take care of our patients but also our donors. Grifols has never had a recall or any manufacturing issue with regulatory bodies.

Grifols has been listed among the top 100 most innovative companies in the world. What role does Spain play in Grifols' research and development (R&D)?

We typically reinvest 6% of our revenues into R&D. This is because Grifols' focuses its research on finding new indications for existing proteins as well as new ones. We use existent and safe products to test our hypotheses. While we do research new proteins, most of our R&D is focused on trials for new indications. In our integrated Alzheimer's research strategy we have been developing AMBAR (Alzheimer Management by Albumin Replacement). This clinical trial uses a combined therapy involving plasma exchange and apheresis together with the administration of plasma proteins, in particular albumin, in different doses and regimens.

Grifols works within the fields of bioscience, diagnostics and equipment. We also work with small biotechnology companies that have select expertise.

How fluid are the relationships between large manufacturers such as Grifols and academic institutions? How can these relationships be improved?

Grifols' relationship with academic institutions plays a critical role within our R&D. In the plasma derivatives and diseases space, it is very difficult to identify patients with protein deficiencies. Because of this, we work with hospitals and foundations that focus on these specific issues and also devise tests to better detect these deficiencies. Some hospitals work with universities, which is of great value to us. We adopt an academic approach in most of our research.

Select biotechnology firms are investing in the development of personalized medicine. What are your views on the evolution of this field? What role will Grifols play?

Grifols itself is not a biotechnology company. Yet its commitment to patients has led the company to pursue a presence in biotechnology. For example, Grifols has a stake in a Spanish company, Progenika Biopharma, which is working in the field of personalized medicine, specializing in genotyping. One of its goals is to administer drugs or treatments that take into account the genetics of the patient, thus personalizing the treatment. This is beneficial and efficient for the patient and the health care system.

What is Grifols' strategic growth plan moving forward?

Grifols is working in three primary areas where we see growth opportunities. Firstly, we are seeking further international expansion of our product range. Secondly, we are working to discover new indications for existing proteins in order to find solutions to existing problems with existing medicine. Thirdly, we would like to introduce new products in countries where we already have a presence. (This applies to both bioscience and diagnostics.) In terms of growth, there is potential in Latin America, Europe and Asia. Grifols is opening new plasma donor centers in the United States because it anticipates that the plasma derivatives market will continue to grow, and Grifols will have the capacity to accommodate this growth. By 2020, we plan to have 220 plasma donor centers in the United States. •

Reig Jofre

ORIGINS

Reig Jofre was first stablished in 1929 in Barcelona (Spain) by Ramon Reig Jofre and at present it is managed by the family's third generation, with Ignasi Biosca Reig at the head as CEO.

Since December 2014 Reig Jofre is the result of the merger with the Spanish listed company Natraceutical, a transaction that gave birth to the fifth Spanish pharma company listed on the Spanish stock exchange.

FOUR STRATEGIC PILLARS

1. R&D

Reig Jofre's R&D team has a broad experience in the following areas of research:

- Bioequivalence studies.
- Clinical pharmacokinetics and bioavailability studies.
- Drug interaction studies.
- Preclinical pharmacokinetics.
- Preclinical toxicokinetics.
- Analysis and identification of metabolites.

Based on this experience, and with a specialized emphasis on the therapeutic areas of dermatology, gynecology and respiration, Reig Jofre directs its R&D to develop new pharmaceutical products or variations on known active principles in order to modify its release, improve its dosage and get new routes of administration or indications. It also develops generic specialties to be manufactured by the company and licensed. Reig Jofre has an outstanding experience in the development and manufacture of injectable lyophilized, beta lactam antibiotics, topical dermatological products and nutraceuticals.

Reig Jofre's R&D team has extensive experience in coordinating and conducting preclinical and clinical (Phase I-IV) ADMET studies required for the development both of proprietary products and of third-party products. To this end, Reig Jofre has a mass spectrometry (LC_MS/MS) service that is mainly specialized in bioanalysis and covered by a "Good Laboratory Practice" (GLP) certification.

2. OWN DEVELOPMENTS AND BRANDS

Together with the product range from specialized technologies (i.e. antibiotics, injectable and freeze-dried forms), Reig Jofre has a broad portfolio of products in its specialty areas (dermatology, gynecology and respiratory). Additionally, at the end of 2014, the company incorporated the Monegasque pharma lab Forté Pharma, one of the top brands in Europe in the field of food supplements.

In this area, Reig Jofre aims to strengthen its own brands oriented to the medical, pharmaceutical, and hospital channels as well as search for strategic opportunities to acquire new products and brands.

Image: Reig Jofre's Dosification Process

3. INTERNATIONAL PRESENCE

Together with four productions sites in Spain and Sweden, Reig Jofre has today direct commercial presence in Spain, France, Belgium, Portugal, Sweden, United Kingdom, the United States, and Singapore.

At an international level, Reig Jofre channels its goals to agreements with licensees in markets where the company has no direct presence, for the marketing of in-house-developed prescription medicines, OTCs, medical devices, cosmetics and the nutritional supplements range of Forte Pharma (out licensing).

Reig Jofre's products are available today in 130 countries.

4. SPECIALIZED PRODUCTION SERVICES

Reig Jofre has four production sites, all of them in Europe, whose specialized technology is also put to the service of other pharma companies:

The company's origins are very much bound to the production site in Barcelona, where Reig Jofre has its headquarters. This site has bespoken technology to manufacture injectable and freeze dried forms and is today a reference in the industry. Barcelona's site can also produce oral solid forms (capsules, tablets, coated tablets and lozenges), semisolid (ointments, emulsions, micro-emulsions, creams) and liquids (oral and topical solutions, syrups, liquids in single-dose sachets and swabs).

The company also has two differentiated plants in Toledo (Spain) specialized in beta lactam antibiotics, namely penicillin antibiotics in all dosage forms and cephalosporin antibiotics in vials with sterile powder.

In 2009 Reig Jofre enlarged its production capacity with the acquisition of a site in Malmö (Sweden) specializing in dermatological products, cosmetics, semisolids (ointments, emulsions, micro-emulsions, creams), liquids (oral and topical solutions, syrups, liquids in single-dose sachets and swabs), and clinical trial material.

To learn more about Reig Jofre, visit www.reigjofre.com

Ignasi Biosca Reig

CEO
REIG JOFRE

Reig Jofre was founded in 1929 as a family-owned business and has since evolved to become the fifth largest player in Spain. Please you walk us through some important milestones that have shaped its growth.

For many years, Reig Jofre has been growing by acquiring local businesses. We have always had a strong focus on the development and production of pharmaceutical products. One of the biggest milestones occurring along our international expansion trajectory was the acquisition of Swedish company Bioglan AB (specialized in topical dermatological products) in 2009. Since then, we have launched operations in the United Kingdom, where we currently sell our own products. Reig Jofre also established a subsidiary in Singapore to bring its operations to South East Asia. At the end of 2014, we merged with Natraceutical, a company that was traded on the main Spanish exchange, resulting in interesting financial and strategic synergies. Through the merger, Reig Jofre became a publicly listed company. Prior to the merger, Natraceutical was about a third of the size of Reig Jofre, but had a strong presence in a complementary business area: food supplements, through its own pharma company Forte Pharma. As a company based out Monaco, Forte Pharma already had a strong presence in France, Benelux and Spain. Since the start of 2015 we have been working together on a joint strategy to grow internationally. We are confident that together we will be able to bring about more growth in France and Spain and achieve new goals internationally.

Today, we are observing the growth of "open innovation" among companies and academic institutes. Given that Reig Jofre is dedicated to the advancement of biotechnology here in Spain, have you adopted this model into your research and development (R&D) practices?

At Reig Jofre, we are very keen on open innovation. As a medium-sized company, there are some projects that require large investment and are not aligned with our capacities. However, we are open to team up with smaller firms in order to engage in co-developments. A large portion of our R&D is conducted according to the open innovation model, in collaboration with many local Spanish firms, research centers, and universities. I also serve as president of Catalonia Bio—the local association for biotechnology companies and research and innovation firms—and am confident that many projects currently underway will succeed in the near future. These new developments will serve as opportunities for us to collaborate with new companies.

Given the current price equality requirements for generics and branded drugs, we have seen many companies shift to the production of nutraceuticals and self-care products. Is diversification the way forward?

Diversification is certainly one way forward. During the last five years in Europe, and especially Spain, the situation surrounding pricing and reimbursement has been difficult, and there have been a great deal of changes in legislation from one day to the next. It has been a time for all of us in the industry. One strategy that we have adopted is diversification into other product ranges, hence the decision to merge with Forte Pharma. However, there are other strategies as well, such as internationalization and specialization, which we have utilized to mitigate risk. Finally, we are placing firm bets on our own R&D capabilities with the aim of creating new products to license out internationally.

Today, Reig Jofre's products are in 130 countries. Which of these markets are most important to the company?

As of today, 40% of our business comes from the Spanish market, 50% from the rest of Europe, and the remaining 10% from the rest of the world. For us, the most promising area of growth is the rest of the world, where we perceive the most opportunities for future expansion. We are working hard to penetrate both the United States and Asia. Additionally, there are some countries that may not be considered very developed from a pharmaceutical perspective, that pose many opportunities. Essentially, we would like to focus the bulk of our attention outside of Spain and Europe, but without undermining our local market position.

Reig Jofre is looking to grow by acquisition. What are some reasons behind this, and in which areas are you looking to expand?

At Reig Jofre we are always considering organic growth as well as any new opportunities that arise that are related to our strategic areas (specialized production technologies, dermatology, gynecology and respiratory products, and consumer healthcare and food supplements).

Do you have a final message for the readers of this publication and those attending CPhI Worldwide?

Reig Jofre established an international presence many years ago and has since been participating in CPhI. At the moment, it is the main event for us not only to identify new partners and opportunities, but to meet with our existing ones as well. CPhI is a great event. •

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Ángel Fernandez

President-Director General
MSD SPAIN

Can you introduce us to MSD in Spain, its operations, and the role that the subsidiary plays within Merck's overall research and development (R&D) activities?

MSD was established in Spain in 1954, through an R&D agreement with a Spanish company called CEPA, which was focused on penicillin and antibiotics. In 1968, MSD established itself as a full-fledged organization that included R&D, marketing, commercial operations, and manufacturing. In the 1980s, MSD opened a center for the discovery of products and solutions to combat infectious disease. Today, the center is a joint venture with the Government of Andalucía and is located in Granada. MSD invests €50 million in R&D in Spain alone. Its total sales are approximately €800 million, making the total amount spent on R&D approximately 6% of total revenue.

What are the various strategies that can be employed to ensure sustainable growth and investment in the healthcare industry in Spain, given the recent financial crisis and its impact on the sector?

At present, total healthcare investment in Spain—both private and public—amounts to approximately 9% of the country's GDP, about 6% of which is public and 3% private. In this respect, Spain is lagging far behind other countries. France and the United States, for example, are investing much larger portions of their revenues in healthcare. While these countries are increasing the amount that they spend on sectors such as oncology research, Spain is not. In order for this to change, the overall economic situation must improve, and we need to see sustained growth. Only then can Spain confidently reinstate its growth pathways and strengthen its investments in health.

The provision of healthcare has been decentralized and transferred to various region, which offers many advantages, including proximity to decision makers. Yet, inefficiencies also stem from decentralization. The various regions and decision makers have to agree on basic rules and goals to ensure that the provision of health services is equal across the country. Currently, investment per capita in healthcare is not consistent across Spain, which will give rise to discrepancies in standards of care.

Could you speak more broadly about Spain's competitive landscape within the scope of the pharmaceutical industry? What sets MSD apart from other Spanish companies?

Spain is like other countries in Europe, where the large R&D companies are multinationals, such as Pfizer, Novartis, and Roche. Spain is also home to reputable local companies that are investing in R&D and manufacturing, for example companies such as Almirall, Esteve, and Rovi. They have excellent capacities and are performing well. MSD works in partnership with these companies to collaborate on marketing, production, and R&D. An important strategy for us is to generate alliances and form agreements with fellow Spanish companies. For example, MSD in Spain has a production partnership agreement with Rovi, who also supports our operations in other countries. We also gave Almirall the marketing rights for one of our products. MSD is a leading company when it comes to collaboration and partnership. •

Joaquin Vila

Director General
SEID LAB

To begin, please tell us about the historical context of Seid Lab, including any significant milestones that have led the company to develop its niche expertise.

Seid Lab was founded in 1958, and my family acquired it later in the 1980s. In the 1990s, the company entered the women's health sector. Towards the end of the decade, Seid Lab received a license from Pfizer for a product called Synarel, which was used in fertility treatments. Today, two local families own the company, which is comprised of 51 employees. 18 of these employees are sales representatives positioned across Spain to cover the gynecological therapeutic area. We do not sell directly to pharmacies, but instead sell to prescribers. Gynecology is our core business, and we are striving to increase our sales in this area. Currently, Seid Lab has a turnover of €10 million, and is looking to grow and increase its market share in Spain and abroad. Seid Lab has a manufacturing plant outside of Barcelona where it produces its own products, as well as products for other companies. Our technologies allow us to produce capsules, creams, gels, solutions, sachets and more. While we do not conduct research and development (R&D), Seid Lab is vertically integrated and able to develop galenic formulas and present dossiers in Spain and in other countries. Essentially, Seid Lab is primarily engaged in product development, while contract manufacturing comprises 10% of our business operations.

Seid Lab decided to enter into the therapeutic area of women's health in 1990. What motivated this change in strategy?

Seid Lab entered the gynecology sector in the 1990s, as a result of a series of opportunities that arose to distribute and sell interesting products. For example, we established commercial relations with a French company Besins Healthcare that led us to obtain authorization for the marketing of one of their products, a natural progesterone for women. Similar opportunities arose repeatedly, leading us to become specialized in this niche. Women's health is a strategic sector, as it is a non-generic market. Most products are branded, making it difficult to find many generics in this area, which is beneficial for companies like us. Larger companies are more suited to the generics business as they are able to produce large volumes.

Seid Lab's vision is to consolidate its position in Spain as one of the national reference laboratories in the scope of women's health, especially in the areas of gynecology, obstetrics, and fertility. What are some steps you are taking to achieve this goal?

As a medium-sized enterprise, we do not have the capabilities to develop new molecules. Hence, we are targeting the over-the-counter (OTC) market. This is the case in most countries in Europe, especially given recent budget constraints. Many governments are delisting reimbursed drugs in Spain and across Europe. In this regard, while the rate of OTC penetration has been relatively low in Spain, we are developing products that fit within this category. They can be publicly advertised, do not require a prescription,

and are sold in pharmacies. Seid Lab is developing drugs, medical devices, and value-added nutraceuticals within the gynecological therapeutic area and beyond. In the case of gynecological OTC products, we are able to cover multiple marketing and sales channels. This is because doctors also recommend the use of select gynecological OTC products, such as folic acid for pregnant women, for example. Thus, the channel for sales may be a doctor or pharmacist.

Many Spanish companies are looking abroad for the sale of their products. Is this a strategy that Seid Lab is interested in pursuing? If so, which markets are of most strategic importance to you?

Our primary market is Spain. But we have decided that we have to be international. The first step is developing a comprehensive product range to present to the international market. We have employed an international business director to handle international business and attend events worldwide. Through such initiatives, we are generating good opportunities, usually in the Middle East and North Africa. Our policy for each product that we launch is that its active ingredient has been used around the continent, and the market share of that product is important in Europe. These policies ensure that the product that we manufacture for Spain can be sold in other countries. In the pharmaceutical industry, regulatory processes are tedious, as each country has its respective legislation. Even within the European Union, many requirements are not standardized.

How do you characterize the competitive landscape for companies specialized in women's health, and specifically gynecology, in Spain?

There are numerous companies that specialize in this niche, and we know all our competitors very well. Yet Seid Lab is well positioned in the area of fertility and is a market leader in certain products. For example, it was discovered that 40% of fertility issues are due to problems stemming from males. In response to this discovery, Seid Lab developed a product especially for men to build their store of antioxidants. Today, we are market leaders in Spain for the sale of this product, and compete against renowned international players. Given our size, this is quite an achievement. Seid Lab has been in the business for more than 15 years, and we boast an excellent penetration rate in the Spanish market, covering approximately 5,000 of the 8,000 gynecologists in the country.

Do you have a final message for the CPhI readers worldwide?

Spain has suffered greatly in the last five years, but remains an important market. The pharmaceutical sector is key in Spain, and the government and institutions should maintain efforts to promote innovation among companies. Spain has the potential to achieve a great deal within the field. At Seid Lab, we are very optimistic about the future, especially given our strategic position within the gynecology segment. I am confident in our ability to grow our market share in both women's health and OTC segments. •

Inés Juste & Fernando García-Lahiguera Cambra

IJ: President
FG: General Manager
GRUPO JUSTE

IJ

Grupo Juste is a family-owned Spanish company that was founded almost one hundred years ago in 1922. Can you please walk us through some of the company's key milestones?

Grupo Juste was founded in 1922 by my great grandfather and began as a small laboratory in the center of Madrid. Years later, my grandfather and aunt further developed Grupo Juste's commercial and industrial divisions domestically. At the time, the company developed products according to the needs of the population. In the 1960s, my father spearheaded the internationalization of the company in Central and South America. Grupo Juste has always been driven by my father's philosophy of partnership, as he believed that companies could complement each other with their unique strengths. Today, Grupo Juste boasts strong relationships with all its partners and suppliers, and continues to thrive as a partner in many joint ventures, licensing agreements and co-promotional agreements, both in Spain and abroad. Additionally, 30 years ago Grupo Juste was the first Spanish company to obtain U.S. FDA approval and has been working there ever since. We also have a monopoly over one product worldwide in the field of contrast media.

What are Grupo Juste's primary lines of business?

Currently, we have two main business lines: pharmaceuticals and chemicals. Juste, the pharmaceutical business, works primarily within the CNS area (depression, insomnia, migraines and epilepsy) and licenses products for companies that do not have a direct presence in Spain. Grupo Juste is a pioneer of radiological contrast media internationally and has a hospital business that specifically works in contrast media agents, which is growing in other countries. This is due to the chemical side of our business, which allows us to produce our own APIs. We also boast a strong presence in Central America and have begun operations in the Middle East and North Africa, as well as in Latin American countries, with a range of products in the following fields: primary care, gynecology, SNC, and contrast media. Justesa Imagen, our chemicals business, exports 100% of its products. We have intensified research and development (R&D) efforts and production of new APIs, and work with some of the major pharmaceutical companies.

How would you characterize Spain's business environment, specifically with regards to pharmaceuticals?

The pharmaceutical sector in Spain has changed dramatically in the last six to seven years. The reduction of government expenditure in healthcare has affected all companies. The National Health System (NHS) covers 90% of Spain's pharmaceutical market, so the authorities fix the prices. Reductions in margins have caused us to adapt very quickly and institute new strategies. For example, we have reduced our debt burden in order to be more financially healthy and readapted our business model to align with new market trends. Grupo Juste has abandoned some businesses that were once successful but did not look promising in the context of the new regulatory environment. Hence, we continue to explore other markets, focus domestically within niche markets and license products that are innovative and address patient needs.

What are your growth projections for the Spanish pharmaceutical market?

Medium-sized companies need to collaborate and consolidate business. Together, we have to maintain innovative niche markets, where companies like us can continue to add value. The main threats to the pharmaceutical market are regulation, specifically with regards to pricing; market access; and cuts in healthcare spending. In the last six to seven years, the market has contracted by one third. New innovations, such the latest portfiolio in Hepatitis C and Oncology for example, have yet to be financed. The debate today is about which healthcare system we can afford to finance. Issues with low quality and service in East Asia, however, are propelling production back to Europe, which is promising for Spain.

Grupo Juste exports over 90% of its products to over thirty countries. What are the prospects for foreign market expansion of other Spanish pharmaceutical companies?

Grupo Juste is a fully integrated company that exports almost its entire portfolio to other markets. During the last few decades, Spanish companies have striven to become more international, with some going to international exchanges to raise funds to grow. In select markets—such as Central and Latin America—we have a strong presence due to our history. In other markets such as China, some Spanish companies have established a presence through producing APIs. Spanish companies must find a niche where they can perform excellently and add value. Accordingly, some have abandoned select markets such as primary care and focused on others with higher growth potential.

Do you have a final message for the attendees of CPhI Worldwide?

Spain is a good country to invest in. There are regions that boast a strong industrial presence and seek investment. Labor reform has also helped us to become more flexible and competitive globally. We have highly qualified and talented human capital and competitive labor costs. Geographically, our position is also advantageous because of proximity to Africa and the Americas. Our infrastructure and legislative structures are well established and transparent. Companies are reliable and eager to grow and be more competitive and profitable. •

Future in Flux

Generics Players Try to Stay Afloat Amidst Regulatory Uncertainty

Spain's generics market is significantly smaller in size than those of its European counterparts. According to the Spanish Generic Medicines Association, AESEG, the country's generics market represents only 18% of the total pharmaceutical market by value and 38% of the market by volume. This falls far short of the European average of 25% and 55%, respectively. These statistics imply that there is significant growth potential for the market, and consequently for cost-savings. The country's generics manufacturers, however, are facing a series of regulatory challenges that are impeding the sector's growth.

The first challenge is associated with price. Spain's Ministry of Health is responsible for drug pricing through the following mechanisms: external reference pricing, internal reference pricing, and price negotiations. Internal reference pricing is used to determine the price of drugs if a generic equivalent exists within Spain. Existing legislation compels brands to reduce the price of their product according to that of a comparable generic. In the past, there was a price differential between any given generic drug and its branded equivalent. Today, this is not the case, severely impeding competitiveness and growth within the sector. "There is a lack of fair competition in the market because of price referencing, which compels brands to reduce their prices to those of the generics. This harms the brands because they have to reduce their prices, and it also harms generics because there is no longer a gap in price," explained General Manager of the Indian generics firm Combix-Zydus Group, Juan Luis Fernández.

Many, including the president of generics manufacturer Mabo Farma, Guillermo Tena Suriani, are afraid that the incentive to prescribe generics is quickly eroding. In addition to price equality requirements, prescriptions are mandated to be written based on the active ingredient so that the consumer can clearly identify the substance. "Today, the price of a generic is required to be 40% lower than the price of a branded drug, and the brand automatically has to drop its price by 40%. This, coupled with the fact that the prescription is INN, implies that there is no reason to prescribe a generic drug over a branded one. This system is clearly not advantageous for the generic industry," said Tena.

Another regulatory uncertainty causing concern among members of the industry is the potential nationwide adoption of a pharmaceutical tender system. Because healthcare has been devolved to Spain's autonomous regions, policies remain inconsistent throughout the country. This has led to the emergence of a tender system in the southern autonomous community of Andalucía, worrying manufacturers across Spain. While tenders have been adopted across Europe in countries such as Belgium, Denmark, and Ireland, Spanish firms are resistant to this change. "There is a great degree of uncertainty surrounding the adoption of the tender system currently being used in Andalucía. In light of upcoming elections, no one is sure of what is to come. There is a risk, in the case that the tender system is adopted, that Spanish firms will have to fire their sales representatives and sell through tenders across Spain," said executive vice president of global licensing and 3P sales at Intas Pharmaceuticals, Marc Comas.

Nevertheless, the industry is evolving accordingly. AESEG is working with the Ministry of Finance and the Ministry of Health on a protocol to ensure the sustainability of the generics industry and obtain a price differential between generics and their branded counterparts.

As executive vice-president of the nation's fifth largest generics manufacturing company, Raul Diaz Varela explained: "Any generic market in the world requires certain measures of support stemming from clear pricing rules that make it easier for products to remain differentiated."

Given the state of flux, the generics market is experiencing slow growth. The average growth rate of the generics market after July 2012, when copayment was introduced, has stood at approximately 5%, down from 25% in the period up until then. Additionally, while market share continues to increase, and was 36.1% in terms of units sold as of March 2013, the sector only represents 17.4% of the market in value. Only through regulatory reform can the generics market fulfill its true potential as a cost-saving measure for the system. •

> "There is a great degree of uncertainty surrounding the adoption of the tender system currently being used in Andalucía. In light of upcoming elections, no one is sure of what is to come. There is a risk, in the case that the tender system is adopted, that Spanish firms will have to fire their sales representatives and sell through tenders across Spain."
>
> - Marc Comas, Executive Vice President, Global Licensing and 3P Sales, Intas Pharmaceuticals

Ángel Luis Rodríguez de la Cuerda

Director General
SPANISH GENERIC MEDICINES ASSOCIATION (AESEG)

AESEG was founded in 1998. What have been some key accomplishments of the association throughout its history?

Our first accomplishment was to gain visibility and make ourselves known to the central and autonomous health administrations. Today we are the reference association that defends the interests of the generic pharmaceutical industry in Spain. Our second accomplishment was to develop and promote the generics culture in Spain. Generics are known accepted as a safe and high quality product that allows financial capital to applied to other health-related expenditures such as research and development (R&D). Third, we have helped promote and facilitate society's access to these medications. While 20 years ago a particular drug may have been accessible to only 1 million people, today it is accessible to over 6 million.

AESEG recently signed a sustainability agreement with the government to resolve the issue of product differentiation between generics and branded products. Please tell us about this agreement and what it seeks to achieve.

AESEG has worked with the ministries of finance and health on a protocol to help ensure the sustainability of the system. The Spanish government is constantly seeking to realize cost savings on medication expenditure through rationalization and price revisions. In the past, this meant that generics introduced to the market were priced at a 40% discount against their branded equivalents. In this regard, we have had a regulatory framework that helped promote the development of generics. Yet this framework has been changing, and today is very restrictive to generics. For example, it is difficult to establish price differentiation from branded products. The law states that when a generic enters the market, the branded equivalent must match its price. There used to be a reasonable time period, between six months to one year, when generics were sold at a 40% discount, allowing them to gain market share. Without this time period, it is difficult to successfully introduce a product. We need a regulatory framework that does not force a branded product to match the price of a generic, so that the brand can compete in the private market (which is about 20% of the market) while we are able to introduce the generic. There was a copayment system in place that we are trying to reclaim. Both ministries have established protocols with associations such as ours, in which they asked us to help free up financial instruments that would enable us to promote generic products and obtain the price differentiation that we seek.

Spain is unlike other European countries in that it is separated into autonomous communities, which have the authority to dictate their own health policies. These entities finance medications and run their own reimbursement programs. Ideally, we would have a consistent framework applied to all communities, but this is not the case in reality, and each community progresses at a different pace in introducing a particular generic product. Additionally, some communities launch their own initiatives that are contrary to those of the central government. The Andalusian auctions, for example, grant exclusive rights to the drug to whomever bids the lowest price. In all of these auctions, no member of AESEG, which represents 95% of the industry, has been awarded rights. Most of the time they go to small, opportunistic firms that do not contribute much to the GDP, forcing us to cut production and employment. This program also limits the access of Andalusian citizens to one product as opposed to having a wider range of products to choose from.

Given these challenges, how do you expect the association and the generics industry to evolve?

The future will be based on four pillars. The first is the rhythm at which patents will expire and allow new generic products to enter the market. The second is that the pace of generics development must keep up with the rhythm at which patents expire. Third, it is crucial that the central administration continue enforcing measures to promote generics in order to increase savings for the system and expand access to medications for its citizens. Finally, it is important that prescriptions continue to be given based on the active ingredient and not specific to the branded product, so that the consumer can identify clearly what substance they are taking.

Many generics manufacturers are looking to export markets for growth. Are they the future for the generics sector in Spain?

Despite the crisis, there has been a serious commitment on the part of our industry to provide employment. We directly employ over 8,000 people and 5,000 indirectly, and have maintained these levels throughout the crisis. Our sector is also committed to maintaining production—seven out of 10 generics that are consumed in Spain are produced in the country. We have also been able to increase productivity and reinvest 3.5% of these profits into R&D, so that new generic products are accompanied with better technologies. Finally, the sector is committed to increasing exports, which have grown by 30% to 40% in the last five years. This shows how important generics are to Spain's GDP as an industrial sector. •

Guillermo Tena Suriani

President
TEDEC-MEIJI FARMA
General Manager
MABO-FARMA

Can you provide us with a brief historical introduction to Tedec-Meiji, including some key milestones that have shaped its presence today?

Tedec-Meiji was founded in 1990 here in Spain, and today is comprised of two laboratories: Tedec-Mejii Farma and Mabo-Farma. The former manufactures new chemical entities and medical devices, which are either exported via licensing agreements, or developed as a result of research and development (R&D) activities conducted in Spain and Japan. Our second laboratory, Mabo-Farma, specializes in the manufacture of generics for the local Spanish market. Our turnover is currently about €50 million; €20 million come from local Tedec-Meiji sales, and €14 million from Mabo-Farma. The rest of our revenue is generated through exports. Tedec-Meji has several license agreements with foreign countries, both on our own and through Meiji Japan, for our best-selling product Adant.

This year, we fulfilled U.S. FDA requirements for the sale of Adant in the United States, and thus we hope to export our product there soon. Here in Madrid, we currently have 25 people working in our R&D center, who are developing, among other products, generics for Japan. Tedec-Meiji is the first pharmaceutical company from Spain that will be exporting pharmaceutical products to Japan in the coming years. We have successfully fulfilled regulatory requirements in many countries and for numerous companies. Tedec-Meiji has a promising future despite the condition of the pharmaceutical market in Spain because we have a strong partner in Japan and open markets for exportation.

How has the generics market evolved in Spain, and how does this evolution align with Tedec-Meiji's goals and targets?

The generics market in Spain has evolved a great deal. Initially, there was a price differential between a given generic drug and its branded equivalent. At present this is not the case, which is a major problem. Initially, the price of a generic drug was 25% below that of a branded drug, and the manufacturer of the latter was not obliged to cut its price (we did not have reference pricing at the time). As the patient and doctor were both aware of a 25% reduction in price, doctors prescribed the generic in order to save money for the system. Today, the price of a generic is required to be 40% lower than the price of a branded drug, and the brand automatically has to drop its price by 40%. This, coupled with the fact that the prescription is INN, implies that there is no reason to prescribe a generic drug over a branded one.

Where you think the generics market is headed?

In Spain we have 20,000 to 25,000 pharmacies, which are all independently owned businesses—the Mediterranean model—that works quite well. The emergence of larger pharmacy chains is unlikely to emerge in the next five years, but we do face the risk of tenders, like the one that has emerged in Andalucía. Regardless of whether this system becomes more widely adopted, the generics industry in Spain must survive. •

Juan Luis Fernández

Director General
COMBIX-ZYDUS GROUP

Juan Luis, can you begin by telling us about your background within the industry?
I began working in 1985 as a chemist and in 1988 became a sales representative. I gradually moved on to the management of large accounts, which allowed me to develop my knowledge of pharmaceuticals and marketing. Specifically, I worked with prescription drugs, over-the-counter drugs, and generics. In 2001, I began working in generics, and have continued to do so since then. My professional career has provided me with great exposure to the technical and regulatory aspects of APIs and generics.

What led to the establishment of the generics market in 2001?
The generics market has various distinctions compared with other markets because it is a completely different segment. Before 1992, patents worked differently in Spain, where copies of the branded products were more prevalent than generics. When real generic drugs entered the market, these companies realized that copies had already occupied the entire market share.

What are some challenges that remain that are inhibiting the development of the generic market in Spain?
There is a lack of fair competition in the market because of price referencing, which compels brands to reduce their prices to those of the generics. This harms the brands because they have to reduce their prices, and it also harms generics because there is no longer a gap in price.

What is the structure of price referencing in Spain?
A majority of European countries use similar mechanisms, however the difference lies in the implementation of such structures in each country. Reference prices indicate a price that brands will get reimbursed for. There have been talks with health authorities to generate attention to generics, without which the market will continue to suffer.

What led to the decision to establish Combix in Spain as opposed to any other region?
Zydus is a successful and global company with strong presence in the United States, India and Asia Pacific. It is challenging to operate in competitive markets such as Europe, but the will of the company allows it to succeed in this market. The company is well positioned in France and Spain, two countries that have strict regulatory frameworks, further highlighting Combix's high standard for product quality.

What are some growth projections for the Spanish market compared with other markets globally?
In Spain, Combix is still modestly positioned, given our entry into the market in 2007. We have developed in the last eight years and are attempting to duplicate market growth and generate high volumes until we achieve sustainable performance. Our sister company in France boasts significant turnover, and ours is modest in comparison. Nevertheless, we are a small but dynamic organization.

Where are most of your manufacturing and research and development facilities that serve the Spanish market?
Currently, about half our products are manufactured in Europe and the other half in India. We are in the process of transferring some of our manufacturing sites to our factories in India. Within Europe, majority of our manufacturing occurs in Spain.

What is the impact of currency volatility on Combix's cost structure?
The currency volatility has had a strong impact on our cost structure, as the Euro has weakened considerably. This has created an imbalance as our revenues are in Euros.

What strategic initiatives are you planning to implement for the rest of 2015 to stimulate growth?
We are planning to add products to our existing line in order to build a more competitive portfolio. We will launch therapeutic products and additives, to name a few.
Are there certain products that are not practical to sell in Spain due to high costs?
Some antibiotics such as Amoxicillin do not generate substantive profits, as there are few APIs for these products, thus raising the cost of raw materials. However, it is important to offer these products on the market in order to meet consumer demands.

What do you hope to achieve with regards to research and development by 2020?
Combix currently invests 15% of revenue in research and development in Spain, some of which is allocated for the further development of approximately 20 products per year.

Where do you see Combix in five years?
In 2017, many product patents will expire for generics. Hence the period from 2017 to 2020 will provide an opportunity for Combix to expand within the generics market. Additionally, we are already commercializing biosimilars in India, which we hope will occupy a large market share by the year 2020. By securing a large customer base, Combix is targeting revenue of €24 million by 2020, which will ensure a sustainable future for the company.
What is your final message to the readers of this publication, including investors and government representatives?
The pharmaceutical industry needs to add value to the sector by investing in research and development. As patents expire, the industry needs to offer cheap products, as this is the only way to ensure market sustainability. •

Marc Comas

Executive Vice President,
Global Licensing & 3P Sales
INTAS PHARMACEUTICALS

Please introduce us to Accord Healthcare here in Spain, including any historical milestones that have led the company to establish its dominant market position today.

Intas is headquartered in Ahmedabad, and remains one of the largest companies in India, generating one billion dollars in sales each year. Ten years ago, I founded Intas Spain, which is today the global headquarters for Intas, comprising management and key departments to service our customers' needs in the context of licensing generics. Traditionally we manufactured products for other companies, operating at a B2B level. Today, we boast a large portfolio of generics developed by us that we out-license to third parties all over the world.

As the company grew, some years ago Intas decided to invest in the placement of Accord Healthcare directly on the market. Today, Accord Healthcare is primarily a hospital company, through which Intas' products are marketed and sold.

What was the strategic decision behind the founding of Intas Spain?

At the time, Intas had one manufacturing site, annual revenues of $100 million, and a fully equipped GMP site that needed to be utilized. Intas recruited me to attract contract-manufacturing business for the company. Over time, instead of waiting for large companies to approach us, we began out-licensing our own portfolio of generics, and today, our contract manufacturing business is limited.

The launch of Intas' first biosimilar in Europe was a key milestone for the company. How do you think the landscape for biosimilar production will evolve over time?

The biosimilar market is very tough because companies invest millions in their development, almost akin to that of a new chemical entity. Then, registrations are necessary and price referencing system requirements compromise profit margins. Additionally, there is a tender issue. There is great uncertainty surrounding the biosimilar market. For the first time, biosimilars will be used for the purposes of treatment, when in the past they have been used solely to support therapies. Intas is the biggest producer of biosimilars in India with a huge pipeline of ten biosimilars that are fully developed and produced by us in our GMP certified facilities. In light of this, we are aiming to bring all of our products to regulated markets, including the United States.

What are some specific growth targets that Intas has for Accord Healthcare?

We are very focused on our extensive pipeline, and aim to bring 50 products currently under development to the market. We want to be a one-stop shop as far as the hospital pharmacist is concerned, as it is our key stakeholder. We will continue to apply to as many tenders as possible. Additionally, as far as packaging is concerned we try to gain as many points as possible in the tenders. We have packaging facilities and labs in the United Kingdom, and recently opened up a new lab in Barcelona for testing and release. We are a profitable company and will also remain vigilant for any opportunities to grow inorganically. •

The Search for Growth
Supply Chain Dynamics

"In recent years, regulatory control and security measures have increased in the market. Customers want to know more about product origin and quality. At present CEP and GMP regulations are mandatory in Spain, and Safic Alcan has also obtained GDP (good distribution practice) classification to ensure maintenance of product safety and quality during distribution."

- Jaume Fortea, Managing Director, Safic Alcan

Image: TEDEC-MEIJI FARMA

Supply Chain Optimization

Striking a Balance between Quality and Price

Image: TEDEC-MEIJI FARMA

Increased international regulatory requirements have pressured all industry stakeholders to rethink their strategies. Issues with low quality and incidents of contamination have pushed players to demand higher quality raw materials across the board and examine their pharmaceutical supply chain more closely. As President of EMEA & CEO of Qualicaps, Ciro Ahumada said: "Globalization begs quick development and demands high quality."

While this pressing demand may serve as an opportunity for European producers to reclaim some of their market share with the production of high quality products, stringent regulations place heavy cost pressures on all parties, including the end consumer. "From a regulatory standpoint, requirements in Europe and the United States are becoming progressively more complex with regards to quality and GMP. Thus, we observe an increasing demand for auditing and verifying the quality of raw materials from API producers," said the president of Asociación Forum Auditorias (AFA), Octavi Colomina.

While Asian powerhouses China and India have long since established themselves as hubs for the supply of raw materials, the quality of Asian products is often not up to par. "These two regions are without rivals in the production of pharmaceutical raw materials that fall below the $100/kilogram threshold. This is also true for chemical intermediates, most of them coming from India or China. However, Europe maintains a competitive advantage for the production of raw materials priced above this threshold, especially for specialized care markets like oncology," said president of SUANFARMA, Héctor Ara Sanz.

In light of this trend, many Spanish players are optimistic about their chance to step in and claim their share of high quality production. Local API producer Gentec, for example, has ventured into the production of high potency active pharmaceutical ingredients (HPAPIs), and is investing in one of the world's few GMP certified HPAPI plants. "Such regulations could be a good opportunity to serve as a barrier for competitors and for us to excel within our niche," said Gentec CFO Daniel Pérez.

Although increased regulations may pose as an opportunity for Spanish suppliers, they also impose higher production costs. A plethora of new requirements are aimed at increasing visibility across the chain, which is convoluted and difficult to control across its entirety. These measures drive production costs up which are eventually transferred to the consumer. For example, compliance with new temperature control requirements means the implementation of new processes. "We are content and satisfied with the regulations in Spain, as we believe that strict regulations are beneficial to ensure high quality of pharmaceutical products. However, there are some challenges associated with these regulations, such as compliance with temperature control requirements. State-of-the-art technology is required to control both humidity and temperature, and when the temperature rises above what is expected, it is difficult to control for quality. This is most challenging when products are held in customs," explained president of Disproquima Jordí Sanchez.

Other requirements, such as those related to traceability, imply that drug manufacturers have to spend more on altering packaging accordingly. Additionally, new GDP (good distribution practice) requirements for distributors have been issued. Today, a staggering 80% to 85% of costs associated with medicines are due to indirect labor costs.

"Companies are forced to employ more quality control and assurance personnel to comply with regulatory requirements, as well as automation and new good distribution practice requirements, driving costs of production further up. These adjustments are reflected in the final price of the product," explained Colomina of AFA.

AFA is working to establish a program and methodology that will ensure the quality of raw material manufacturers that are supplying to API producers. A few years ago the firm also began auditing distributors and warehouses. Many would agree that in the field of healthcare, these initiatives are paramount in ensuring quality and safety and eventually striking a balance between price and cost. •

Sergi Trilla

CEO
TRIFERMED

You founded Trifermed in 2002. Please begin by providing us with a historical perspective of the company's evolution.

I founded Trifermed thirteen years ago, as a result of my personal experience, both as a medical doctor and within the industry in various medical and marketing roles. Trifermed provides business development and management services to companies within the life science market. We like to call ourselves a life science business partner, as we support a diversity of players from startups to well established multinationals (local subsidiaries) with their business management needs.

Initially, we supported European players by introducing their existing products into Latin American markets. We then transitioned to serve European pharmaceutical companies by sourcing commercial distributors for them within Europe. In 2007, I seized an opportunity to collaborate with Biocat in Catalonia, to assist and train entrepreneurs in the field of business development. This marked our entrance into the biotechnology sector, (a shift from commercial assets to underdeveloped assets) which today ranges from the development of partnerships, sourcing of co-development opportunities, industrialization, capital raising and coordination of regulatory expertise (provided by third parties), to name a few. That year, Trifermed began its operations in Canada, where we successfully helped a small startup company out-license their product to a large multinational in Europe. In 2012, we recognized the need to establish a more international presence, and upgraded our project management services to more sophisticated e-cloud platforms. We set up our first regional affiliate in London in 2013, and established Trifermed in Germany, Canada and Australia in 2014. Today, Trifermed also has sales offices in Mexico and Boston.

Trifermed formed an alliance with the intention of satisfying a need for additional expertise in partnering teams to move forward on the life sciences value chain. How does this alliance fit within your business model?

Formed in 2012, Trifermed alliance is a team of selected service providers. It was founded upon the conclusion that any given project requires a variety of expertise. For example, when managing a project, Trifermed requires local experts on regulatory processes and sometimes even within specific therapeutic areas. Our alliance consists of experts on market access, public funding, regulatory procedures, intellectual property and many more areas. This selection of service providers is growing, allowing us to refer one another and work together to serve our clients. We never incorporate any company into our alliance prior to working with them.

What is your typical client profile?

Today, our clients are equally split within the biotechnology and pharmaceutical sectors. We regularly work with subsidiaries of multinationals requiring local assistance, medium-sized pharmaceutical companies looking to expand their presence internationally, and small biotechnology startups. We support startups across all stages of development including incorporation, business modeling and strategy and selling and licensing of products.

What is the competitive landscape for service providers such as Trifermed?

The competitive landscape can be divided into two major segments. The first is comprised of former c-level business development executives, marketing their knowledge, expertise and network, on a personal basis. The second includes well-organized business development firms, largely concentrated in the United Kingdom. Currently, the market is not very crowded, and is growing steadily due to increased demand for our services. The value chain is becoming progressively more fragmented, more expertise is required, and the need for partnering is growing.

Trifermed is associated with nine academic institutions and situated within the ESADE Innovation Park. How do you utilize academic resources and collaboration to help achieve your operational goals?

Trifermed's intensive academic involvement and activities have several advantages. Firstly, being a professor, mentor, and member of the Entrepreneurships Institute at ESADE, helps us to remain consistently updated. We are active players within the knowledge economy, and being linked to a university such as ESADE guarantees our latest knowledge in business. Secondly, academic engagement is a great opportunity for us to offer our knowledge to different programs worldwide, while simultaneously learning form entrepreneurs through programs such as Biocat and ACCIO. And finally, such types of collaboration serve as a marketing channel for Trifermed.

Trifermed works with numerous startups and entrepreneurs in biotechnology. What is the most pressing challenge they are facing today?

The primary challenge is not lack of capital. Instead, there is a lack of economical value propositions that are good for both the patient and the healthcare system. Today, it is simply not enough to offer a value proposition for a certain niche. Entrepreneurs need to consider the related cost, as most health systems, especially public ones, have limited budgets. They are faced with an ageing population and need to manage expensive, chronic diseases. Hence, costs are increasing every year. The biggest challenge for new startups is not only to find health solutions but also to discover solutions that provide savings. •

Ciro Ahumada

President of EMEA & CEO
QUALICAPS

Qualicaps has a multinational presence, why did the company choose Spain to establish their European operations?

Qualicaps originated as part of Eli Lilly and Co., which had manufacturing sites in the UK, Benelux and Italy. Eli Lilly and Co. wanted to consolidate their operations into one site, and chose Madrid to do so. Eli Lilly and Co. then sold Qualicaps to the Japanese pharmaceutical company Shionogi and Co., Ltd. Hence today we have manufacturing sites in Japan, the United States, and Europe. All three were created and developed by Eli Lilly and Co. and further strengthened by Shionogi and Co., Ltd. who later sold Qualicaps to The Carlyle Group. While in the hands of this venture capital firm, in 2008, Qualicaps opened a state-of-the-art production facility in Romania. Today, as a wholly owned subsidiary of Mitsubishi Chemical Holdings Corporation, we have two important sites in Europe.

Can you introduce us to Qualicaps here in Spain? What percentage of your manufacturing takes place here?

Large pharmaceutical firms conduct 75% of their research and development (R&D) in the United States and Europe. Because of this, it is a great competitive advantage for Qualicaps to be present in Europe, and strengthen longstanding relationships with these companies. Many global pharmaceutical companies are located in the core EU5 and Switzerland, which allows us the opportunity to work with the originators and build a strong base to continue within the field of generics. Today Qualicaps manufactures its products in Japan, United States, Romania, and Spain. From Spain we manufacture our gelatin capsule (Quali-G™), our HPMC capsule (Quali-V®), which was the first of its kind, and our specially designed inhalation capsule for use in Dry Powder Inhalers (Quali-V®-I), also an industry innovation.

What is Qualicaps' competitive advantage?

Qualicaps has over 115 years of experience in pharmaceutical capsule manufacturing, and its consequent longstanding relationships with global and local pharmaceutical companies are important assets. The global pharmaceutical industry has evolved greatly with regards to regulation by way of consolidation, mergers and acquisitions. These changes require companies to have a solid understanding of proceedings, and an ability to support swift change. Qualicaps is able to handle registration flawlessly, even in the complex European region, where each country has distinct regulations. We engage with our key interest groups beyond customers, such as relevant industry associations and regulatory bodies, and collaborate with many organizations from suppliers to universities. Due to our history, our partnership with customers, and to other stakeholder interactions, at Qualicaps we have a 360-degree vision of what ultimately affects patients and what they need within the healthcare system.

As recently appointed CEO in March, you developed two main global strategic objectives. Could you expound on each objective and its relative importance to Qualicaps moving forward?

The first is to accelerate growth and international expansion of Qualicaps to become a more efficient global partner, and the second is to strengthen the company's competitive advantage within an increasingly challenging industry.

Clearly one of the most dramatic movements we have seen in the market during the past decade is the globalization of companies. They are operating all over the world, and thus we need to understand the customer base much better in the global sphere. The first step is to examine the BRICs, as the entire world economy is looking at Brazil, Russia, In-

dia and China in the context of the ways in which they can improve healthcare. It helps to understand how important it is to look at health globally, even from a capsule perspective. For example, for many years pharmaceutical companies used gelatin almost exclusively as the raw material in the production of capsules. We were the first to launch the HPMC capsule—a plant-based capsule. We invent in order to adapt to the needs of customers and patients for different alternatives. On an international level, we have to continue along the path of innovation and understanding the needs of individuals and society.

The second step is to remain ahead in the field of technology, and live up to our motto: "Engineered to perform." Globalization begs quick development and demands high quality. We can further develop the use of capsules against those of the tablet or pill. More and more complex molecules and new technologies are helping to speed up development of new medications. Technology and science are key competitive advantages in which we will continue to invest.

What new innovation has Qualicaps recently brought to the market?

Qualicaps recently launched an inhalation capsule, and as such quickly became the leader for using capsules within specific therapeutic areas. Initially, we were competing with tablets because the method of ingestion was only oral. But now through dry power inhalators, the capsule is a much more versatile device to deliver medication.

What are some of Qualicaps' strategic goals for the next three to five years?

First, Qualicaps aims to align both its operations and values with those of the Mitsubishi Chemical Holdings Company. We would like to embody the group's concept of value, or "KAITEKI", which is the ability to add value to individuals, society, and the Earth. Whatever we do, we do with great responsibility, and hence we seek to do things right. Secondly, we are investing heavily in the proper management of resources, to eliminate waste and inefficiencies associated with production. The third strategic goal is for Qualicaps to strengthen its contribution to health, not only within pharmaceuticals, but also in the field of nutrition and wellbeing. We have a great role to play in preventive medicine, and we want to ensure that each person within our organization is eager to contribute in this direction. Our long-term goal is about globalization, as previously mentioned, as Qualicaps must be present throughout the world and deliver health to all of society. •

Jordi Sánchez

President
DISPROQUIMA

Disproquima celebrates its 40th anniversary this year. Please tell us about the company's historical evolution within the Spanish pharmaceutical market.

Disproquima was founded in 1974. Years later in 1991, my family acquired 100% of the company, of which we continue to be the sole owners today. In 2002, we conducted our first international acquisition in Portugal, where today we have our own logistics and GMP platforms from which we can serve the Portuguese market. In 2009, we established Disproquima Morocco in Casablanca, and some years later, set up an office in China. From our China office, we have 10 people working to source products for both import and export. In 2011, Disproquima acquired a company in France, established a subsidiary in Germany, and purchased new facilities in Spain. In 2013, we founded Disproquima Brazil in Sao Paulo bringing us to four continents, with offices in China, Brazil, Morocco, Portugal, Germany, France, Italy, and Spain, where we are headquartered. Today, we are a team of 70 worldwide with an annual turnover of €50 million.

Disproquima caters to various segments within the life sciences market. How important are pharmaceuticals to the company's revenue?

Disproquima offers a wide range of services and products to the pharmaceutical sector, which is responsible for approximately 50% of our revenue. Our vision is to provide our clients with the products they need, and we aim to do this by serving the life sciences field at an international level. We source products globally, including APIs, excipients, and finished dossier forms (FDFs), to name just a few. At Disproquima, we are also active outside sales and invest on all levels, including technological development and patent studies.

What is Disproquima's competitive advantage in the market?

Disproquima's relationships with both customers and suppliers are very important to us. Because of our worldwide presence on almost all continents, we are able to ascertain valuable information that helps us provide our customers with what they want. We also have dedicated sales teams and project managers for each line of products.

Disproquima maintains a strong presence in countries all over the world. Are there any new markets of interest that the company is looking to penetrate in the near-term?

In terms of market penetration, we are trying to be very active. Disproquima is working to enter the Asian market, specifically focusing on India, Korea, Vietnam, and Japan. We strongly believe there is opportunity for growth in the pharmaceutical industry within these emerging markets. Additionally, we are working to place our staff in the United Kingdom, Turkey, and North-Central America.

Today, we are observing tremendous growth within the personal care market. How has this affected Disproquima's business?

Disproquima's commitment to the personal care industry has been solid for the last 15 years, evolving according to market needs and trends. Today, we have an exclusive team devoted to the support and development of new products, as well as technical, regulatory and commercial advisory. The pharmaceutical industry in Spain is suffering, which compels companies to seek alternatives. One of the easier alternatives has been to resort to personal care. Disproquima is here to help companies adapt to this trend and cover the personal care segment by bringing relevant products to the market.

Given the emergence of stricter and more complex regulatory requirements, including demands for product traceability and distributor audits, measures to ensure quality are being implemented throughout the supply chain. How do these requirements affect your business?

We are content and satisfied with the regulations in Spain, as we believe that strict regulations are beneficial to ensure high quality of pharmaceutical products. Yet there are some challenges associated with these regulations, such as compliance with temperature control requirements. State-of-the-art technology is required to control both humidity and temperature, and when the temperature rises above what is expected, it is difficult to control for quality. This is most challenging when products are held in customs, for example, and is one area where the authorities can improve. Disproquima's next initiative is to establish a quality control laboratory, for which we are currently in discussions with the Spanish authorities to obtain the necessary approvals.

How would you characterize the competitive landscape for distributors like Disproquima?

There are too many players in the market, several of which find it difficult to comply with regulations and abide by the required quality standards. Financing is also an issue for some of these companies. For these reasons, the number of pure distribution companies will decrease in the coming years, leaving the companies that remain well positioned in the market.

What are some strategic goals that Disproquima is hoping to realize in the near-term?

We hope to expand our global presence, and aim to enter the American market within the next three to five years. Additionally, Disproquima is always open to acquisitions.

Do you have a final message for attendees of CPhI Worldwide in Madrid?

All pharmaceutical companies should enforce strict standards to ensure the high quality of their products, as this will benefit customers and the industry alike.

The market will change significantly in the coming years, and Disproquima´s goal is to lead this evolution as a services and solutions provider and partner. •

Octavi Colomina

President
ASOCIACIÓN FORUM AUDITORIAS (AFA)

You hold positions as the technical director of TDV as well as the president of AFA. Please introduce us to both organizations briefly and provide us with an overview of AFA's service offering.

TDV is a consultancy firm, specializing in GMP and regulations, primarily within the pharmaceutical industry. We have been in this sector for over twenty years and provide validation, auditing and quality and consultancy services, to name a few. Ten years ago, we became heavily involved in the provision of supplier audits, but the number of audits demanded increased, and we found ourselves auditing the same supplier for various customers. Thus, we spearheaded an initiative, AFA, which benefited all parties— pharmaceutical companies (our customers), suppliers, and regulatory authorities—through the performance of joint audits. AFA was formed as a third-party auditing organization, initially comprised of an affiliate network of Spanish pharmaceutical companies. The initiative drives costs down by providing companies with a novel option of sharing costs and saves suppliers time by avoiding repetitive audits. Today we are a non-profit association of pharmaceutical companies, and have been operating as such for the past ten years. Our network has expanded to other countries in Europe, North America and Asia, which constitutes the bulk of our business. We have also created an important database of over 400 audit reports that are available to those companies in search of supplier audits. These reports, however, are tailored to the requirements of every given customer. In the past five years, the distribution of reports has grown to be a significant business activity. AFA boasts a growing team of highly qualified personnel to perform audits worldwide across the United States, India, Europe, Israel, and China, allowing us to offer competitive prices.

Today, there is growing demand for higher quality raw materials. How has AFA perceived the results of this increasing demand? What effect has it had on the need for audits?

Our final customer is the pharmaceutical company, and approximately 70% of all the suppliers that we audit are API producers. From a regulatory standpoint, requirements in Europe and the United States are becoming progressively more complex with regards to quality and GMP. Thus, we observe an increasing demand for auditing and verifying the quality of raw materials for API producers, who are experiencing pressure from pharmaceutical companies to do so. Three months ago, we pioneered an initiative to promote this kind of audit, which will be released next year. This trend has taken hold largely due to incidents of quality issues, stemming from lack of control among suppliers. Raw materials suppliers perform quality tests according to their own specifications and will not detect impurities outside these tests. Fortunately, there are many measures of control implemented within the supply chain, and in the most cases issues are detected in some link of the chain. Yet changes in factors such as facilities or technologies can often result in contamination. Additionally, it is difficult to implement quality standards across the supply chain, especially beyond the scope of pharmaceutical companies and API producers. For example, quality standards are not the same in the chemicals industry, whose members may comply with the same requirements. At AFA, we are working on a program and methodology that will ensure the quality of raw material manufacturers that are supplying to API producers.

Regulatory and quality requirements are getting progressively more complex and strict, driving costs of

production up. (Indirect labor costs now account for 80% to 85% of costs associated with medicine.) Is there a future for standardization across countries? How does this affect AFA?

The standardization process has already taken hold. Globalization of the pharmaceutical industry has led regulatory authorities to demand similar requirements across the world. Standards are coalescing, and companies have to get themselves up to the level on par with the FDA, the European Union, and other authorities. This does not drive costs down, though. In fact, costs are increasing. The burden of new quality requirements, and the implications that they have for companies are very high. Companies are forced to employ more quality control and assurance personnel to comply with regulatory requirements, as well as automation and new technologies, driving costs of production further up. These adjustments are reflected in the final price of the product.

AFA organizes conferences on the control of the supply chain of pharmaceutical raw materials and is well acquainted with suppliers of all kinds. What are some challenges that AFA has identified along the pharmaceutical supply chain?

The challenges in Spain are the same as they are elsewhere in Europe and the United States, given that supply chains in these countries are similar. One universal challenge is the difficulty associated with traceability. It is challenging to track a given product throughout a complex supply chain comprised of warehouses, suppliers, brokers and other stakeholders, as a stakeholder does not have control over the product along the entire length of the chain. Two years ago, AFA started an initiative to audit and control distributors and warehouses. We began a campaign and audited approximately fifteen distributors in order to observe practices, quality systems and warehouse management. Since then, we have continued to audit distribution and transport companies to help provide security and visibility along the supply chain. This is not easy given the number of players involved. To maintain quality, it is necessary to remain consistent and comply with standards across the entire supply chain. Even if a given manufacturer is performing well and in accordance with quality requirements, once the product leaves the warehouse, such measures are not always implemented thereafter. Today, the pharmaceutical industry is facing this challenge, and AFA is working to address it.

Do you have a final message for attendees of CPhI worldwide?

As members of the industry, we should look for the best suppliers of APIs and materials. In this regard, price is important, but quality is also crucial. Hence we should strike a balance and refrain from attaching too much importance to price, which could result in serious setbacks. Fortunately, many companies today are considering all the factors to determine who their suppliers are going to be and are taking into account quality and price according to the right ratio. •

Spain's Strategic Sector Biotechnology

"From a biomedical perspective, Spain is well positioned due to the high quality of the country's educational institutions (schools of medicine, pharmacology and biology) and basic research capabilities, which are recognized around the world. We also boast strong healthcare services, both through the public health system and our first private hospital in Spain: University of Navarra Hospital."

- Dámaso Molero, General Manager, 3P Biopharmaceuticals

Image: Vlad Teodor - Shutterstock

Breaking Biotech

Spain's Place in the Global Biopharmaceutical Industry

Spain's biotechnology industry is a strategic sector for growth within the country's larger economy. According to the Spanish Bioindustry Association, ASEBIO, Spain's biotechnology sector contributed to 9% of the country's GDP in 2014. The sector is comprised of 554 pure biotechnology firms, employs 173,000 people, and is second in the world after the United States by total number of biotechnology firms. Just last year, 58 new biotech firms were founded. And while the sector has come under pressure as a result of the economic crisis, 976 patents were published last year, up by 8% from the year before, indicating recovery on the horizon.

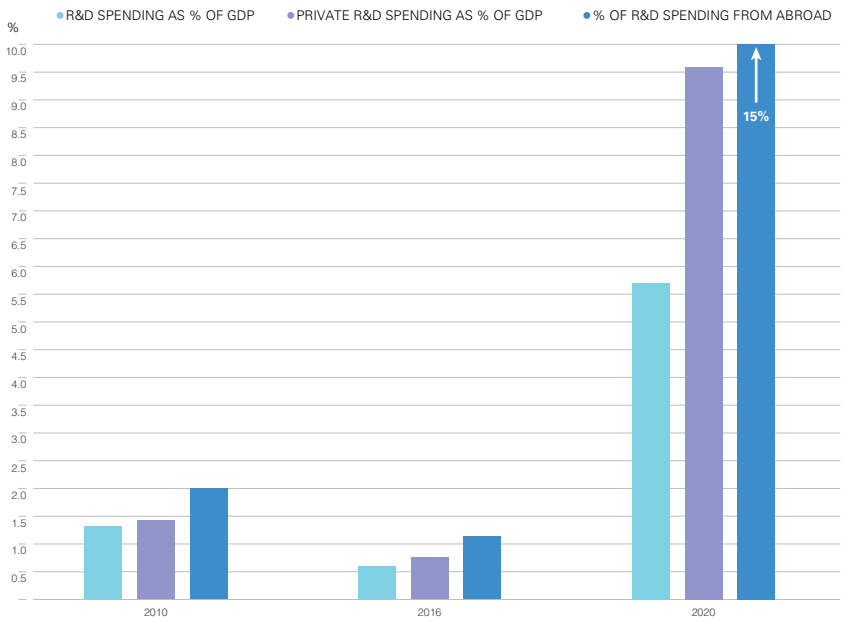
Today, the autonomous community of Catalonia is home to the highest concentration of biotechnology firms (14.9%), followed by Madrid (12.1%) and finally the Basque Country (11.9%). In fact, three of the world's 25 most reputed scientific centers in the field of health are located in Catalonia, alongside four science and technology parks. According to the government of Catalonia, the region produces 1% of the world's scientific output and invests 1.7% of its GDP in research and development (R&D).

Spain's industry has evolved due to the country's well-developed research capabilities, highly talented human capital, and prevalence of public and private assistance programs. While many claim that Spain lags far behind other players in terms of public and private investment, there are select programs in place to promote the development of the sector both at home and abroad.

Founded in 2008, EuropaBio, for example, manages an internationalization plan for the Spanish biotechnology sec-

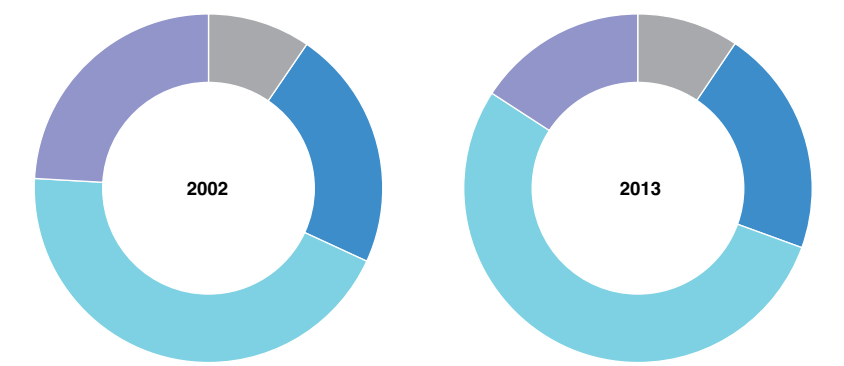
R&D SPENDING (2010-2020)

Source: Farmaindustria



SPENDING ON CLINICAL RESEARCH (2002 VS. 2013)

Source: Farmaindustria



	2002	2013
Phase I	9.6%	9.5%
Phase II	22.5%	21.2%
Phase III	43.9%	53.7%
Phase IV	24%	15.7%

Image: Shutterstock

tor, helping to promote and facilitate cross-border expansion. Various innovative public spending efforts are in place, including InnovaSUMMA, Castilla La Mancha's CLAMBER project (through which the EU has invested €20 million into a bio-economy project), and the SUMMA project. Spain's Ministry of Economy recently established an agency devoted to innovation that was included in the new law of science. "The government is promoting transnational cooperation among companies, universities and research and technological centers, as well as implementation of sectorial technology platforms such as the Biotech Platform (managed by ASEBIO)," said President of ASEBIO, Regina Revilla.

Biotech firms utilize the Center for Industrial Technological Development (CDTI) in Madrid or ACCIO in Catalonia to secure public funding. ICREA has also been established for the last 15 years with the aim of promoting R&D in Barcelona. Yet many R&D assistance programs have limitations, especially for members of the biotech sector. "Spain remains far from adopting a mentality similar to that in the United States, where research grants are issued. Here, loans are granted in a field where commercial success is far from guaranteed. About 20 years ago, angel investing and other means of raising capital were nonexistent. Nowadays, there are more associations emerging to invest in startups. For example, ESADE has a business angels association to invest in such endeavors. All these aspects are very new, and the culture in Catalonia today is becoming progressively more entrepreneurial," said the president of GP Pharm, Antonio Parente.

Even with existing programs and emerging financiers, investment in Spain's biotechnology sector falls short. According to ASEBIO, lack of financial resources remains the main barrier to internationalization for 79% of companies. Internationalization is first on a biotech firm's list of priorities and many are looking to the United States as both a market for their goods and a model for entrepreneurship. "Circumstantial modifications stemming from an adverse environment have occurred and today Spain does not prioritize investment in biotechnology. We still remain far behind more advanced countries that have favorable fiscal and financial frameworks, including patronage actions and incentives such as stock options for research participants. Local companies need to go abroad in order to grow; there is no other option," said managing director of PharmaMar, Luis Mora.

Moving forward, both government support and economic recovery will be key to ensure the sector's success. Public spending on R&D needs to increase to pre-crisis levels and the country has to build a financial environment that is more conducive to private investment. ASEBIO is actively working to support the growth of the private equity sector in Spain in order to attract foreign capital for the country's biotechnology firms.

In addition to targeted capital, however, cost-saving innovations will help ensure biotech firms' success. According to Sergi Trilla, the CEO of Trifermed, a business development firm that provides services to biotech entrepreneurs, "there is a lack of economical value propositions and solutions that are good for both the patient and the healthcare system."

As budgets are strained due to ageing populations and chronic diseases, worthwhile innovations are those that save money for the system. These types of innovations will make it to the market. "Today, it is simply not enough to offer a solution or value proposition for a certain niche. Entrepreneurs need to consider the related cost of any given solution. The biggest challenge for new startups is not only to find health solutions but also to discover those that are in favor of these budgets. It is becoming clearer that solutions also have to provide savings," said Trilla.

Bearing these factors in mind, Spain is uniquely equipped to maintain its stature as a leader in biotechnology. With an abundance of biotech startups stemming from universities, the emergence of new investment schemes, and an economic recovery in sight, Spain's biotech industry is primed for growth. •

Regina Revilla Pedreira

President
SPANISH BIOINDUSTRY ASSOCIATION (ASEBIO)

ASEBIO was established in 1999. What have been its key accomplishments over the past 16 years?

ASEBIO was founded with the support of the Ministry of Industry and began with a small member base of 50 companies. Today, ASEBIO is comprised of organizations that have various applications to biotech, ranging from small firms to large multinationals. Our membership is also comprised of various ministries, hospitals, research foundations, administrations, emerging startups, scientific associations, universities, and business schools. ASEBIO engages all stakeholders, including BioSpain, Biolatam, and various trade missions. We assist in the raising of European funds, and engage in innovative public procurement spending efforts such as InnovaSUMMA, Castilla La Mancha's CLAMBER and the SUMMA Project. ASEBIO has also participated in legislative processes to help convey the interests of the sector, such as INNVIERTE BIO, Law of Science and Law of Entrepreneurs. Additionally, we helped promote the CEU Masters program, a joint Master's degree with ASEBIO called Master de Gestión de Empresas Biotecnológicas, which will begin next October. From 2011 to 2015, ASEBIO grew its base from 159 to 280 members, and helped found 500 new biotech companies.

In the past, ASEBIO has worked to develop a strategic plan of action to grow Spain's biotech sector. In crafting this with the government, what challenges did you identify for the sector?

The most significant challenge that the sector faces is the lack of an ecosystem to transform basic research into commercialized products. We are ranked 10th in the world in publications of basic research, but we need to develop our capacities to identify market interest and produce proofs of concept. There are enough funds to establish research programs, but not enough is invested in the development of proofs of concept. In other countries, there is an abundance of private capital invested in these models, whereas in Spain this type of targeted capital is less abundant. Currently, ASEBIO is working to resolve this issue by providing economic incentives such as tax breaks. These incentives are in place for other sectors, but not in the biotechnology sector, due to its long (10 years) gestation period.

We are currently at a delicate moment. Despite good progress from companies such as Oryzon and Zeltia, shortage of capital, lack of liquidity, and shrinking government budgets have weighed on the sector, right in its prime. The biotechnology sector is largely composed of small companies still in their investment phase. Because of this, only the most well funded companies survived the first half of the crisis with regards to employment and turnover. However, now that the economy begins to recover, the sector is going through its most difficult period. Hence, it is now that we need institutional and financial support.

As the president of ASEBIO can you tell us about strategic initiatives that you would like to realize over the next five years?

Firstly, I would like to develop a firm strategic plan. We are growing very fast and expanding our coverage into many different sectors including the pharmaceutical, agricultural, energy, and environmental sectors. The EU has invested €20 million into a bio-economy project, CLAMBER, and we are in the process of establishing a new bio-refinery in the coming years in Puertollano (Castille-La Mancha). We would also like to optimize our management processes, and increase our member base.

Secondly, the development of biomarkers and innovative procurement purchasing is a priority for ASEBIO. For example, we have been working with 100 of the most prominent hospitals to ascertain the demand for developing biomarkers, and liaising with different administrations and the minister of health. Once hospital demand has been evaluated, a program has been launched for innovative procurement purchasing, so that companies can develop biomarkers in accordance with the given demand of each hospital.

Thirdly, ASEBIO would like to address legislation to facilitate quick access to biotechnologies at both central and regional levels, as currently it is difficult to coordinate.

Lastly, we need to help smaller companies grow, either organically or by promoting mergers and acquisitions, increasing access to capital markets, reducing dependence on public funds, developing specialized communication programs, and increasing investment in research and development (R&D). Innovative projects require a lot of support, and other countries have had laws in place to encourage entrepreneurship, such as tax incentives for companies engaging in R&D. ASEBIO is working to help ensure the adoption of fiscal incentives for innovation next year. As a result of the crisis, these measures were approved in 2013. The Minister of Economy also just established an agency devoted to innovation that was included in the new law of science.

How do Spain's capacities for R&D and academia fare in comparison to other countries?

Spain is ranked tenth in the world for its scientific capabilities and fifth in Europe. The OECD ranked us as the second country in the world for biotech firms, behind the United States, which has 6,860 companies. To maintain this stature, we need to develop centers of excellence with sufficient capital to fund projects. At present, due to a drop in R&D investment, only 1.24% of GDP goes towards R&D, which is well below the 2% target. •

Antonio Parente Dueña

President
GP PHARM

Please introduce us to GP Pharm and its top-notch facilities and technologies.

GP Pharm was founded 10 years ago by a group of partners. The idea was to build a local company, specialized in its own technologies, rather than a generics company. For this reason, our manufacturing facility is one of the top four in the world, with capacities to produce cytostatic, microspheres, liposomes, and peptide and oligos finish forms. We were inspired by the American mentality to form as a spinoff from a university, but this is often difficult in Spain, given the challenge in raising capital for such endeavors. Today, GP Pharm has three manufacturing sites and 100 employees, 30% of who have a PhD degree. Given our extensive capabilities, specialized technologies and worldwide approvals, we are able to produce our own products, as well as products for third parties. GP Pharm engages in value-added contract manufacturing, contract development, and the sale of our own products.

What is GP Pharm's typical client profile?

We work with all players, ranging from large pharmaceutical companies to small biotechnology startups. GP Pharm offers specialized technologies to companies worldwide. More specifically, we tend to work for companies that are looking to produce some type of liposome or depot formulation, with whom we engage in contract manufacturing and/or development. Contract development engagements often evolve into contract manufacturing opportunities for GP Pharm.

GP Pharm is committed to research and development (R&D), and Spain is home to a host of intellectual resources. Are there sufficient public programs to incentivize research?

Today, there are many programs instituted to prevent the loss of Spain's high quality human capital. Generally, government assistance is not targeted towards large projects. For instance, the cost of a phase III clinical trial is very high, and a few million euros granted by the administration is not sufficient. Companies therefore need to maintain their shareholder investments. There are, however, various programs to incentivize research. For example, CDTI in Madrid is the best means to secure public funding. In the case of local administration, Generalitat de Catalunya's program, ACCIO is also helpful. ICREA was formed 15 years ago to promote R&D in Barcelona, through which talented researchers were recruited from all parts of the world to conduct their research in Spain.

Compared to 20 years ago, when angel investing and other means of raising capital were nonexistent, there are more associations emerging to invest in startups. For example, ESADE has a business angels association to invest in such endeavors. All these aspects are new, and the culture in Catalonia is becoming progressively more entrepreneurial. Biotechnology startups stemming from universities are concentrated in local large scientific centers, and Catalonia has become home to three of the 25 largest scientific centers in the world in the field of health, including CRG and IRBB are among the ten most recognized centers for public health R&D.

Do you have a final message for attendees of CPhI attendees worldwide?

Spain offers a very unique and special opportunity. With an abundance of technologies, small companies and new manufacturing sites, we are ready to bring our innovations to the rest of the world. In fact, 80% of our turnover comes from outside Spain, and is linked to other countries. Yet the pharmaceutical sector is changing, and the disparities among large and small companies is staggering in comparison to five years ago. Today, the industry is segmented into generics and big pharma. This leads us to ask what our position will be in this new market? The answer is the same as it was five years ago: technology. •

Catalonia Biotech: An Upcoming Success Story

Melqui Calzado,
General Secretary,
Catalan Association of Biotechnology Companies (CataloniaBio)

Biomedicine is rapidly gaining priority in many countries as a key engine for long-term economic growth. This is also the case in Catalonia, which now has the largest share, more than 20%, of firms with activities related to biotechnology in Spain. According to Biocat Report 2013, the life sciences sector in Catalonia is made of 512 companies, with joint turnover of €11,527 million (2011). These companies have more than 33,000 employees and contribute to 5.8% of the Catalan GDP. Of these, 194 are biotechnology companies, with more than 66% being red biotechs, 40 are pharmaceutical corporations, and 54 are medical technology firms. The rest are investors, service companies, and suppliers. In the last fifteen years, the number of companies has doubled. More than 80% are small and medium-sized enterprises (SMEs) and the majority of them are micro-companies. The international crisis may have halted this upward trend in 2010, but Catalan biotechnology remains relevant to Spain. In order to evaluate Catalonia's competitive strengths and weaknesses in biotechnology, one should take a more international perspective and compare it to other biotechnology regions.

The Catalan effort in research has been improving steadily and, it has overcome the position of other European biotechnology regions. One of the most useful indicators of the quality of research is the international funds attracted. Between them, the most recognized is the number of grants from the European Research Council (ERC). According to the Catalan government, from 2007 to 2014 Catalonia has been awarded more than 50% of all those grants that were awarded in Spain, which was almost 3% of total awarded in Europe. It ranked 4th in Europe (per 1 million people). Likewise, Catalan research groups have received almost 30% of the funds granted to Spain under the 7th Framework Program. Catalonia has also top large-scale scientific facilities like the Barcelona Supercomputing Centre (BSC), ALBA synchrotron, and National Genome Analysis Center (CNAG).

It is also important to note that Catalonia is a leader in clinical research thanks to an excellent network of international hospitals. In order to position Catalonia among the top European territories for the conduct of clinical trials, Catalonia is developing the Barcelona Clinical Trials Platform (BCTP), which brings together the outstanding hospital research institutes into a platform for improving the coordination, integration, quality, inclusiveness and speed of clinical research.

Access to funding still remains an important challenge for Catalan biomedicine firms. Part of this could be due to the following two facts: the average size of the related industries is relatively small compared to the size of industries hosted in other European biotechnology clusters. These firms are the ones that have the capacity to generate demand for biotechnology in several intermediate stages of the value chain production process and such a demand is eased by proximity. The second fact is that potential investors are unfamiliar with this type of investment and its high uncertainty and long value chains. However, this last aspect has considerably improved recently with the constitution of several Spanish venture capital firms exclusively focused on biotechnology. From January 2012 to September 2013, investment in companies in the life sciences sector in Catalonia more than doubled from 2010 and 2011.

The health sector is facing new challenges. In most developed countries, healthcare expenditure represents 9% to 10% of GDP (17% in the United States) and is growing faster than GDP each year. We are living longer and population is progressively ageing. These facts, and also other challenges (drop in sales due to loss of patent protection, increasing cost of research without resolving productivity), requires us all to be more efficient and are forcing the global pharmaceutical industry to rethink their business model, particularly their R&D strategy. As a result, we have seen new collaboration methods among institutions (companies, investors, academic, etc.) and they are accelerating innovation and increasing the efficiency. Given this brief analysis, we propose the following considerations in order to transform the sector:

First, it is critical to provide the right incentives to promote quality research and facilitate the implementation of such research into a business model, regardless of the sector it involves.

Second, Catalonia can attract investors by fostering understanding of the long timelines, high uncertainty, but also high potential of the biotechnology sector. Moreover, the investment is often not on the development of a final product but on achieving the next step in the value chain, such as reaching phase I of the clinical trial, and hence, the investment timeline might end up being shorter than initially expected.

Third, Catalan biotech is still small by European standards and needs local champions to invigorate the ecosystem. Most of our companies are SMEs and less than 10% of them post turnover of more than €100 million.

Finally, our greatest challenge is transferring research, and the capitalization of our innovation in the clinical arena. We have to learn from other regions how to link business and research, in order to improve our innovation indicators.

Local investors, leading new transactions, pharmaceutical corporations, looking for innovative projects, and the growing interest in instruments like the MAB will play a key role in the future.

Since 2000 and as a result of good economic times and big efforts of people who believe in the sector, we have seen significant growth. We as a sector have overcome an international, financial and economic crisis. We now need brave decisions and explicit goals that will allow us to prioritize the basis on which we want to grow. We have more than enough assets to make the biosciences a driving force for the economy in Catalonia, and most important, we are determined to do it!. •

Roman Stampfli & Concha Serrano

RS: CEO
CS: Government Affairs Director
AMGEN

This year Amgen is celebrating its 35th anniversary. Please begin by providing us with a historical perspective of Amgen's activities here.

CS: Amgen Spain was one of the first subsidiaries that the company established in Europe 25 years ago. Initially we marketed our drugs through licensees, but quickly began selling our own drugs in Spain. Amgen Spain has always sought broad partnerships in the healthcare system, not only with clinicians but also with hospital managers and pharmacists, so as to become truly part of the system. This commitment to our different stakeholders has always differentiated us. Amgen is also proud to carry out a bulk of our clinical research in Spain, from early to late phases. In fact, Spain has played a role in clinical development for all the drugs that Amgen has launched. In Europe, we were the first company to contribute with clinical trials and patients for registrational studies, which required a large effort on our part. We want to continue to carry out research in Spain—in collaboration with academic institutions—in order to be able to offer patients and clinicians the most innovative products.

RS: Amgen is concentrating efforts in clinical research and in partnering with local companies in Spain. The Spanish government recognizes our strong footprint in research in the Plan Profarma. On the other hand, our local partnerships were especially beneficial given the difficult environment, and helped strengthen our presence here.

Amgen has nine biosimilars on the market today. How will the landscape for biosimilars evolve moving forward?

RS: Since the appointment of our new CEO a few years ago, Amgen has shifted its strategy and entered the field of biosimilars. Amgen will be especially strong in this field given our expertise in manufacturing biotechnology products. With this diversification we can also deliver solutions for the healthcare system. On one hand, there has been a strong push towards saving expenditures by using biosimilars. On the other hand, the investment required is very high due to the high costs of development associated with biosimilars (clinical comparison studies are required). Nevertheless, certain margins should be maintained to make sure companies stay interested in developing their biosimilar portfolios. •

José María Fernández Sousa-Faro & Luis Mora

JMF: Chairman
LM: Managing Director
PHARMAMAR

JMF

LM

To begin, can you provide us with a brief history of PharmaMar?

JMF: PharmaMar (formerly known as Zeltia Group) was founded in 1939 and is currently the holding company of three biopharmaceutical companies: PharmaMar, Genomica and Sylentis. Today, PharmaMar constitutes 90% the group's value and has recently absorbed Zeltia Group in a reverse merger. PharmaMar's was founded to develop novel, anti-cancer drugs that would transform oncology treatments. To do this, we decided to venture into a largely unexplored territory as a source of new molecules and inspiration: the sea. In 2007, PharmaMar successfully registered the first marine anti-cancer drug worldwide, YONDELIS® (trabectedin), for the treatment of soft tissue sarcoma. Two years later, we secured approval for another cancer indication, platinum-sensitive ovarian cancer. Today, YONDELIS® is marketed in 78 countries worldwide, six of which where we have a direct presence. It has been licensed to Janssen Products (a Johnson & Johnson company) in all territories outside of Europe (except Japan, where we licensed it to Taiho Pharmaceutical), giving them commercialization responsibilities in many countries. Through our partner, the drug has been approved all over the Americas, except in the United States, where we expect to receive approval within the next few months.

Please tell us more about YONDELIS® and the other novel drugs that PharmaMar has in its pipeline.

JMF: This anti-cancer agent is a first-in-class molecule that works through a mechanism of action that is entirely different from anything else on the market. It is a true novel agent, which can also be combined with other drugs for the treatment of various cancers. Other than YONDELIS®, which has been approved for two indications, we have two other candidates in the pipeline: APLIDIN® (plitidepsin) and PM1183. Plitidepsin just finished the recruitment of a Phase III trial in multiple myeloma, a blood cancer, in which has shown activity, and is characterized by a completely new mechanism of action. Our third anticancer agent is the most interesting in terms of potential. It has yet to be named and is referred to as PM1183. This drug seems to be quite effective against small cell lung cancer (a deadly disease) and platinum-resistant ovarian cancer. PharmaMar is channeling all its efforts to commercialize PM1183 directly in the United States. Additionally, we have a fourth and very promising drug called PM60184 in phase I trials. •

José Escaich

CEO
BIOIBERICA

Founded in 1975, what have been Bioiberica's important milestones?
Bioiberica was founded in 1975 to produce Heparin (the most used anticoagulant in the world) derived from porcine intestinal mucosa. Since we began extracting Heparin, the company established an international presence and adopted a multi-output approach with the aim of developing biomolecules with significant biological and therapeutic properties. We discovered many agricultural and animal nutrition applications. Bioiberica then expanded to work with other raw materials and animal tissues, such as cartilage and cockerel combs, to obtain chondroitin sulfate, glucosamine and hyaluronic acid, chondroprotective molecules for treating osteoarthritis. At this time we were selling APIs and determined that in order to maximize the potential of these newly discovered biomolecules, we had to develop products and enter the market directly with our own brand. We further integrated internally and invested in clinical studies, product modification, and strategic alliances. Bioiberica established a factory in Brazil, the United States, Poland and Italy to optimize its supply base, but our state-of-the-art production facility is located in Spain. We eventually specialized in osteoarthritis and developed the first biomarker and genetic test for the disease. Today, we are also actively researching cell therapy for osteoarthritis. Bioiberica is looking to expand to new tissues such as porcine brain, lung, and pancreas. We have many research projects in 2015 that are in the early stages of development, including a new compound isolated from porcine brain that has shown positive results in slowing down the progression of Alzheimer's in seven animal studies.

What are the prospects for personalized medicine?
Personalized medicine is the future, and new technologies are emerging to track and monitor health. Bioiberica is developing an application for osteoarthritis patients in collaboration with Columbia University, which will soon progress to clinical trials. In Granada, we are working within the field of cell therapy to extract cells from the knee, and then grow and inject them to recover one's own cartilage. We are also working to develop bio ink for 3D printers and biomarkers in the area of diagnostics. Personalized medicine will allow for the use of one's own cells for regeneration. Bioiberica has also founded an osteoarthritis medical center (currently in its pilot phase) where services are centered on the patient. •

Jordi Martí Pi-Figueras

Vice President and General Manager
CELGENE SPAIN

What key milestones have shaped Celgene into the company it is today?
Celgene has always been committed to fulfilling the needs of patients. The company established itself in 2006 in Spain as a wholly owned subsidiary, and two years later acquired Pharmion. In 2010, Celgene established a research and development (R&D) center in Seville. The EMA and Spanish Agency of Drugs recently approved our oral treatment for patients with psoriasis and psoriatic arthritis called OTEZLA® (apremilast).

Celgene prides itself on heavy R&D investment, around 30% of its revenues. Why did Celgene establish the Celgene Institute for Translational Research Europe (CITRE) in Seville in 2010?
At the time, the government was keen on promoting science within the region, and offered attractive facilities, hospitals and clinics, and Spain has fantastic human resources. Today, CITRE is a major establishment for Celgene's R&D activities after the United States. From 2012 to 2013, Celgene invested over €32 million in local R&D activities and approximately €5 million in equipment and scientific development. The company has more than 30 clinical trials underway in phases I, II and III. Five of these trials are in phase I and are conducted in CITRE. Two are in phase II, 17 in phase III, and six observational studies post-approval in phase IV.

What challenges does the biotechnology industry face?
Local public investment has decreased substantially due to the onset of the economic crisis. Access to innovation is becoming more challenging. This is relative to the early 1990s, when research groups and hospitals were better able to commit to advancing new developments. The future depends on achieving trust and demonstrating value. The government has to decide which kind of country they want, and prioritize investment accordingly.

What are some of Celgene's strategic goals for the next five years?
Celgene is planning on launching new products, with new indications. We want to demonstrate value for patients and will innovate within the area of product research. We are also committed to evolving our business practices and will employ innovative pricing models. Celgene seeks to go beyond the pill, and improve services such as patient management. Our main goal is to generate €20 million in revenue by the year 2020. •

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Into the Future
Final Thoughts, Company Index, and Credits

"Europe is our natural first step, and our secondary focus is the United States. In order to compete in that market, we need to offer highly differentiated products. The market is well dominated with Asian products, making price an issue for us. In this case it is crucial to be able to defend value and quality with scientific studies. We also would like to continue focusing on China and India, where we have been very successful thus far."

- José M. Roset,
Managing Director,
Biosearch Life

Image: S-F - Shutterstock

"Today, [China and India] are without rivals in the production of pharmaceutical raw materials that fall below the $100/kilogram threshold. This is also true for chemical intermediates. Yet Europe maintains a competitive advantage for the production of raw materials priced above this threshold, especially for specialized care markets like oncology. This is in part attributable to the fact that Asian manufacturers find it difficult to fulfill high quality standards required by western health authorities. We expect, however, that Asian manufacturers will reach this level of quality within a short period of time."

- Héctor Ara Sanz, CEO, SUANFARMA

"The long-term collaboration we engage in with Esteve has been critical for us. We currently have visible results to show for our combined efforts, and are expanding our technological concept to apply pharmaceutical co-crystallization within the field of process chemistry. This strategy is unique to Enantia."

- Joan Feixas, PhD, CEO, Enantia

"Alcalá Farma's competitive advantage is that we have a wide range of state-of-the-art technologies within our plant, including 90% to 95% of the manufacturing technologies available on the market. Additionally, Alcalá Farma's employees have excellent technical knowledge, which is key to handle all our manufacturing equipment."

- Alvaro Soto Mengotti, Corporate General Manager, Alcalá Farma

"Solutex strives to sell products with a special and unique flavor profile, for example, products with extra flavoring or strong caffeine content. Solutex has gradually evolved to service the technological side of the pharmaceutical, nutritional, and cosmetics industries. We manufacture premium natural and specialty ingredients for these industries as well as materials for several products."

- Fernando Moreno, President, Solutex

"Self-care has already taken hold in other countries, but is new to Spain. Both the mindset and business model among pharmacies have to change, in order to adapt operations to those more akin to a retail store. In order to maximize profitability, pharmacists need to begin thinking from a marketing perspective. Today, the number of self-care products in pharmacies is growing significantly, making it critical for the future of the pharmacies to grow and adapt in this regard."

- Miguel Gómez Prado, CEO, Logista Pharma

"Gentec is one of a few companies that produce HPAPIs. We are currently in talks with Spanish authorities to obtain GMP certification and necessary approvals for our Gentec/Pharmanoid plant, which specializes in the production of prostaglandins. Our intention is to produce a range of ophthalmologic products for the market."

- Jaime Melendo, CEO, Gentec

"PanReac AppliChem seeks customers with a sustainable future. We have identified customers globally that are sensitive to quality and these are the types of customers we want to have. When PanReac AppliChem looks for customers in developing countries, we ensure that they have passed several international standards audits."

- Joan Roget, Vice-President and General Manager, ITW Reagents

"Opko Health Spain has a competitive advantage because traditional pharmaceutical companies are entering the nutraceutical industry, a new market that is unfamiliar to them out of necessity. They are doing so because they are finding difficulties in a market that they already know very well. Opko Health Spain has been in this market for long because we love providing people with the resources to improve their quality of life."

- Julián Agut Sánchez, Ph.D., CEO, OPKO Health Europe, S.L.U.

"Due to the crisis, there has been a decline in consultations with doctors specialized in homeopathy, leading to a stagnation in demand for homeopathic medicine. On the other hand, branded medicines—that are well known by the public and used as self-care alternatives—are seeing increased demand."

- Gualberto Diaz, Medical Director, and Miguel Barelli, Director, Institutional Relationships, Boiron

"Vivia Biotech turned its attention to hematological cancers, given that it was the most direct and translational tissue we could access, and the best fit for our technology. In fact, there is not a single company that can do what we do at Vivia Biotech; we can see the effects of thousands of drugs or combinations in a fresh sample. We moved our operations to Spain because the legal system in the US made it difficult for us to access samples of patients at scale for research. Today, we are working with large pharmaceutical and biotechnology companies in the United States and considering reestablishing a presence there."

- Andrés Ballesteros, CEO, Vivia Biotech

"The landscape in dermatology is characterized by competition between large, medium, and small companies. The big ones are slower and less flexible, while the small ones are local and cannot innovate as the competition requires. In the middle, there are companies like us, ready to fill the gap with flexible structures, with a high innovative performance and with the right people to answer what the market requires, here in Spain, Europe, and worldwide."

- Marian Puig, CEO, ISDIN

"We are not focused on the Spanish market, where there is often unfair competition protection."

- Eduardo Bravo, CEO, Tigenix

EDITORIAL AND MANAGEMENT TEAM

Senior Project Director: Vanessa Benz (vanessa@gbreports.com)
Journalist: Neha Ghanshamdas (nghanshamdas@gbreports.com)
Journalist: JP Stevenson (jpstevenson@gbreports.com)

Executive Editor: John Bowlus (jbowlus@gbreports.com)
Graphic Designer: Gonzalo Da Cunha (gdc@d-signa.com)

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THANK YOU

We would also like to sincerely thank all the governmental bodies and associations that took time to share their insights into the market as well as their experience and knowledge.

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