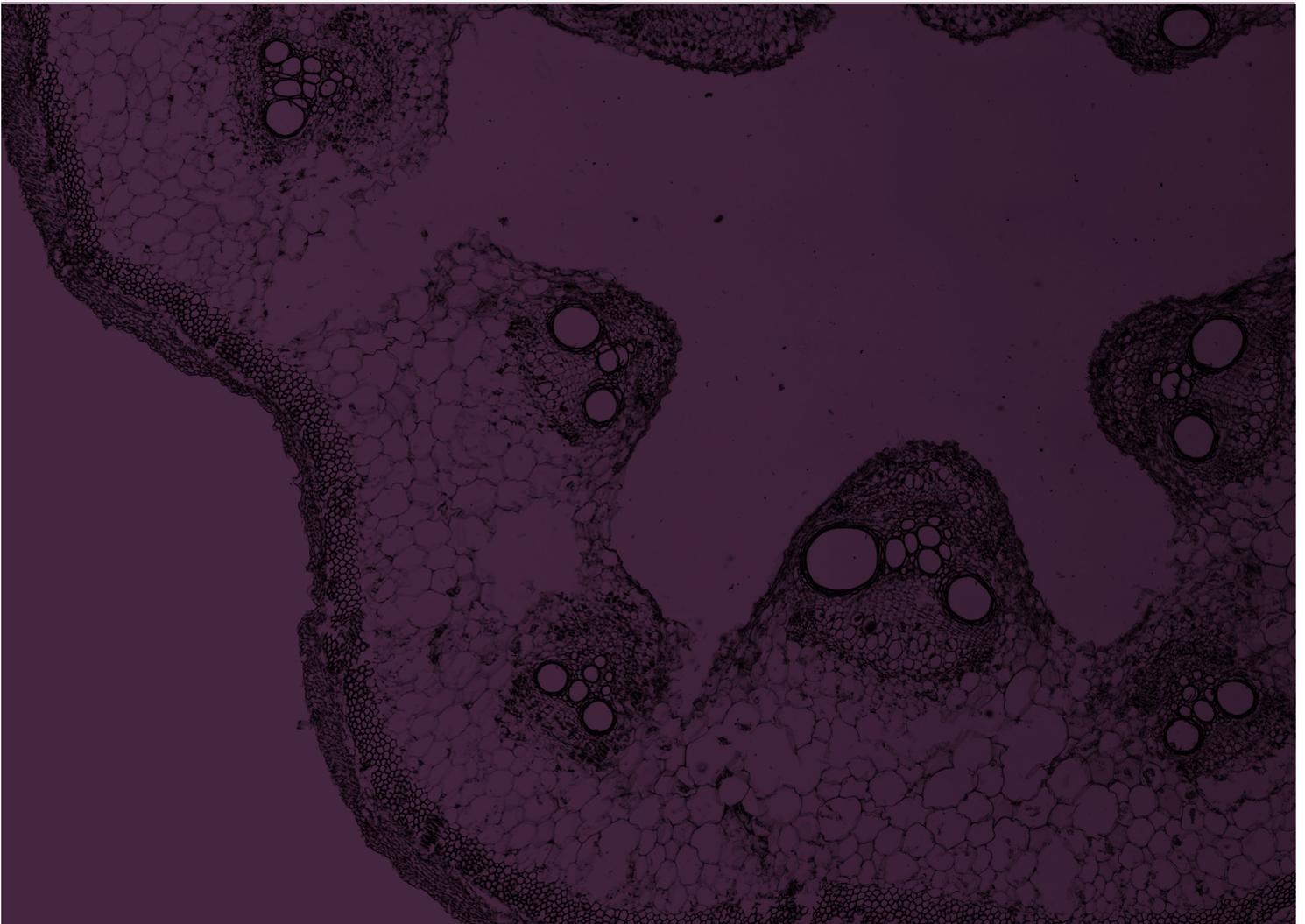


Rethinking the life sciences: the emergence of biopharma firms

Interview with Ignasi Biosca
President of CataloniaBio and CEO of Reig Jofre





Changes in the health and life sciences sector are forcing biotechnology and pharmaceutical companies to work together, in ever-closer collaboration, in a new model of co-existence in which each contributes the best of its know-how. Ignasi Biosca, president of CataloniaBio and CEO of Reig Jofre, goes over the reasons behind this new era of biopharma companies and the challenges and opportunities this poses for stakeholders in the sector.

There is a growing move towards outsourcing R&D from pharmaceutical companies. How does this affect the relationship between pharmaceutical and biotechnology companies?

The way pharmaceutical R&D is done has changed a lot in recent years. We'll never go back to the traditional fully integrated, vertical model of doing research in pharmaceutical companies. In some cases, pharmaceutical companies are still doing in-house research but the growing trend is for it to be done externally.

Why?

One of the reasons is funding, as research is becoming increasingly expensive and risky. Projects in the early stages

need a specific funding structure (venture capital funds, individual investors, friends, fools and family, etc. who are willing to assume these risks) but once projects become consolidated and reach certain milestones, they need to be brought into the fold of pharmaceutical companies so they can evolve with them. Biotechnology and pharmaceutical companies, therefore, are destined to understand each other and find a way to co-exist.

What does this co-existence look like?

There is currently a wide range of ways the pharmaceutical and biotechnology sectors collaborate: start-ups, spin-offs, collaboration and development agreements, licenses, strict sales, accelerators... We're an innovative sector not only in terms of products, but also in relations among stakeholders.

Is this collaboration a must to be competitive?

In other industries, research is done behind closed doors, so no one will find out what's going on! In our sector, however, there is a surprising degree of openness and collaboration.

Public grants should help set trends, without intervening directly. In this re-

“Biotechnology and pharmaceutical companies are destined to understand each other and find a way to co-exist”

gard, the grants from the Government of Catalonia, as well as those from Spain (CDTI) and Europe, have incentivized collaborative projects. And this has been very positive for the sector because we have gotten used to working in consortia. Now, however, these grants should incentivize international collaboration, forcing us to look for foreign partners. European projects already have this requirement but the Catalan and Spanish ones don't yet.

One paradigmatic example of biopharmaceutical collaboration in Catalonia is the agreement between Oryzon Genomics and Roche. Will this type of agreement become more commonplace in coming years?

We're in a good place right now. Companies in the sector have suffered a lot, and that has sharpened their wits. The case of Oryzon and Roche is paradigmatic because it was the first, but there were others in 2015 that have confirmed the feasibility of this model: for example, the agreement between Palobiofarma and Novartis or significant funding agreements like the Minoryx capital increase with national and international capital.

These examples substantiate the fact that the science being done in the Bio-Region is good: the most important thing is to keep doing projects of the very highest scientific caliber, and the results will come.

How are competition from generic drugs, the lack of blockbusters and the appearance of biosimilars transforming R&D in pharmaceutical companies?

“We're an innovative sector not only in terms of products, but also in relations among stakeholders”

The move away from in-house research has been fuelled by these changes, which have tightened profit margins for pharmaceutical companies and forced them to find other sources of income. The capacity to invest in research has been especially hard hit at Spanish pharmaceutical companies, given their particular idiosyncrasies, as a result of a widespread drop in prices and, above all, the shrinking market, approximately 30% in recent years. That means many thousands of euros that have disappeared from the market and can no longer go towards funding research.

The changes we're seeing, with large pharmaceutical corporations moving towards a *beyond the pill* mentality including telemedicine, big data, wellbeing programs and, in short, new ways of interacting with patients, demonstrates the huge shift as a result of the digital transformation. What opportunities and obstacles does this challenge pose?

Technology, which is already part of many areas of our life, has to be part of health. We're already seeing projects like Devicare and Ascidea, as well as many diagnosis and data-analysis projects, that are starting to link health and technology. We now have access to absolute data, not just statistics, which will allow us, for example, to take clinical studies much further and monitor the effects of a drug on each individual patient even after it's gone on the market.

It's a huge opportunity, but given the strict regulations in our sector, there's a risk that regulatory bodies may curb the growth of these trends instead of fueling them if they can't see them for the opportunity they are.

This could mean companies like Google and Apple end up setting the standards and then regulatory bodies have to come in behind them and establish a regulatory framework that encompasses all of the technological advances that arise. Now we have the chance to

“New technology opens up immense opportunities in health, but if regulations hamper their advance, technology companies like Google and Apple will set the standards”

do it the other way around.

Could the pharmaceutical industry's traditional conservatism be a threat to these trends?

The pharmaceutical industry is conservative because it is used to acting in a highly regulated arena. Until the regulations have been established, not much exploration will be done: the industry has lost the freshness of other sectors, like technology, where the lack of regulation has led to much faster innovation.

How do public healthcare cuts and expiring patents affect the business plans of pharmaceutical companies? How are they adapting?

Public healthcare cuts are putting a lot of pressure on income statements at Spanish pharmaceutical companies, which don't have the capacity to absorb some movements and have to survive on their own local markets.

As a result, their capacity for investment is limited. The government has to be aware that it plays an important role in dynamizing technology developed here, and that's why innovative public procurement continues to be very important for driving local companies.

Pharmaceutical companies are looking for different open innovation models. There is a wide range of possibilities between radical innovation companies (often large multinationals) and generics companies, which is where most companies are found. Here they have to find a way to set themselves apart through incremental innovation, which

isn't always given the importance it deserves.

Funding continues to be the main obstacle facing biotechnology companies, especially small ones. What role can collaborating with pharmaceutical companies play in funding these companies?

The relationship with pharmaceutical companies is key for small biotechnology firms, not necessarily for their role in directly funding projects –there are financial institutions for this- but for long-term collaboration.

Biotechnology firms must demand co-development projects in which each party contributes what it does best: the pharmaceutical company should handle clinical design, industrial scaling, international clinical trials, market access, medical sales pitches, etc. The biotechnology firm has to stay true to its own identity and remain independent in order to focus the project and reach the goal.

In this regard, the most important thing is for pharmaceutical companies, above all multinational corporations, to be willing to pay well for successful projects from biotechnology firms: for the reward for good projects to be high. If the compensation is good and biotechnology entrepreneurs and early-stage investors see good return on investment, the system will work and projects involving risk will continue to be undertaken.

What other funding alternatives does the sector need?

In Catalonia and Spain we have an unresolved matter: proper access to capital markets. We have seen positive experiences like Reig Jofre and Oryzon on the Spanish Continuous Market, or Inkemia and AB-Biotics on the Alternative Stock Market (MAB). It's an alternative way to access capital that is looking for return on investment, with small shares with liquidity that allow investors to enter or exit the project when they want without

getting involved. There have to be more of these experiences, which prove the sector's maturity.

On the other hand, the role of specialized venture capital funds in the BioRegion is noteworthy, funding bigger and bigger projects and bringing international capital along with them.

“Pharmaceutical companies have to pay well for successful projects from biotechnology firms: the system will only work if the reward for good projects is high”

What are the main needs of the biopharmaceutical sector in Catalonia to be able to compete on an even playing field internationally?

The most important, here and anywhere in the world, is to have projects of the very highest scientific caliber.

In Catalonia we have top-notch research centers, hospitals and universities and this is where projects have to come from, which will later be consolidated into companies to cover patient needs. We have to stop relying on the idealized figure of the Renaissance man that is a scientist and entrepreneur rolled into one. We have to differentiate between the different profiles needed in the chain. That's why anything associated with valorizing research is extremely important, to ensure we identify as many good projects as possible and that they reach the market.

*Ignasi Biosca is CEO of pharmaceutical company Reig Jofre, which he joined in 2006, and president of CataloniaBio, the association of health and life sciences companies in Catalonia. Biosca is on the board at Farmaindustria (National Trade Association of the Spanish-based Pharmaceutical Industry) and at several biotechnology companies. He has a degree in Telecommunications Engineering from the Polytechnic University of Catalonia and

master's degrees from Telecom Paris Tech, IESE Business School and the University of California at Berkeley.

Biotech – Farma

Bioibérica

Josep Escaich
CEO

 **1975**
Year founded

 **358**
Employees

 **246.8M€**
Turnover (2015)

www.bioiberica.com

Company mission

Bioibérica is a biotechnology company that specializes in identifying and extracting biomolecules with significant therapeutic value from animal tissues. These biomolecules are applicable in any field of the life sciences: in the Western world, we are the leading producers of heparin, the most widely used anticoagulant and antithrombotic in the world; we specialize in osteoarthritis and joint health, producing chondroitin sulfate, which has been proven to slow the deterioration process. In the area of human health alone, we treat more than 15 million patients each year all over the world. We have also developed a line of ingredients for animal health and natural products to help crops overcome plant stress and improve yield.

What innovation do you bring to the market?

We have two strategic lines of innovation: one in biotechnology and the other in internal talent management.

Here at Bioibérica we are always doing research and developing new compounds, obtained from animal tissues, that can be applied in the field of the life sciences. So, we bring value to these animal-based raw materials, through science and scientific proof. Herein lies our innovation and contribution to the market. For example, one of the projects we have been working on is a compound isolated from pig brains, which has shown positive results slowing the progression of Alzheimer in pre-clinical studies.

In terms of innovation in managing talent, we've launched a program called Bioflow, based on positive psychology, which encourages the personal strengths of each of our collaborators in order to help them tackle personal and professional challenges with the best chances of success.

What is the most important milestone you've reached so far?

Since the company was founded, we've achieved two great successes: becoming a global benchmark in heparin production and leading scientific research and innovation in osteoarthritis. We work with one hundred research centers around the world and forge strategic alliances with the main researchers and institutions in each of our areas of expertise.

What would you like to read about the company in the news a few years from now?

That Bioibérica has a team that happily works for the good of society. We want to achieve business and science goals, but always based on the wellbeing and happiness of our team.

Biotech – Farma

Grifols

Javier Jorba
President Grifols Bioscience Ind.
Group

 **1940**
Year founded

 **14,737**
Employees (2015)

 **3.93B€**
Turnover (2015)

www.grifols.com

Company mission

Grifols is a global company and a world-wide benchmark in the healthcare sector. The mission of the nearly 14,000 people in 30 countries that make up the Grifols team is to help improve human health and wellbeing by researching, developing, manufacturing and marketing biological drugs derived from plasma, clinical diagnostic systems and pharmaceutical specialties for hospital use. Founded in 1940, Grifols is celebrating its 75th anniversary in 2015. 75 years of commitment to patients and healthcare professionals; of commitment to innovation.

What innovation do you bring to the market?

At Grifols, innovation is one of our founding pillars and part of our commitment to patients and healthcare professionals. This commitment has made us one of the 100 most innovative companies in the world according to Forbes magazine.

1. Through the Bioscience Division, our main line of activity, we bring together the legacy of our 75 years of history and supply proteins derived from plasma that save and improve patients' lives. Grifols is currently third in the world in the sector and first in Europe. Our main proteins include:

- Immunoglobulin, especially intravenous (IVIG), to treat immune deficiencies
- Albumin to reestablish and maintain circulatory volume
- Factor VIII for treatment and prophylaxis of hemophilia
- Alpha-1 antitrypsin, which protects against the breakdown of lung tissue (emphysema)

2. As specialists in diagnostics, our products and services also help care for patient health and help medical professionals make decisions. The Grifols Diagnostic Division focuses on two key areas of specialization: transfusion medicine and clinical analysis.

We are leaders in transfusion medicine with our line of blood-typing products, NAT technology and production of antigens for reactivities in immunoassays. We are currently the only company that offers comprehensive solutions for blood and plasma donation centers to control the whole process, from donation to transfusion.

3. Through our Hospital Division we provide non-biological pharmaceutical products and healthcare supplies for hospital pharmacies.

Here at Grifols we drive innovation through research into new plasma proteins with a therapeutic effect or new indications for existing proteins. In this regard, we devote between 5% and 6% of our yearly income directly to R&D. In 2014, specifically, we invested around €181 millions in R&D.

Plus, Grifols is also working in new fields of research through companies it holds stock in. So, Grifols also promotes biotechnology initiatives by investing in research companies to fund R&D projects in fields like Alzheimer and personalized medicine, among others.

Grifols is the majority shareholder in research companies like Araclon Biotech, Nanotherapix, Progenika Biopharma and Kiro Robotics. Plus, the group also holds stock in Aradigm Corporation, TiGenix, Alkahest and VCN Biosciences.

What is the most important milestone you've reached so far?

Over 75 years we've achieved a lot of goals and gone through many different stages. We've been able to adapt to the new times, going from a family-run company to a multinational corporation; we've prioritized international expansion to become a global company; and we've determinedly promoted activities in the field of plasma derivatives while also maintaining intravenous and diagnostic solutions, which were the base of the company for decades.

Success stories

Today Grifols is a diversified, international company with direct presence in 30 countries and sales and distribution in more than 100.

From a business standpoint, going public in 2006 was key. As were several strategic acquisitions, like that of Talecris (2011) and the Novartis transfusion diagnostics unit (2014).

From a scientific standpoint, over our 75 years of history, Grifols has contributed to advancing plasma derivatives to benefit patients. The company has been a pioneer in developing techniques and processes to obtain and produce plasma proteins currently used in the industry.

Innovation as a goal has been, is and will be fundamental. This focuses on increasingly efficient and safe production methods; new indications for plasma products to treat more minority diseases; and products adapted to make treatment easier. From this perspective, the best is yet to come.

What would you like to read about the company in the news a few years from now?

The work we do here at Grifols doesn't aim to make headlines. We're hardwired to contribute to advancing science and society.

For the company, it is essential to promote research into Alzheimer, in light of the ageing population in developed societies and the high social and economic impact of this disease. Our strategy covers the three main fields of action: new treatment to slow progression, early diagnosis and development of a prophylactic vaccine.

On our 75th anniversary, the AMBAR study (Alzheimer Management by Albumin Replacement), which is testing a combined treatment of plasma exchange and hemophoresis with albumin, is moving forward. Furthermore, the company is also working to validate a diagnostic

kit and to develop an Alzheimer vaccine, currently in phase I clinical trials.

The success of these projects would undoubtedly be good news for society.

Biotech – Farma

Kern Pharma

Manuel Garrido
General Manager

 **1999**
Year founded

 **776**
Employees

 **171M€**
Turnover (2014)

www.kernpharma.com

Company mission

Kern Pharma is a pharmaceutical laboratory committed to the people and to providing the best solutions for patients, doctors and pharmacists, every day.

What innovation do you bring to the market?

In the area of generic drugs, in which we are a leading laboratory, we have our own development and manufacturing facilities. This allows us to work with improved pharmaceutical formulas and presentations that foster proper administration of drugs in patients. Plus, we're developing products with greater value added that will allow us to be even more competitive in the future.

What is the most important milestone you've reached so far?

The most important strategic decision in recent years was to move into the biosimilar drug market through our division Kern Pharma Biologics. In February 2015, we launched Remsima® (infliximab), the first biosimilar monoclonal antibody (mAb) to gain approval from the European Medicines Agency (EMA). This has made us the first national laboratory to market a biosimilar monoclonal antibody in Spain. It is the first product we are marketing in this area, thanks to an agreement with Celltrion Healthcare, one of the most qualified, experienced biotechnology companies in the field of biosimilars. It is a project with a very broad scope that will be an essential part of the company's road map for the coming years.

What would you like to read about the company in the news a few years from now?

We would like to be recognized as a laboratory committed to the people that provides the best solutions for patients, doctors and pharmacists.

Biotech – Farma

Minoryx

Marc Martinell
CEO

 **2011**
Year founded

 **16**
Employees

 **—**
Turnover

www.minoryx.com

Company mission

To develop drugs for minority diseases, mainly those caused by congenital metabolic disorders, like adrenoleukodystrophy and lysosomal diseases.

What innovation do you bring to the market?

Pharmacological treatments for diseases that are currently incurable, through interaction with stakeholders in the sector, contributing our expertise in the initial stages of drug development through our proprietary technology platform.

What is the most important milestone you've reached so far?

Having begun regulatory studies on our first drug candidate for adrenoleukodystrophy (MIN-102); having built a committed, solid, well-prepared team and having been able to attract the interest of international venture capital funds with a €19.4-millions round of funding led by Ysios Capital, with participation from Caixa Capital Risc, Kurma Partners, Roche Venture Fund, Chiesi Ventures, Idinvest Partners and Health Equity.

What would you like to read about the company in the news a few years from now?

That one of our drugs has reached the market and is healing people with diseases for which no treatment was previously available.

Biotech – Farma

Oryzon

Carlos Buesa
CEO

 **2000**
Year founded

 **35**
Employees

 **4.3M€**
Turnover (2015)

www.oryzon.com

Company mission

To identify and manipulate genes and proteins that allow us to develop new therapeutic tools to improve human health, focusing on unmet clinical needs.

What innovation do you bring to the market?

Oryzon is a pioneer and one of the benchmarks in epigenetics, an area of innovation in which large companies have only recently begun to invest and in which few people believed. Large pharmaceutical companies have recently started to bank on targets we have been working on for years: we do things no one had ever considered doing before.

Oryzon started out providing genomics services thanks to our technological platform and in 2004 moved into researching and developing biomarkers for gene expression in vitro diagnostics projects. In 2008, Oryzon began its current focus: epigenetics research for therapeutic use. This led to the first innovative therapy project focusing on an epigenetic target for an oncology need, specifically leukemia, licensed to Roche in April 2014 and currently in phase I clinical development.

What is the most important milestone you've reached so far?

Having advanced in therapeutic areas that weren't even considered previously from an epigenetic standpoint: this success can be seen in the global license agreement signed with Roche to research, develop and market epigenetics drugs for onco-hematology and solid tumors. The most important, however, is the science behind this project and others we continue to work on, because we're not a one-product company: after our agreement with Roche, we could sign new agreements with other top pharma companies in the future. We continue to move forward with other programs, like the one addressing neurodegenerative diseases, which we hope will move into clinical phase I in 2016.

What would you like to read about the company in the news a few years from now?

The great decision-makers in multinational pharmaceutical corporations know us. We already are a benchmark in epigenetics, especially in Europe, but we would like to become a benchmark company integrated into society. We want people here and abroad to know Oryzon as a healthcare company which contributes value by discovering and researching beneficial therapies for conditions with unmet clinical needs.

Biotech – Farma

Reig Jofre

Ignasi Biosca
CEO

 **1929**
Year founded

 **850**
Employees

 **157M€**
Turnover (2015)

www.reigjofre.com

Company mission

Our mission is a commitment to health. This is why we focus our activity on researching, developing, manufacturing and marketing drugs and nutritional supplements, as well as specialized manufacturing for third parties. Internationalization is one of the pillars of our business strategy. Reig Jofre (RJF) products are available directly in a dozen countries, and in more than 40 additional markets through licensing and distribution agreements with companies with solid local commercial capabilities.

RJF is clearly committed to supporting the development of the life sciences sector with the desire to create a solid fabric that is as wide reaching as possible, from which RJF can occasionally extract significant projects for its own future. This is why the company works to analyze projects being developed in specialized therapeutic areas with the aim of actively participating in their progress and facilitating their success.

What innovation do you bring to the market?

RJF contributes an innovative way of working, committed to health and to the life sciences sector. RJF aims to play an active role in dynamizing the sector, promoting research projects countrywide and in small biotech firms, participating and trying to guide them on the path to market. In this regard, we've gone from doing everything internally to breaking up the development process and looking to open innovation models, which we are very comfortable with. We're moving into the early stages of development with small research companies in this ecosystem that have been created in our sector and are becoming increasingly important in Catalonia. We believe that this ecosystem is where we have to be and where we should

try to act as a driving force. We see this as a responsibility and an opportunity. As proof of this commitment to the sector, we've been on the board of directors of CataloniaBio (the association of companies in the life sciences arena that carry out research and innovation in Catalonia) for years now, currently acting as president.

In addition to radical innovation, we are also committed to incremental innovation, which means looking for new uses, applications or formulations for molecules that exist and have been proven safe and effective in order to better meet the needs of patients and healthcare professionals.

What is the most important milestone you've reached so far?

The merger with Natraceutical/Forté Pharma, which has been a leap forward in terms of business with more than 100 workers in France, Belgium and the Netherlands. It has also been a leap in terms of shareholders, going from a family-run company to one with a new equity partner to one traded on the Spanish Continuous Market.

The operation came out of our desire to grow, seek out complimentary partners and diversify. It has led to diversification in terms of location but also type of product. We were very focused on pharmaceutical products and, so, on "curing". Now we are moving into the nutritional supplement arena and, therefore, towards "prevention" and future health, when people are more well informed thanks to the Internet and self-management.

We believe that companies working in health must strike a balance and act as a nexus between these two forms of medicine to foster holistic health. In this regard, integrating Forté Pharma has also been an important move strategically.

What would you like to read about the company in the news a few years from now?

That RJF is a benchmark in our country for its contribution to health, to growth and for its global presence. That its role as a driving force for research projects here at home has been significant and that we can see some of the projects created in our universities on the global market, ideally marketed by RJF. And that all of this has happened while the 815 families behind RJF have grown to 1,630.