REPORT
biocat

Catalonia Life Sciences and Healthcare Outlook

2015

Biosciences
and innovation

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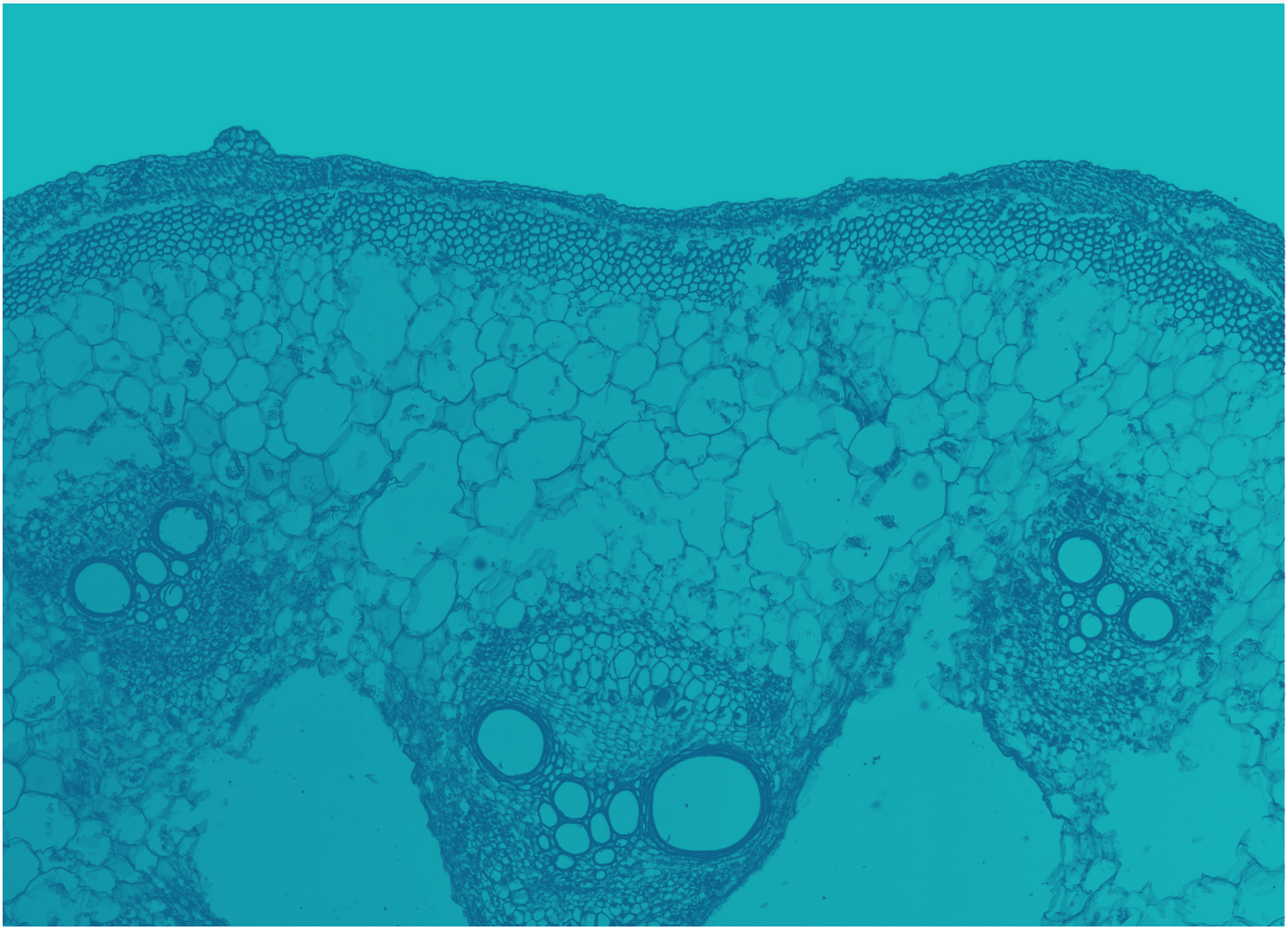
Many thanks to all of you.

Towards a position of leadership in a competitive world

Josep M. Martorell i Rodon
Former Director General of Research for
the Government of Catalonia (2011-2015)



Europe is slowly pulling out of the greatest recession we've seen in decades and we now find that we need to establish long-term strategies to boost competitiveness. The EU is committed to providing greater financial resources and to encouraging private participation in the innovation process, encouraging flexibility and openness to new ideas. These are the concepts that are being strengthened in the program underway, Horizon 2020, and they are also the main guidelines of the smart specialization strategy for European regions (RIS3), both covering the 2014-2020 period.

Taking this situation into account, I invite you to look back at what has been done in recent years in Catalonia, in terms of the university and research system, broadening the scope to look at the past thirty or forty years (a period of time that has been key in building the top-notch system Catalonia has today in the knowledge arena). Then, I will take a closer look at the past two years, which is the time that has elapsed since our latest reflection in this same space.

With the perspective we've gained over these more than thirty years, we can divide this period into three eras.

The first runs from the decade of the 1980s to just before the year 2000, marked by the consolidation of democracy in Spain and progress towards our own self-government. In those years, Catalonia focused its efforts on aspects of higher education. The goal was to extend and guarantee universal access throughout the country, growing the public university offering to fit a global population that was also growing due to the baby boom.

After that, towards the year 2000, and with a quality higher-education system accessible to all, the challenge was to focus it globally on research. The system, despite having a certain level of quality, wasn't competitive internationally as a whole. Therefore, a number of actions were put in motion that have helped us reach our current level of excellence over the past fifteen years: tools that have allowed us to overcome some of the strict limitations in terms of governance established –and still in place today- by the Spanish system (the Law on Universities in Catalonia and the Catalan University Quality Assurance Agency), and some of our own instruments that allowed us to influence how institutions are governed (CERCA and ICREA), making them flexible and focused on internationalization and excellence, and to attract and retain foreign talent.

Towards the year 2000, a number of actions were put in motion that have helped us reach our current level of excellence over the past fifteen years

Taking advantage of the fact that the latest version of this report was published in 2013, I will choose that year as the end of the second era. By this time we had established a good university system: the UB (University of Barcelona) is among the top 200 and 300 universities in the world on what is known as the Shanghai ranking (Academic Ranking of World Universities) and this was also the year that both the UAB (Autonomous University of Barcelona) and the UPF (Pompeu Fabra University) moved into the higher part of that ranking, which is one of the most renowned among universities worldwide.

In 2013, Catalonia also overtook Sweden in per capita grants received from the European Research Council (ERC), moving into second place in the EU.

We also reached that same year with a good system of research centers, found at the top of global rankings (Scimago 2013) in chemistry, physics and biomedicine. ICREA was also found at the top of these rankings, confirming the decisions made over the years, kept in place by administration after administration and consolidated with the signing of the National Pact for Research and Innovation in 2008.

Over these years, and comparing competitive grants obtained through national (Plan Nacional, now Plan Estatal) and European (7th Framework Program and now Horizon 2020) programs, the system has proven to be more effective the more competitive the call or ranking, with most indicators between 50% and 100% above the expected level for population size in Europe and in Spain. Again, the decisions made in terms of openness, flexibility, accountability and commitment to excellence are reflected in these indicators, which put groups and bodies governed by the Catalan R&D&i model in extremely noteworthy positions, even within our own system.

And the third era runs from 2013 to the present. Now there are 3 Catalan universities among the top 200 on the 2015 THE ranking (Times Higher Education) and 3 universities on the 2014 QS Top 50 Under 50. In fact, Barcelona is the second city in the world with the most universities on that ranking (the first is Hong Kong, a city with a population equal to all of Catalonia). Catalonia has the most universities among the top 50 under 50 years old, per million inhabitants, in Europe, and nearly seven times more than the rest of Spain. Likewise, we've pulled away from the country that follows us on the ranking of ERC grants by population (thanks mostly to the success of the biomedical sector, which receives 35% of all these grants). Therefore, it is clear that we've done a good job, thanks to the hard work of thousands of people working in the system and despite the difficulties we are all aware of.

Previously, the challenge had been to put in motion actions that would have an impact on the R&D model and on higher education. Now, the challenge is to consolidate the quality of the system, no easy feat given the difficulties in the environment, and to transform this knowledge into social benefit and economic growth. Now, the challenge is to put research at the heart of our economic model and that requires policies of state.

Now, the challenge is to consolidate the quality of the system and to transform this knowledge into social benefit and economic growth, and that requires policies of state

The fact that, at this point in the story, I am emphasizing that the Government is prioritizing knowledge transfer in this third era in no way means that the institutions haven't already been working in this line. And the biomedicine and biotechnology sector is a very clear example of this. However, looking at figures that include all innovative sectors, we know that the current global volume of collaboration between academia and companies –which can be considered knowledge transfer– for all of the stakeholders together is approximately €200 millions per year. And by type of stakeholder, we see that universities play a key role, with a growing contribution in recent years from the CERCA centers, especially those conducting research in the health sciences.

Given the capacities of the stakeholders in the BioRegion, the strategy promoted by the Government focuses on strengthening three main lines: training (talent), facilitating (legal and fiscal matters) and funding (incentivizing investment). Although these aren't large-scale structural measures (they structure instruments in line with our scope of action in terms of competence and, at times, somewhat further despite the obstacles), they are working in the right direction. I'll give three examples of government actions in each of these lines.

In terms of **training**, industrial PhD programs, inspired by successful programs in countries like Sweden and Denmark, address the challenge of influencing talent-training programs to encourage technology and knowledge transfer to the industrial fabric. In its three editions, the program has led to the kick off of more than 150 projects, with 120 participating companies ranging from start-ups to large corporations, 26 of which are from the life sciences. Last July, the first industrial PhD candidate in the country presented his dissertation.

Regarding **facilitating**, we must look to the measures introduced in the *Government Budget Acompanying* Law for 2014: noteworthy in the legislative arena is the Catalan income-tax deduction, raised from 30% to 50% for angel investors in companies created out of universities and research centers.

Finally, the *Knowledge Industry* program is the main action in the area of **funding**. In terms of encouraging science-based companies through knowledge and incentivizing investment, the program will

leverage up to €30 millions over 5 years for different stages of development, from idea to market (seed, product and market). It must be noted that, in the first edition of the program, 50% of all projects granted funds in the seed stage and 60% in the product stage were from the healthcare and life sciences.

All of the actions that have been put in motion in this era, which are key in consolidating the drive from knowledge to market, aim to align our policies for the coming decade with those in Europe. For now, through the RIS3 instruments, but also following the commitment to a model that encourages competitive resources (we only have to look at the impact of our policies on the funds attracted under the Framework Program), and putting in place measures that allow us to improve indicators used in Europe to assess regional innovation levels. And to commit to the node of the IET InnoLife consortium (current EIT Health) and all of the large-scale European projects in which our institutions participate as significant stakeholders in the respective consortia, as well as institutions that, on a systemic level, promote and make it more agile and capable. This is the case of Biocat, a clear catalyst for the success of the Catalan bio sector.

The strategy promoted by the Government focuses on strengthening three main lines: training (talent), facilitating (legal and fiscal matters) and funding (incentivizing investment)

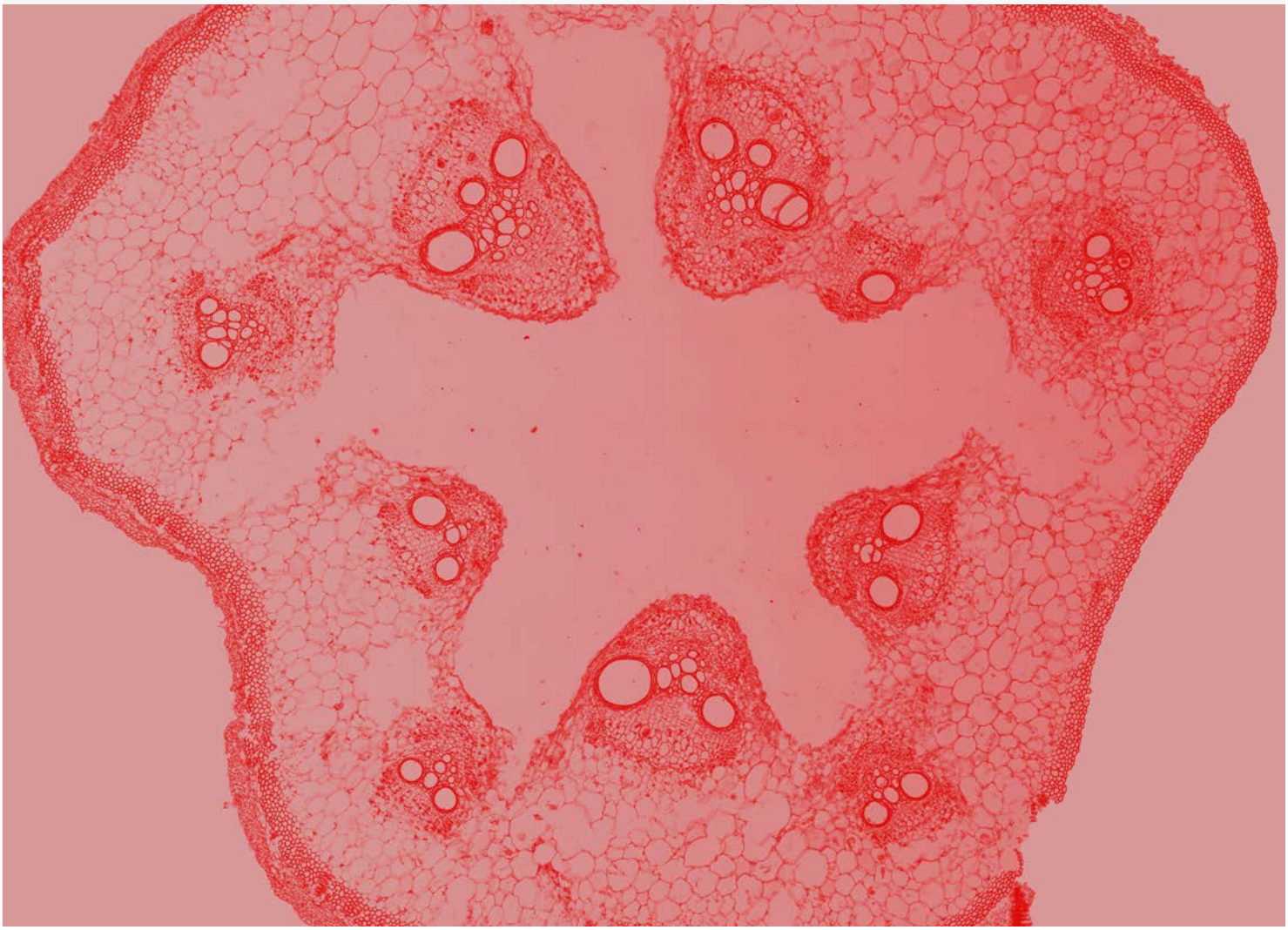
Yet, as I said before, there are still challenges to be tackled. And to take the next step, we need a significant change: we must have the ability to set fiscal policy (especially in terms of business taxes), the ability to regulate credit operations, regulate venture capital mechanisms and angel investors, the capacity to intervene in employment regulations and the governance system, to participate in international bodies, and more. These points require political action that is only possible if Catalonia becomes a state.

I would like to finish up this reflection, and the vision with the perspective of what has gone before and what has happened since the previous Biocat Report was published, by recognizing that it is true that without the recession the situation would have been better. But the crisis has also made us more efficient as a system. The fact that we have maintained indicators and been able to promote measures designed to grow the system is proof that we have become stronger, which puts us in an advantageous position to make the most of opportunities that will come in the future from the bourgeoning economic recovery, and from the political process our country is immersed in.

Global trends.
Local challenges.

Consolidation, efficiency and transformation.

Albert Barberà
CEO of Biocat



The fourth edition of the Biocat Report, once again, aims to present updated indicators and main figures on the healthcare and life sciences sector in Catalonia in order to provide a holistic view of the BioRegion.

This year, we've worked hard to synthesize the ideas and the document in general. For the first time in digital format with a more visual design, it now includes both the situation of the main stakeholders in the ecosystem and the opinion of international experts and relevant initiatives, which we hope will help better understand the reality of a complex industry that is in transformation.

Noteworthy new elements in the 2015 report also include a series of success stories from local businesses showcasing the great quality of Catalan research, entrepreneurial spirit and a job well done at a growing number of companies on the front lines of the European and international league. Because the success of the BioRegion can be seen globally, with data, but also through specific projects and the teams behind them. It wasn't easy to choose these cases, given that we're starting to have quite a few examples from each subsector (biotech and pharma, medtech and digital health) to choose from, but we tried to put together a representative sample reflecting criteria of consolidated business development, financial success, large operations and innovation in terms of product/service.

A series of figures and stakeholders from the *champions league* that encourage us to continue working to boost the potential of a BioRegion that is advancing, despite the difficult situation, with an ever deeper commitment and greater capacity to address the large healthcare challenges of today, and to boost economic and social growth in a small country that is competing on a global market.

Trends and Global Challenges

The intrinsic globality of the healthcare and life sciences sector requires us to pay close attention to the ongoing changes and evolving international trends that affect the markets and organizations working in them. Growth over the past two years has been marked, on one hand, by the demographic changes, increase in chronic diseases, expansion of emerging markets, advances in treatments and technology, and, on the other, by the demand from governments and suppliers to cut costs, improve results and prove value. Therefore it is clear that we are in a period of transition.

In the following section we highlight important considerations (some of which are also found in the articles in the report) that demonstrate the need to adapt, innovate, collaborate and become more efficient over the coming years:

First trend: Convergence among industries

Breakthroughs in science and technology over the past decade are causing the traditional lines among sectors in the healthcare and life sciences (providers, pharma and biotech, medtech, digital health) to be blurred.

Over the past 3 years, these sectors have begun to converge: not only is each of these sectors important in its own right, they are increasingly important to each other. If pharma wants to offer *beyond-the-pill* or *beyond-the-molecule* solutions, it has to look to medtech and digital health. Hospitals that want to cut pharmacy spending look at how to get pharma involved in risk-sharing agreements, etc.

On the other hand, we're moving towards a world of consolidation not only in our sector, but also among traditionally disparate sectors. The next big M&A operation (mergers and acquisitions) could be between a large pharma company and a large telecommunications company.

This trend implies that it will be even more important than ever to collaborate with other stakeholders over the coming decade. The question is: who will take the reigns in these new situations?

Second trend: Each subsector must face new challenges

Each of the subsectors (providers, pharma and biotech, medtech, digital health) and the main activities tied to knowledge (research and innovation) are facing new challenges. Over the coming decade, we will need a lot of talent (intelligence), soft skills (collaboration), and multidisciplinarity to tackle this new paradigm.

Healthcare providers

· There is an increased feeling that there is a difference between the cost assumed and the value created. Governments (when healthcare is mainly funded publicly) and companies or individuals (when funded privately) are calling into question the effectiveness of healthcare expenditure.

· On a systemic level, governments and administrations question the value of money spent in providing healthcare services. Of the 200 countries in the world, not even one is reasonably satisfied with its healthcare system. The latest crisis has forced governments, the main source of funding for healthcare, to reduce their contribution to healthcare budgets. In the hospital arena, the decline in public funding has put extreme pressure on institutions to increase efficiency.

· The value-based healthcare delivery[1] strategy proposed and promoted by Michael Porter (Harvard Business School)[2] is behind some of the main efforts of several countries around the world (including Germany, the UK and Singapore). In an increasingly data-driven world, healthcare services are forced to be based more on clinical outcomes and not just on the perception of the intrinsic benefits of highly sophisticated technology.

· In recent decades, healthcare spending has risen considerably faster than the GDP (which is not sustainable). And that's not all; this sector hasn't been able to boost productivity as others have. In fact, according to a study by McKinsey & Co.[3], the healthcare sector is at the bottom of the ranking on increase in productivity since 1990.

· This trend will require all healthcare service providers (hospitals and primary care) to improve efficiency and productivity.

· In order to face these challenges, hospitals will increasingly work together. In fact, the number of areas in which they collaborate has grown compared to those in which they compete. Important examples include: High Value Health Collaborative (HVHC), International Consortium for Health Outcomes Measurement (ICHOM) and Children's Hospitals' Solutions for Patient Safety National Children's Network.

· So far, cutbacks have been executed better than reforms. The two main reforms in hospitals will include: 1) changing the focus of the model (preventing not curing); and 2) leaving behind a business model that is highly dependent on physical structures (buildings, equipment) and very little on technology (online care and big data).

Pharma and Biotech

· Pharmaceutical companies are increasingly advancing in the process of transforming their value chains. A decade ago, the value chain for a pharmaceutical product was totally or mainly controlled and carried out within the company. Later, different waves of outsourcing, first of secondary activities and later, in some cases, of core or main ones, allowed pharma companies to cut costs and use resources more flexibly. Now, we are seeing a disintegration of the value chain, towards different partnering structures (small biotech firms are no longer companies bought by pharma corporations but partners in different sorts of collaboration agreements).

· The challenge facing the pharmaceutical industry is to evolve from being drug suppliers to being health and disease management companies. This will require increasingly fluid communication between healthcare agents and the community of patients.

· The main driving force for growth in the pharmaceutical industry is unavoidably innovation. Faced with the challenge of the decreasing produc-

tivity of research (Eroom's Law[4]), the pharmaceutical industry will increasingly look to open innovation processes, offering up platforms as collaborative spaces that give external partners access to research tools.

· In terms of products, the trend is to move towards *beyond-the-pill* solutions. Faced with the risk of generics and the patent cliff, how can they transform their products (without possible differentiation attributes) into services ("medicines as a service[5]")? Medical devices (hardware) and digital health (software) are the perfect travel companion for the pharmaceutical industry.

Medtech

· Before, it was enough for innovations to offer better results than the existing product or service. Now there is a new trend towards new products being both clinically superior and (more importantly) able to cut costs in the system. Historically, the medical technology sector has had better results but it has also helped push up the cost of the system.

· In response to the shift towards value-based payment systems, medtech companies must become strategic partners for the healthcare systems (governments and hospitals) and leave behind their traditional role as medical technology suppliers.

· Right now, the global medtech market is a concentrated market: more than 80% of the market share is in the hands of the top 15 medtech companies in the world. On the other hand, 95% of all medtech companies in Europe are SMEs[6].

· In their traditional strategy of acquiring medical technology SMEs, large medtech companies are moving towards services and digital health companies. The case of Medtronic (the largest medical technology company after merging with Covidien in 2015) is a good example, acquiring Diabeter (a Dutch company focusing on providing diabetes management services for children and teens using monitoring and follow-up technology).

· Over the coming years, we'll see how medical technology companies (Medtronic, J&J Medical Devices & Diagnostics, GE Healthcare, etc.) throw themselves into a race to buy up small and medium-sized companies in the field of services and digital health.

Digital Health

· What in the beginning seemed like just another layer of computerization (digitalizing the analogical) has become the most disruptive force in the healthcare sector.

· In 2014, venture capital investment in digital health companies in the USA totaled more than $4 billions, equal to the sum total from the previous three years (2011-2013). In 2015, this trend continued, with nearly the same volume[7].

· What are known as digital therapies are starting to appear, which are reimbursable (initially by insurance companies, not yet by healthcare systems). In Europe, there are two good examples: Caterna (digital treatment for amblyopia, reimbursable in Germany) and MySugr (monitoring and managing diabetes, reimbursable in Austria).

· The challenge facing digital health in the coming years will be to use big data for predictive analytics, which allow us to transform the services provided, making them more focused on preventing than curing. If we use data properly, we'll be able to create information that will transform: 1) medicine (as a science): when we can improve our knowledge of the biology of a disease (our greatest limitation now); 2) healthcare (as an industry): by introducing new stakeholders, mainly in technology, both industry giants (all the big ones are already working in the health arena: Apple, Google, Facebook, Amazon, Microsoft) and start-ups (the latest report from CBInsights has more than 800 start-ups with products and services in this field); and 3) healthcare (as a service): as we're moving towards precision or personalized medicine, which will give each patient the specific treatment they need and not that determined by a generic protocol.

· In terms of investment, digital health activity has been wild: in 2015, there were more digital health deals (891) than biotech deals (473), although the total volume of the biotech deals was slightly higher ($6 billions vs. $5.7 billions)[8].

Third trend: collaboration to leverage a new configuration of the ecosystem

The two main processes to generate value in a knowledge economy (research and innovation) are both, due to their specific nature, extremely inefficient. It is therefore key to choose the right strategies, policies and methodologies to get maximum return on investment in this setting of extremely tight budgets. Because, moreover, the option of transferring costs to other stakeholders in the system is diminishing.

Given the characteristics of our sector (diverse, regulated and with numerous interdependent stakeholders), in health it is relatively easy to create and deliver value (with activities that generate costs) and fairly complicated to attract value (generate income).

In this regard, one way to make processes as efficient as possible is to improve technology transfer activities, which not only contribute to the great tree of science but also to creating companies that market products and services that, on one hand, have a positive impact on

patient health (if they don't reach patients they are of no use to anyone) and, on the other, work to leverage economic and social growth in cities-regions-countries.

Because in our sector, the participation and joint leadership of all stakeholders is becoming more and more important. We can't ask others to take all the risks. We have to share the risk: not only entrepreneurs, not just the private sector, not the public sector alone. Herein lies the difficulty of the challenge: in doing it together. Those who collaborate best will have more capacity not only to generate and deliver value but also to attract value. The sustainability of both healthcare systems and cities-regions-countries as tools of economic development in the future will take this path.

Situation in the BioRegion

As of September 2015, the BioRegion of Catalonia has 734 companies (221 biotechnology enterprises, 46 pharmaceutical corporations, 94 innovative medical technology companies, 208 suppliers and engineering firms, 139 professional services and consultancy firms and 26 active investment bodies) and 89 research bodies (41 research centers, 15 university hospitals, 11 universities with degrees in the life sciences; 13 science and technology parks active in the life sciences; 7 technology centers and 2 large science facilities).

All of these assets make the BioRegion a highly competitive, innovative ecosystem that has gained importance compared to other leading European clusters, most of which it has collaboration agreements with.

We'll start with a **business overview**, with the balance of these two years leading us to a positive global assessment. On one hand, the greater number of companies (due to sustained growth, new service companies in this sector and the expansion of the database for the Biocat Directory especially with medtech and digitalhealth companies[9]), the increased size of companies (the number of medium-sized companies has increased and the number of small firms has dropped), the noteworthy amount of funds invested (especially in 2015) and the large business operations are signs that demonstrate the progressive consolidation of our ecosystem. Because the Administration's commitment more than 10 years ago to promoting the BioRegion is now beginning to yield more significant fruit. The quality of our research, the scientific level of projects, the maturity of companies, the entrepreneurs and specialized local investors –increasingly connected internationally- have contributed effectively to the success seen over the past year.

In the field of biotechnology, for example, just three operations in Barcelona (Minoryx, Oryzon and Aelix Therapeutics) surpass all private investment in 2014. It must be said that the effervescence of international markets, above all in the USA, with important IPOs, many mergers and acquisitions and large capital increases, has surely had an influence on this positive period.

In terms of **scientific excellence**, Catalonia continues to be among the top regions in Europe in quality and quantity, thanks to a model based on the autonomy of centers, results-based hiring, independent peer assessment and a commitment to programs to attract and retain talent. Nevertheless, the need to gain critical mass and international competitiveness has motivated a series of mergers and the concentration of bodies and facilities over this period, noteworthy among which is the creation of BIST (Barcelona Institute of Science and Technology), which brings together six large research centers, and EURECAT, which has united six large technology centers. In academia, Catalonia has three universities among the top 200 in the world[10] (UB, UAB, UPF) and two of the 10 best business schools in Europe (IESE, Esade)[11]. Most research indicators still put us between 50% and 100% above population-based expectations in Europe, with an increase in the grants received from the ERC (European Research Council) and through competitive national and European funds, and scientific production in the life sciences that continues to grow, now making up 3.15% of all that in Europe.

In this sense, and despite the recession, Europe, which also hopes to improve innovation indicators, has launched instruments like the RIS3 (*Regional Smart Specialization Strategies*) in order to get all the stakeholders in the system to work together to consolidate innovative strategies in the main industrial pillars of each region, and other initiatives like the Knowledge and Innovation Communities promoted by the EIT (European Institute of Innovation and Technology). Of these communities (KIC), the one focusing on health and active ageing has a node in Barcelona (EIT Health) and is one of the most ambitious publicly funded projects in the health arena over this period and a resounding success for the BioRegion.

Nevertheless, the analysis the report is based on continues to highlight challenges that are still unresolved, which must be addressed and overcome:

- Public and private R&D expenditure as a percentage of the GDP is very low. It was 1.47% in 2014, still far off the 3% EU target. Companies (down 13%), institutions of higher education (11.5%) and the public administration (3.7%) have been cutting investment in research since 2009. It is essential that we increase support for basic research and clinical research, with the commitment of the business sector, in order to have treatments and products that improve people's health.

- The R&D&i systems capacity to generate economic activity (patents, licenses and spin-offs) is not proportional to scientific production. The top-notch research isn't made into socioeconomic value. Therefore, there is still a gap be-

tween business and research, a gap too large between our indicators regarding scientific excellence and those on innovation. We must continue improving the quality of the system and be able to transform knowledge into economic growth.

- Despite the investment success seen in 2015, access to capital continues to be one of the main obstacles facing our companies, which need large injections of capital throughout the different stages of their projects, from start up to research to market. We must establish funding vehicles to develop proof of concept (and overcome the death valley of projects), expand our pool of investors, attract more foreign private capital, boost visibility of investment opportunities, take advantage of new alternative funding platforms and, also very important, have the legal mechanisms to incentivize patronage of research and innovation, given the progressive decline in public resources.

- We need to attract and retain the best talent, because apart from creative, innovative entrepreneurs, we also need good managers with the ability to make and communicate decisions. Managers with experience that have the skills needed to lead companies in a unique sector, which requires the coexistence and confluence of science and business profiles, in order to value the technology opportunities, deal with investors and ensure the viability of the business throughout its growth.

These local handicaps emphasize the need to continue working to achieve a true ecosystem with shared commitment desires and strategic actions –with the public and private sectors working together- that will help boost value and be essential to gaining international competitiveness and differentiation in a sector that is transforming. We must, therefore, push forward to maximize the excellent potential of the BioRegion of Catalonia, shown in this report, which guarantees the progress and the future of our country.

1 https://hbr.org/2013/10/the-strategy-that-will-fix-health-care

2 http://www.isc.hbs.edu/health-care/vbhcd/pages/default.aspx

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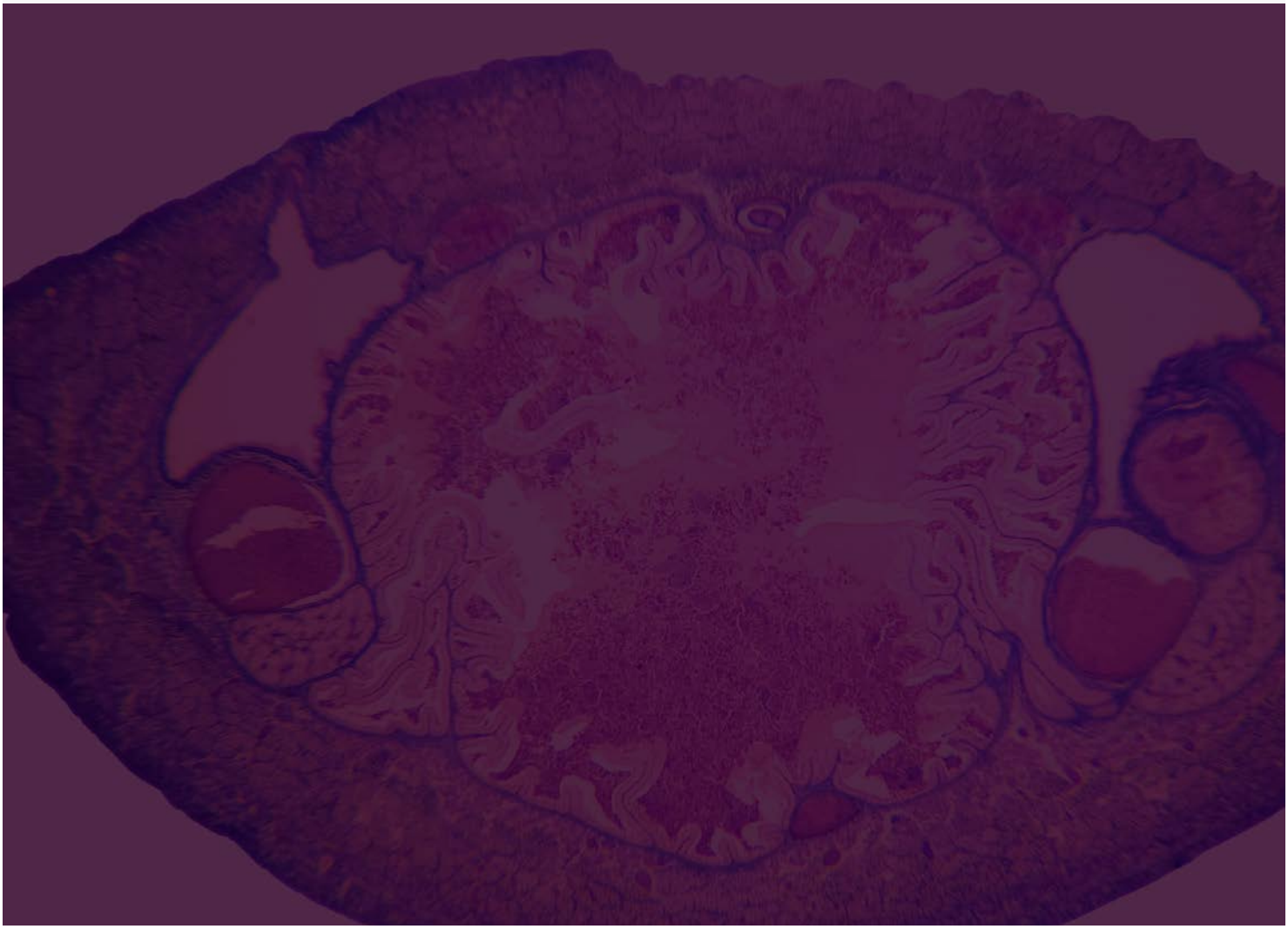
8 https://www.cbinsights.com/blog/digital-health-versus-biotech-startup-investing/

9 Main source of data for the report.

10 2015 The Times Higher Education ranking (THE).

11 2015 Financial Times ranking.

Key Facts & Figures



GENERAL FIGURES

The healthcare and life sciences industry in Catalonia has **734 companies and 89 research bodies.**

Turnover and employment: The companies in the sector post yearly turnover of €14.36 billions, 7% of the GDP of Catalonia (2014 data) and employ 42,133 workers. These figures are up 24% and 25%[1], respectively from the 2013 Report.

Investment: Between 2013 and 2015, companies in the BioRegion attracted more than €100 millions in investment, more than half over the past year, with large operations like the Oryzon-Roche and Palobiofarma-Novartis deals or the Minoryx Therapeutics and Sanifit rounds of funding, led by the main Catalan venture capital funds Ysios Capital and Caixa Capital Risc.

Creation of companies: Between 2013 and September 2015, 75 new companies were set up in the BioRegion, 14% more than the previous period.

R&D Investment: public and private investment in R&D in Catalonia dropped nearly 11% between 2009 (which was the turning point after a decade of steady growth) and 2014. Nevertheless, R&D expenditure makes up 1.47% of the Catalan GDP (data from 2014), which is above the Spanish average (1.23%). Moreover, Catalonia leads R&D investment in biotechnology in Spain, with a total spending of €416 millions (28.7% of the total) (2014 data).

Scientific excellence: Catalonia is awarded 53% of the grants from the European Research Council (ERC) to go to scientists in Spain (180), 35% of which go to life sciences. Regarding scientific production in life sciences, Catalonia produces 3.15% of all scientific production in Europe and 0.99% in the world, and 29% of publications in Spain.

Research personnel: In Catalonia, there are 43,898 people working in R&D (in all sectors), 25,474 of which are researchers. One in five researchers (21%) in Spain work in Catalonia.

Students: the 11 Catalan universities that offer health and life sciences degrees graduate 5,500 students each year. Three of these universities (UAB, UPF and UB) are among the top 200 in the world (Times Higher Education ranking, 2015).

Hospitals: Catalonia has 15 university hospitals and 9 associated research institutes, where 5,000 researchers work.

INDUSTRY

Companies in the BioRegion: joint figures for the sector

Turnover: in 2014, the 734 companies in the BioRegion posted revenue of €14.36 billions, of which:

· €6.85 billions was from pharmaceutical companies (48%)

· €2.91 billions from biotechnology companies (20%), the segment that saw the greatest growth compared to 2011

· €3.09 billions from medical technology companies (22%)

· €1.51 billions from other companies (€16 millions from digital health companies)

GDP: Companies in the BioRegion account for 7% of the GDP of Catalonia (up 1.2% from the 2013 Report).

Funding and investment: between 2013 and 2015, companies in the BioRegion attracted more than €100 millions in investment, more than half (€55.16 millions) in 2015.

· According to ASCRI[2], Catalonia is home to 38% of all companies in any sector to receive investment in 2014, with 60% of all capital invested. In the biosciences, the €10 millions raised by Catalan companies makes up 36% of all venture capital invested in Spain in 2014.

Main operations:

· Oryzon-Roche licensing agreement valued at $500 millions

· Deal to transfer Almirall respiratory division to AstraZeneca for €1.56 billions

· Palobiofarma-Novartis licensing agreement valued at €13 millions

· Merger of Reig Jofre and Natraceutical, and later IPO on Spanish Continuous Market (sixth biopharmaceutical company to go public after Almirall, Grifols, Faes Farma, Oryzon and Rovi)

· Grifols purchase of the Novartis hematology diagnostic division valued at $1.67 billions, acquisition of 50% of Kiro Robotics and 45% of Alkahest

Large rounds of funding:

· Oryzon: €16.5 millions (2015)

· Minoryx Therapeutics: €19.4 millions (2015)

· TopDoctors, Clinic Point, Medtep, Galgo Medical: about €1 million each (2015)

· Ysios Capital led the largest round of funding in a Spanish biotech firm, Sanifit, valued at €36.6 millions

The BioRegion has 26 investment bodies, noteworthy among which are:

· 8 venture capital firms, 4 of which specialize in the sector with significant investment volume: Caixa Capital Risc, Ysios Capital, Inveready and HealthEquity.

· 7 associations of business angels.

· 4 corporate investors.

· 1 institutional investor (Catalan Institute of Finance, ICF).

· 3 new crowdfunding and crowdequity initiatives.

Business creation: between 2013 and 2015, 75 new companies were set up in the BioRegion, most of which are biotechnology firms (27), up nearly 14% from the 2013 report, with a predominance of those offering R&D services (14).

· There is a significant group of new consulting and professional services companies (17) and medical technology firms (14).

· Between 2005 and 2015, 337 new business projects were launched in the BioRegion. Over the same period, only 9% of the projects have had to close down (compared to the mortality rate of innovative companies in Spain and in Catalonia, which is nearly 50%).

Employment: companies in the life sciences sector employ 42,133 workers (up 25% from the 2013 Report), an estimated 4,000 of which work in R&D.

Size: 88% of the companies in the BioRegion are SMEs. Nearly half of these are microenterprises with fewer than 10 workers and annual operating income under €2 millions. Over the past two years, the number of medium-sized companies (between 50 and 250 workers and annual revenue of between €10 millions and €50 millions) has doubled and accounts for 22% of all companies, which is a sign of progressive consolidation in the sector.

Internationalization: the main market for Catalan life sciences companies continues to be Spain. Europe is the main destination for exports and international marketing (mainly Germany, Italy and France) along with the United States.

Location: the province of Barcelona is home to 95% of the business fabric in the life sciences sector in Catalonia; the capital concentrates 51% of the sector and 81% of investors.

Companies in the BioRegion, by subsector[3]

The BioRegion has 734 companies: 221 biotechnology, 46 pharmaceutical, 94 innovative medical technology, 208 suppliers and engineering firms, 130 consulting and professional services and 26 active investment organizations.

The BioRegion has 221 biotechnology companies, of which:

· 45 do research and development into new therapies and diagnostic tools, mainly focusing on the following areas of activity: research into

peptides and proteins, often linked to new drug delivery solutions and the production of antibodies.

· 92 specialize in R&D services, mainly in the following areas of activity: CRO (contract research organizations), analytical services and diagnostics. Growth in genomics and diagnostic instruments has been noteworthy.

· 84 develop products and services in areas including veterinary health, agriculture, food, cosmetics and transforming industrial processes.

Catalonia is the leading region in Spain in the number of biotechnology companies and businesses that use biotechnology (followed by Madrid and Andalusia).

The BioRegion has 46 pharmaceutical companies:

· The main areas of activity of those who work in therapies and diagnostics are: generics, small molecules and anti-infective drugs.

The **main therapeutic areas in which biotech and pharma companies work** are: cancer (often focusing on rare diseases) and neoplasms, dermatology, infectious diseases, and diseases of the nervous system and the respiratory system.

The BioRegion has 200 medical technology companies[4], of which:

· 94 research, develop, manufacture and market medical devices and systems (named "innovative"). Their main areas of activity are: producing reusable instruments, dental devices and electromagnetic devices.

· 93 are distributors, produce medical instruments, manufacture laboratory equipment and fungibles, engineering firms and electronics companies.

· 11 are biotechnology companies that produce and distribute in vitro diagnostic devices (IVD).

· 2 provide information technology services.

The BioRegion has 40 companies working in digital health[5]:

These companies work in:

· bioinformatics and computational research

· medical visits or appointments

· monitoring and following up on patients

· medical imaging and virtual reality

· personalized cognitive services and patient services

· software solutions

RESEARCH

The BioRegion has 89 research bodies and facilities: 41 research centers (32 of which are CERCA centers), 15 university hospitals, 11 universities that offer life sciences degrees; 2 large science facilities; 7 technology centers and 13 science and technology parks with activity in the life sciences.

Scientific production: Catalonia contributes 0.99% of all global scientific production in the health and life sciences.

· The number of health and life sciences publications has increased 168% between 2000 and 2015, making up 3.15% of all scientific production in Europe.

· Catalonia produces 27% of all scientific publications in Spain. From 2007 to 2015, the region has obtained 53% of all ERC grants awarded to scientists in Spain. Of these 180 grants, 62 went to the life sciences.

Patents: between 2010 and 2015, 286 patent applications in healthcare and life sciences were generated in Catalonia and filed with the OEPM (Spanish Patent and Trademark Office), 17% of the total nationwide.

Research groups: Catalonia has 780 research groups in the healthcare and life sciences, which is 47% of the 1,652 consolidated research groups recognized in the 2014-2016 call.

Spin-offs: between 1992 and 2015, 92 life sciences spin-offs were created, 85 of which are still active (2015)

Mergers and groupings: in 2014, a process began to group together separate entities under a shared banner in order to gain critical mass and boost competitiveness by taking advantage of the synergies at different research institutes. The results of these mergers are as follows:

· BIST (Barcelona Institute of Science and Technology): an initiative that brings together 6 large research centers (CRG, ICIQ, ICN2, ICFO, IFAE, IRB)

· EURECAT: merger of 6 large technology centers (ASCAMM, Barcelona Media, BDigital, CETEMSA, CTM, CTNS)

· Integration of CRESIB and CREAL into ISGlobal

· Integration of CReSA into IRTA

· Integration of ICCC into the Research Institute of the Sant Pau Hospital

· Merger of IMPPC, IJC and IGTP.

New initiatives:

· BCTP (Barcelona Clinical Trials

Platform): a platform fostered by Biocat and the Government to improve the coordination, integration, quality, inclusiveness and speed of clinical research, bringing together the 8 most important institutes in Catalonia by volume of clinical trials.

· I3PT (Parc Taulí Institute of Health Research and Innovation): an initiative promoted by the Parc Taulí Health Corporation, Sabadell Service Centre for the Elderly, UDIAT Diagnostics Centre, the Parc Taulí Foundation and the Autonomous University of Barcelona, which have signed an agreement with the aim of using this formula to join the nationwide map of health research institutes accredited by the Institute of Health Carlos III and join the ranks of CERCA centers.

· BIB (Bioinformatics Barcelona): an association that aims to act as a catalyst for initiatives in advanced research, knowledge transfer and technology in the field of biomedicine.

CENTERS

Employment: The 41 research centers working in the biosciences and related fields have a joint total of 8,716 people on staff, 5,499 of which are researchers.

Budget: the CERCA centers (44 centers, 32 of which work on life sciences) have a joint annual budget of €400 millions. The Government of Catalonia contributes approximately 40% of these resources.

UNIVERSITIES

Health and life sciences graduates: approximately 5,500 students/year

R&D Budget: in 2013, they saw €187 millions, a figure that has dropped since 2010. 65% came from competitive calls: 47% from national calls (a percentage that is decreasing) and 53% from European calls (making up an ever-greater proportion).

Transfer: Catalan universities generated 59% of all life sciences spin-offs active in 2015 (50 companies).

UNIVERSITY HOSPITALS AND ASSOCIATED RESEARCH INSTITUTES

Composition: the Catalan hospital system has 195 establishments, 65 publicly owned hospitals (13 of which are university hospitals), 36 private (2 of which are university hospitals), 62 social health centers (government subsidized), 17 psychiatric and/or social health centers (with or without government subsidies) and 15 psychiatric centers (subsidized).

Employment: as a whole, these centers employ more than 89,000 workers, approximately one third of which are at the 15 university hospitals.

· The 15 hospitals and 9 associated research institutes employ about 5,000 researchers.

Scientific production: the hospitals and their research institutes produce 32% of all scientific publications (2007-2011), have 24% of all accredited research groups in the health and life sciences and generate 7% of all patent applications filed with the OEPM (2014).

1 The increase in this percentage is due to: the steady creation of new companies, the fact that many service companies that previously didn't work in the sector have been added to the Directory; and Biocat's efforts to identify all the active stakeholders in the various subsectors, especially in the area of medical technology and digital health.

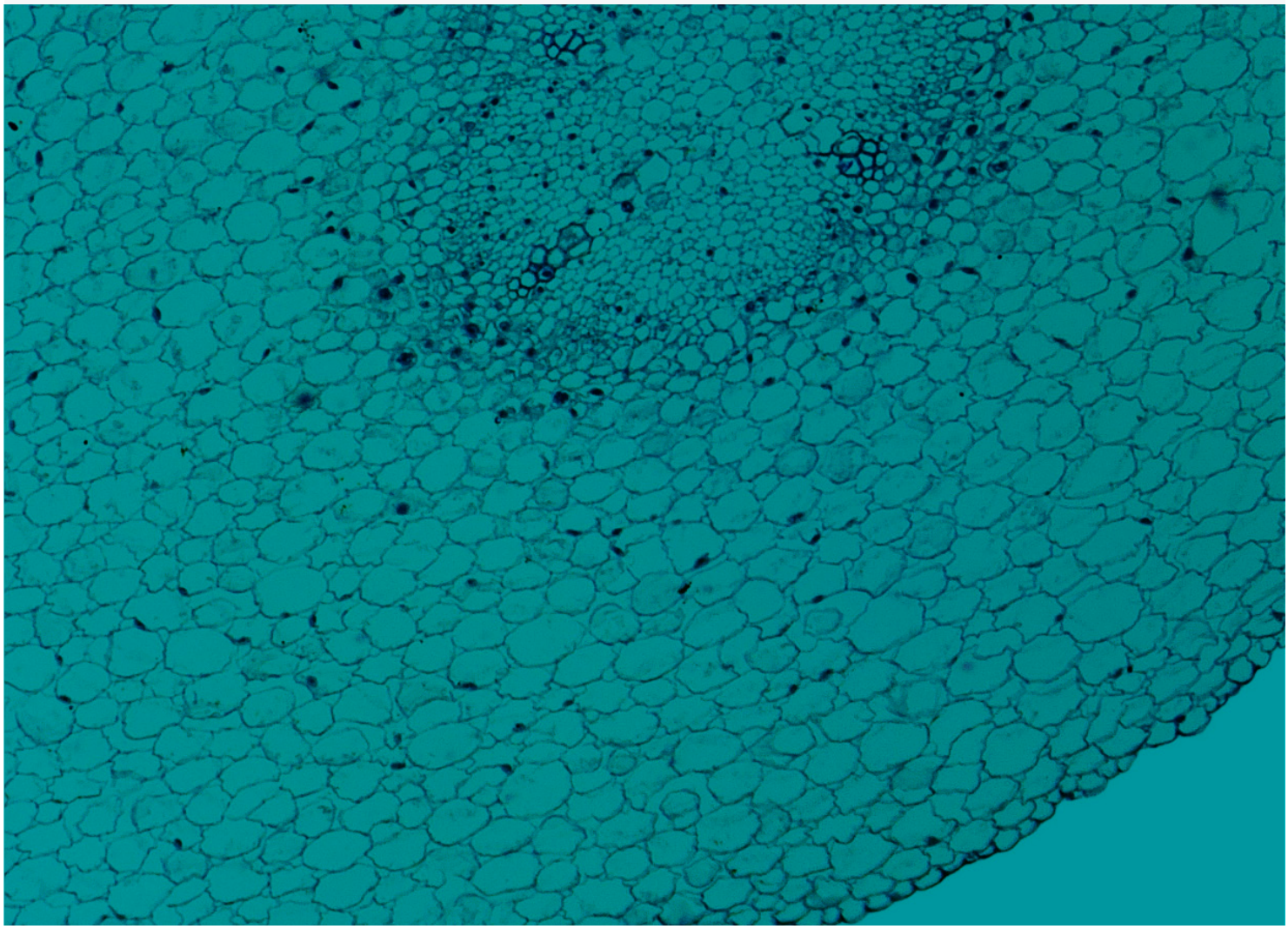
2 Spanish Association of Venture Capital Firms.

3 Companies have been categorized into biotech, pharma, medtech and digital health by cross-referencing the categories in the Biocat Directory (for more information, see the "Methodology" section of the Biocat Report).

4 The 94 innovative medical technology companies are those classified in the *Medical Technology* category of the Biocat Directory. The rest (up to 200) are included in other categories (*Suppliers & Engineering, Biotechnology and Professional Services & Consulting*), although they carry out activities in the medtech arena.

5 Included under the *Providers & Engineering* category in the Biocat Directory.

The BioRegion: The Catalan life sciences and healthcare sector. Status and analysis



On a global scale, the 2013-2015 period was extremely positive for the life sciences sector, particularly for biotechnology companies. The turnover of these companies in the four main markets—United States, Europe, Australia and Canada— totaled $123.096 billions in 2014, up 24% from 2013, which in turn was 10% higher than the previous year.[1] This spectacular growth is mainly due to the results obtained by Gilead Sciences. With the launch of its new hepatitis-C drug, this company doubled its turnover ($10.8 billions to $24.5 billions),[2] clearly demonstrating the extreme importance of innovation in this sector.

The financial indicators are even more spectacular: the capital raised by biotechnology companies that went public in 2014 —94 in total: 58 in the US, 32 in Europe, 3 in Canada and 1 in Australia— totaled $6.8 billions, 93% more than the funds raised on the stock market in 2013, and the highest since 2000. Over the first six months of 2015, 50 biopharmaceutical companies went public, raising more than $5 billion dollars, however the market stagnated in the second half of the year.[3] Venture capital investment in biotechnology grew 28% in 2014, to a total of $7.6 billions. The funds raised through capital increases launched by publicly traded companies also showed notable growth, up to 49%, and the number mergers and acquisitions (M&A) was also up, with 68 operations valued at over $49 billions in 2014 –up 46% from 2013.[4]

The intense M&A activity, which in 2014 was at its highest in the past 10 years, is driven by pharmaceutical companies looking to accelerate innovation in their pipelines by acquiring biotechnology firms. In any case, despite the market pressures –particularly due to healthcare budget cuts in both Europe and the US, and growing competition from generics— the global turnover of the pharmaceutical industry –which was more than one trillion dollars in 2015— is expected to hit $1.4 trillions by 2020, with annual growth rates between 4% and 7%.[5] According to analysts, this growth will be fuelled in particular by greater consumption in emerging markets—China, Brazil, Russia and India— and by innovative drugs, specifically those to treat cancer and rare diseases, in developed markets.

As the 2013 Biocat Report highlighted, human health isn't the only field where biotechnology can be applied. It is also having a growing impact on areas like animal health, agrifood, cosmetics,

In 2014, turnover in biotechnology companies in the United States, Europe, Australia and Canada was 24% higher than the previous year

environmental conservation and energy production. However its potential to provide innovative solutions to treat diseases that currently have no cure —Alzheimer, cancer, multiple sclerosis, and thousands of minority genetic diseases— has make biotechnology the keystone of innovation in the pharmaceutical industry, which is the sector with the most investment in R&D in Europe and the United States, even ahead of the ICT sector.

According to the EFPIA (European Federation of Pharmaceutical Industries and Associations), the pharmaceutical industry invested €30.4 billions in R&D in 2013 in Europe. In the same report, the Federation shows that pharmaceutical and biotechnology companies invest up to 14.4% of their sales turnover in R&D, compared to software and IT services, another high-investment sector, which only invests 10.4%.[6] Additionally, PhRMA (Pharmaceutical Research and Manufacturers of America) states that its members' R&D investment in 2013 totaled $51.6 billions, which is 17.9% of their sales.[7]

In 2014, the pharmaceutical industry's commitment to biotechnological innovation yielded a record-breaking number of new drugs approved by the FDA (Food and Drug Administration). This US agency approved, for the first time in 10 years, all of the applications submitted: 41 new products, which is also the highest since 2005.[8] Of particular weight among these new drugs are those known as orphan drugs, to treat rare diseases (17 out of the 41, or 41%). This trend can also be seen in the European market, where in 2014 the European Medicines Agency (EMA) recommended approval of 82 new medications for humans, 17 of which were orphan drugs. The growing number of approvals is a consolidated trend in Europe: in 2013, the EMA recommended approval of 81 medications (38 of which were new compounds) compared to 57 in 2012 (with 35 new active ingredients), confirming the sustained growth over the past five years.[9]

Apart from biotechnology and pharmaceutical firms, medical technology companies are at the heart of the life sciences sector. Global figures for the medtech market, however, aren't as exceptional. Although turnover continues to grow —up 2% in 2014 to $341.8 billions[10]— it is doing so very slowly, outpaced by the growing number of companies (up 9%) and R&D investment, up 6% to $14.3 billions. For some analysts, this increase in medtech research efforts isn't so much a clear commitment to innovation as a response to the growing pressure this industry faces to prove the unique selling point of its products and devices, which in many cases requires clinical trials and testing.

Over the past two years, some of the most important business operations have taken place since the life sciences sector in Catalonia began to take shape between 2000 and 2005

Whatever the case, large medical technology companies in Europe and North America have found firm support in financial markets, which allowed them to maintain venture capital levels above $4.7 billions in 2014 and 2015 and post the highest results in the past seven years for new IPOs, with valuations totaling $2.3 billions (July 2014 – June 2015).[11] Nevertheless, the number of operations and investors for early-stage projects is decreasing, while pressure is mounting to find disruptive innovations that can be proven and, thus, overcome the budget restrictions of healthcare systems.

In the academic and research arenas, the weight of the life sciences –and its economic impact in particular— is also growing, with knowledge transfer beginning to yield results in some areas that until recently were only associated with engineering and IT. In this regard, the analysis published recently in *Nature Biotechnology* is particularly revealing, stating that of the $861 millions obtained through licensing agreements by the top 11 universities in the United States in 2014, $734 millions —85%— was from licenses in the life sciences. Specifically, these universities began marketing 1,072 biosciences licenses out of a total of 1,510 and the life sciences generated 136 spin-offs of a total of 217. Noteworthy data from this analysis includes the fact that both the number of licenses and the companies created was 40% higher than in 2013.[12]

Overview of 2013-2015 in the BioRegion

In the BioRegion, the two years since the 2013 *Biocat Report* was published was a time of highs and lows. Although far from the investment numbers in more developed markets, we did see extraordinary growth in the funds attracted by Catalan companies in the sector, especially biotechnology firms (graph 17), which was more than €54 millions in 2015, nearly double the already significant levels seen in 2013.

Also on the positive side is the resilience shown by Catalan life sciences companies, which are far from the high mortality rates innovative companies are suffering in Spain as a whole, especially since the beginning of the crisis. These companies are not only withstanding the situation but are also showing a tendency to grow, although SMEs still account for 88% of the sector.

Over the past two years, some of the most important business operations have taken place since the life sciences sector in Catalonia began to take shape between 2000 and 2005.

In April 2014, biotechnology firm Oryzon Genomics closed an agreement with Swiss pharmaceutical company Roche to develop their experimental drug ORY-

1001 to treat acute myeloid leukemia. The operation, valued at a total of $500 millions, is the most important to date by any Spanish biotech company, and a transcendental leap forward in Oryzon's development.

In June 2014, Catalan biopharmaceutical company Reig Jofre closed a merger deal with Valencia-based Natraceutical, making it the fifth pharmaceutical company to be traded on the Spanish Continuous Market. Furthermore, in July 2014, pharmaceutical company Almirall reached an agreement with British company AstraZeneca to transfer its respiratory business line, valued at €1.56 billions.

In 2015, we saw another significant licensing deal: biotechnology firm Palobiofarma —which continues to do most of its activity in Catalonia despite having moved its headquarters to Navarra in 2013— licensed the rights to a lung cancer drug to Novartis for €13 millions.

The effervescence of the business sector, however, is in sharp contrast to the recession in terms of R&D investment, both public and private. The most recent data available on R&D expenditure in Catalonia, for 2014, shows a drop of nearly 11% from 2009, which was a turning point after a decade of steady growth. As seen in graph 1, the communities that spend the most on R&D in both absolute numbers (Madrid, Catalonia and Andalusia) and in relative terms (Basque Country and Navarra) have rallied somewhat over this period. However, in 2014 every Spanish community saw a decrease of between 7% and 32% from R&D levels in 2009 (except for the Basque Country and Murcia, where spending only dropped 3%).

In Catalonia, R&D expenditure fell most sharply in companies from 2009 to 2014, down 13%, while higher-education spending was down 11.5% and that of the public administration, down 3.7%. The final figure deserves special comment: except for the case of the Basque Country —which, although in the middle of the crisis, has increased government R&D spending by nearly 20%— the Government of Catalonia has made the clearest effort to maintain R&D expenditure. This reduction of less than 4% in Catalonia contrasts sharply with the 18% drop seen in Spain as a whole between 2009 and 2014, with the rest of the autonomous communities seeing investment down between 18% and 58%.

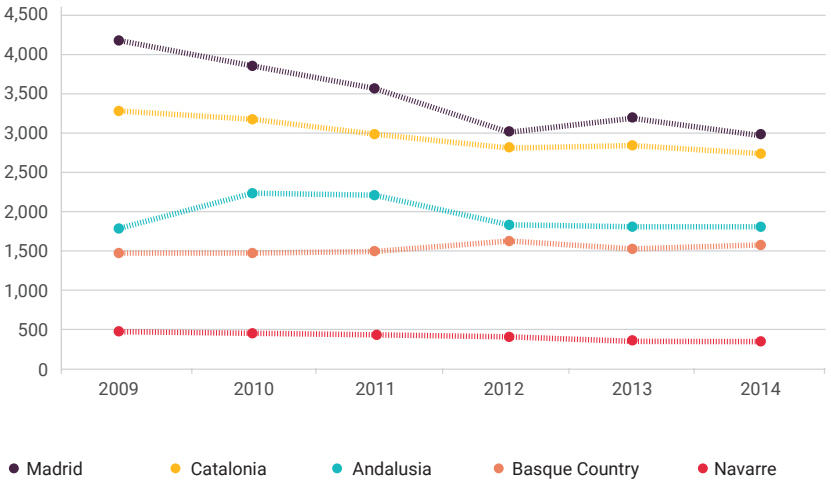
This relative stability in the Catalan government's R&D budget and the high levels of excellence at Catalan research centers, which lead the nation in attracting competitive funds, has allowed our large research institutes to sustain the upward trend in personnel, projects and research results, despite the situation. However, notwithstanding the positive indicators, the size of Catalan research centers, which in the best of cases have yearly budgets of between €15 millions and €30 millions and 200-300 researchers on average, is still very small when compared to their international counterparts, and the lack of critical mass is a handicap in this highly competitive global setting. Therefore, one of most characteristic traits of the period studied in this report, as we will see further on, is the joining of efforts to propose mergers and strategic alignments of different research centers.

In Catalonia, R&D expenditure fell most sharply in companies from 2009 to 2014, down 13%, while higher-education spending was down 11.5% and that of the public administration, down 3.7%

Catalonia continues to be above the Spanish average in R&D spending as a percentage of the GDP, which was 1.47% in 2014 (graph 2), however this indicator has fallen continuously since 2009 —when R&D investment was 1.7% of the GDP— and, in any case, is far from the European target of 3%.

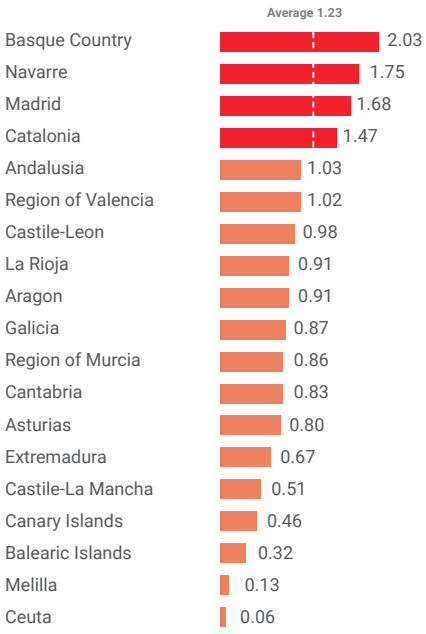
It is plausible to think that the positive results beginning to be seen in Catalan life sciences companies —many of which are spin-offs of universities and public centers— are due to the firm

Graph 1
R+D internal expenditure (2009-2014)
(in million Euros)



Source: INE

Graph 2
Percentage of GDP invested in R+D (2014)



Source: INE

commitment to research in this country since 2000. It is essential to maintain public and private efforts to drive top-notch science and improve the transfer mechanisms that encourage innovation if we want the sector to continue to grow and have a positive impact on the social and economic development of Catalonia in coming years.

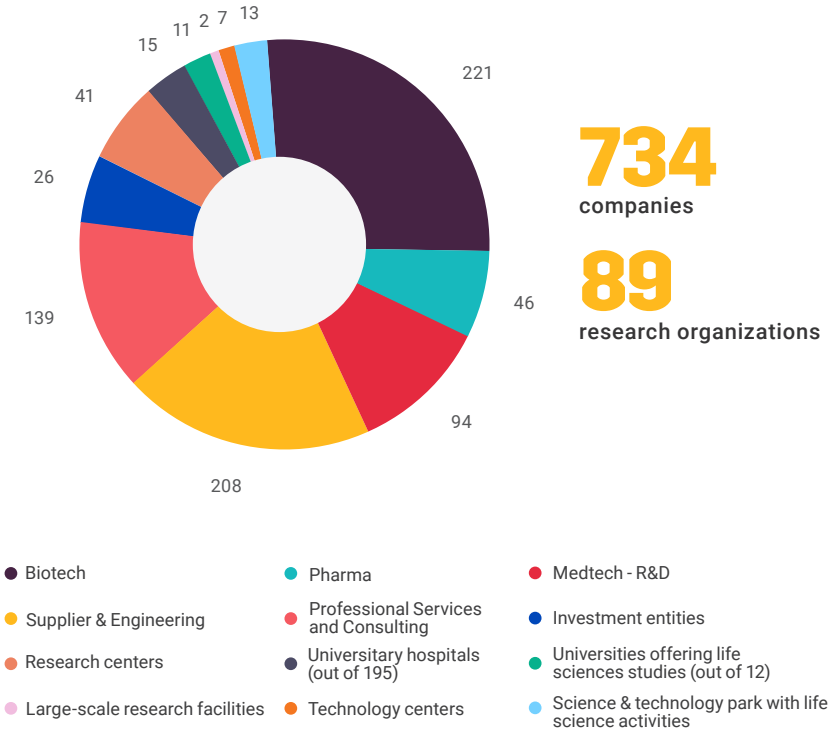
Map of the BioRegion of Catalonia

The map of the BioRegion of Catalonia underwent some significant changes in the 2013-2015 period. On one hand, there was a notable increase in the number of companies, for a total of 734, caused by the convergence of several factors that will be discussed in the next section.

On the other hand, the number of research centers working in the life sciences has dropped, as a result of the aforementioned merging, as has the number of technology centers, six of which have united to form a new organization called Eurecat.

The following sections provide an in-depth analysis of the stakeholders on this map of the life sciences in Catalonia.

Graph 3
The BioRegion ecosystem



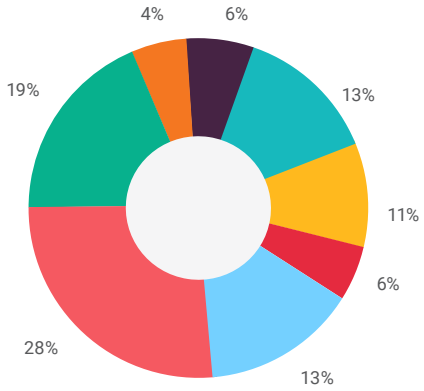
Source: Biocat Directory

COMPANIES – OVERVIEW

The BioRegion of Catalonia is home to a total of 734 companies, 49% of which carry out R&D activities. The largest group is made up of biotechnology companies (221), which focus their activities on new therapies and diagnostics, providing R&D and biotechnology services applied to various fields including agriculture, food, cosmetics and industrial processes, to name just a few.

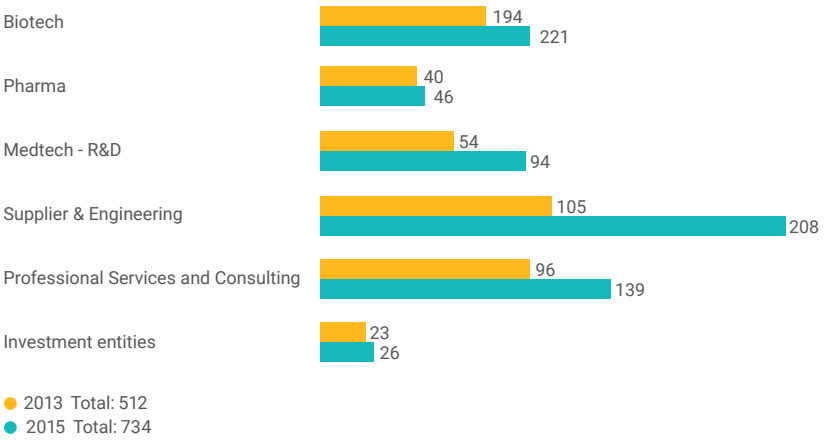
The BioRegion has 94 companies that do R&D in medical technology and 46 pharmaceutical corporations. The large group of suppliers and engineering firms (208 companies) includes many firms with links to two subsectors, medtech and pharma, but that don't do their own product development. This group is basically made up of distributors, technology suppliers and digital health companies.[13]

Graph 4
Percentage of companies in the BioRegion by main sector



Source: Biocat Directory

Graph 5
Evolution of companies in the BioRegion (2013-2015)



Source: Biocat Directory

Professional services and consulting companies make up 19% of those in the BioRegion and there is a small but stable group of investors (4%).

This large number of companies (734) has grown significantly from the make-up of the sector at the end of 2013, when the previous *Biocat Report* was published. At that time the count was 512. This increase is due, firstly, to the steady creation of new companies; and, secondly, to many service companies joining the sector from other arenas; finally, Biocat's efforts to identify all active stakeholders in the different subsectors, and in particular those working in medical technology and digital health, has also had an impact.

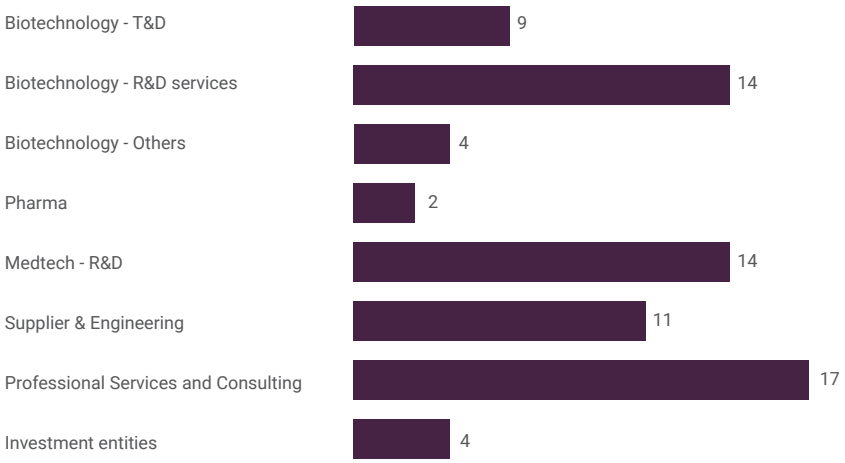
Graph 5 shows the growth seen in each segment since the previous report was published, with a total increase of 222 companies. 33.5% were set up over that period.

Between 2013 and 2015, 75 new companies were created in the BioRegion. Most of these were biotechnology firms (27), among which those providing R&D services were predominant (14). There was also a significant group of new professional services and consulting firms (17) and medical technology companies (14). Although in lesser numbers, there are new companies in every subsector, as can be seen in graph 6.

Given their short history, we have relatively little data on these new companies, most of which are micro-enterprises (fewer than 10 workers) and 25% of which are spin-offs of universities, research centers or hospitals. Among the most recently created companies in the BioRegion, just a handful are subsidiaries of international companies (3), which have opened offices in Barcelona to focus on sales or managing R&D agreements. However a significant number (16 companies, 22%) are the result of, or have benefited from, initiatives to encourage entrepreneurship, like BioEmprenedorXXI and Design Health Barcelona. In this regard, it is worth highlighting that since it was created in 2007, the BioEmprenedorXXI award —a training and mentoring program for entrepreneurs that includes a business plan competition— has led to the creation of 62 new companies, 48 of which are still active in the BioRegion.

Of the companies created over the past two years, three are crowdfunding platforms. This formula is gaining ground as a source of resources for early-stage companies.

Graph 6
Companies created by sector (2013-2015)



Total: 75

Source: Biocat Directory

In addition to the 75 companies created between 2013 and 2015, the Biocat Directory has added 147 companies active in the BioRegion for which no data was available at the time the previous report was published. As seen in graph 5, the bulk of these companies work in medical technology —a segment that has 40 new companies, 14 of which were created over past two years and 26 newly identified— or belong to the group of suppliers and engineering firms. This group nearly doubled, from 105 to 208 companies, only 11 of which were created between 2013 and 2015. Nearly half of the companies that make up this segment (56) are active in medtech (distributing medical devices, manufacturing instruments-and-lab equipment, etc.) and 21 are developing digital health technology. When, further on in the report, we analyze the subsectors of activity for the companies in the BioRegion, we will see that the weight of health and medical technology companies is growing significantly.

If we look at the rate at which new companies were set up over the past two years and compare that to organic growth in the sector between 2005 and 2015 (graph 7), we see a decrease that, however, requires clarification: this figure is only through 30 September 2015 and the detection of new business projects outside of core areas often slows over time.[14]

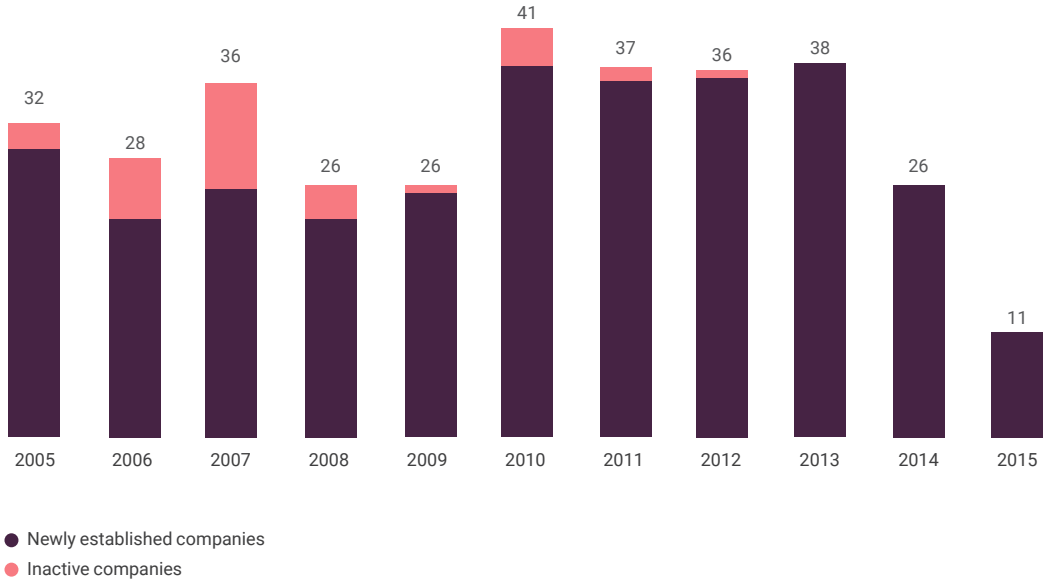
In total, 337 new business projects have been set up in the BioRegion over the past ten years, 30 of which —shown in the lighter color on graph 7— have shut down over this period (with an average lifespan of 5 to 6 years). By subsectors (graph 8), the majority of the new projects were biotechnology companies (133, 39% of the total), and most of the aborted projects were also biotech firms (19 out of the 30). These companies closed for a variety of reasons, although two do stand out: on one hand, a lack of conclusive scientific results for their technology or product to make the company attractive to investors; and, on the other, a weak initial business project or one of its key aspects, like identifying a clear market niche or having a good management team.

It is worth noting the great resilience of Catalan companies in the life sciences sector compared to other innovative sectors. So, we see that only 9% of business projects started up in the BioRegion between 2005 and 2015 came to an end, while several sources show the general mortality rate for innovative companies in Spain and Catalonia is close to 50%. According to a recent study by the Economic and Social Council on R&D in Spain, the number of innovative technology companies dropped from 30,000 in 2009 to just 16,000 in 2013.[15] In Catalonia, according to data from Idescat, in 2009 there were 7,045 companies working in technological innovation, down to just 3,396 by 2013.[16]

The size of companies in the BioRegion

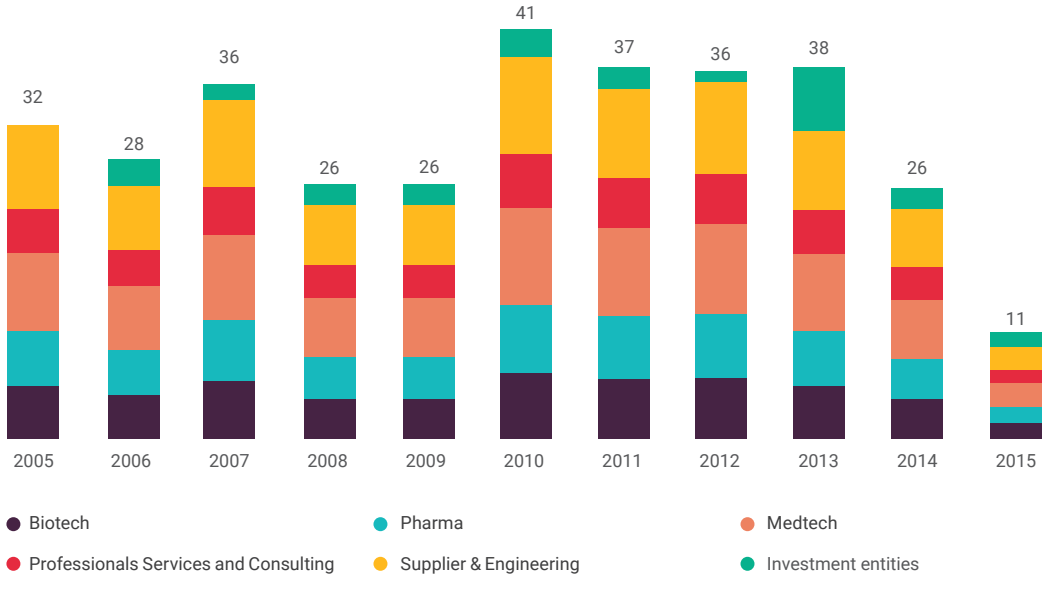
88% of companies in the BioRegion are SMEs and, of these, nearly half are micro-enterprises with fewer than 10 employees and annual operating income under €2 millions. Although in relative terms the proportion of SMEs is higher than it was in 2013 (88% compared to 85%), a more exhaustive analysis shows

Graph 7
Companies created in the BioRegion of Catalonia (2005-2015)



Source: Biocat Directory, September 2015

Graph 8
Companies created by main sector (2005-2015)



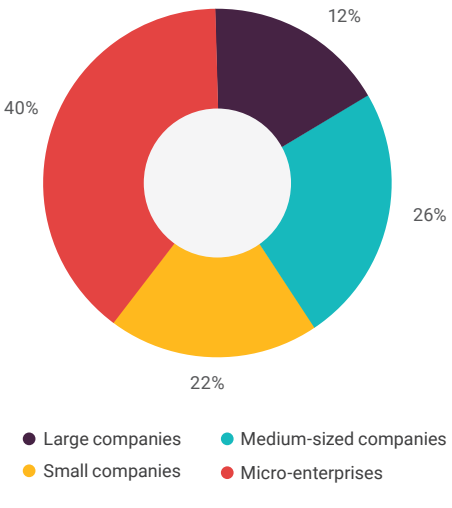
Source: Biocat Directory

that the proportion of micro-enterprises and small companies has dropped (from 43% in 2013 to 40% now and from 29% to 26%, respectively), bolstering that of medium-sized firms (with between 50 and 250 employees and yearly turnover of between €10 millions and €50 millions) that now make up 22% of the BioRegion compared to 13% in 2013.

Although it is true that the increase in the pool used for calculations means there are more companies in all segments, the increase in medium-sized companies – which doubled— and the relative drop in micro-enterprises and small firms shows that business projects are also growing, which as we mentioned in the previous report is absolutely essential to the consolidation of the sector.

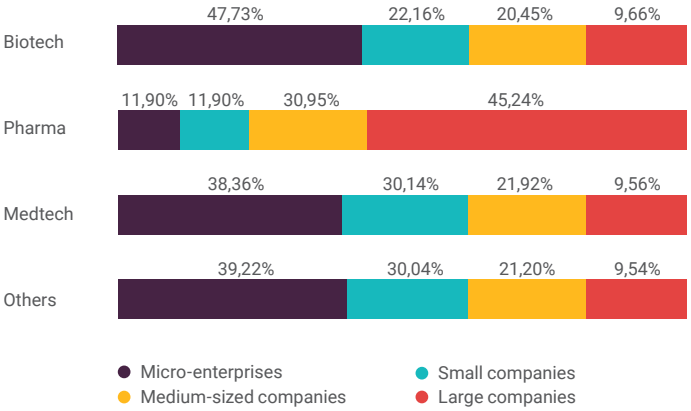
If we turn to look at the subsectors (graph 10), we see that medium-sized companies now make up 20% of all biotechnology firms, when two years ago this segment was only 14% of that total, while the proportion of small firms dropped from 26% to 22%. Among biotechnology firms, there is still a high percentage of micro-enterprises (48%), however we cannot forget, in this regard, that most entrepreneurial projects in biotechnology kick off with a bare-bones team and see no revenue for the first four years, seeking the support they need to develop their products or technology in venture capital or other public or private investors.

Graph 9
Percentage of companies in the BioRegion by size (revenue and workers)



Source: Biocat Directory / SABI

Graph 10
Percentage of companies by size in each subsector



Source: Biocat Directory / SABI

The medical technology subsector also shows a much higher relative weight of medium-sized companies (21% of the total compared to 10% in 2013), while small firms have dropped from 42% to 30% of the total and micro-enterprises, from 42% to 38%. In this case, adding a significant number of companies with years of history and consolidated projects to the pool analyzed has undoubtedly had an impact, unlike the biotechnology subsector (whose growth was purely organic, with 27 new companies created between 2013 and 2015).

The drive towards internationalization, the growing number of licensing agreements between biotechnology and pharmaceutical companies and the interest of investors —which has led to significant operations over the past two years— are good indicators that this upward trend will continue over the coming years.

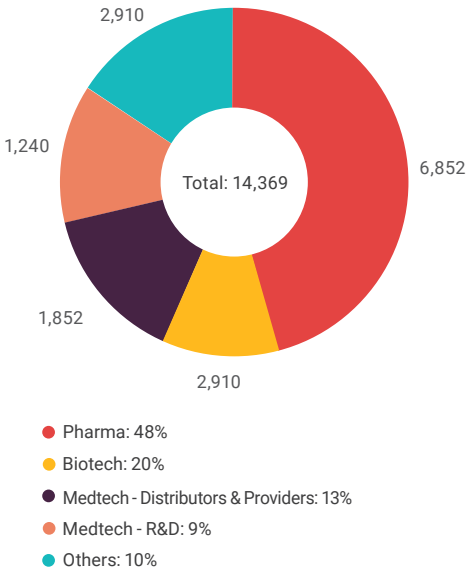
Turnover of companies in the BioRegion

Companies in the BioRegion of Catalonia posted joint turnover of €14.36 billions in 2014, which **accounts for 7% of the GDP of Catalonia**. 48% of this income is from pharmaceutical companies, with €6.85 billions,[18] while 20% (€2.91 billions) corresponds to biotechnology companies. The medical technology subsector, as a whole, makes up 22% of all revenue generated by the sector, which is broken down as shown in graph 11, between medtech R&D companies (€1.24 billions or 9%) and the group of medtech distributors, specialized providers and manufacturers of instruments and lab equipment (€1.852 billions or 13% of the total).

If we compare these figures to those in the *2013 Biocat Report* (graph 12), we see that the segment with the highest growth is medical technology, which with total income of €3.09 billions doubled the results seen in 2011. We must remember, however, that the number of companies analyzed is also twice as big as that in 2013: then the medtech segment had 106 companies and in this report the group studied is made up of 200 companies.[19]

The most significant growth, in terms of sector consolidation, is that of turnover in biotechnology firms. This has increased 20% from 2011 with practically no impact from the increase in number

Graph 11
Revenue of companies in the BioRegion 2014
(in million Euros)



Source: Biocat Directory / SABI

of companies. This data confirms the upward trend we've already noted in analyzing the size of companies, and is also in line with the increase in personnel shown in graph 13.

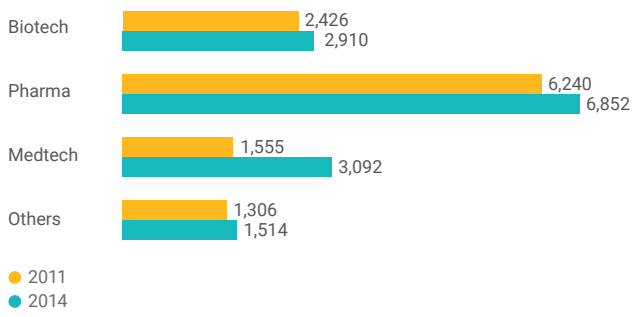
As we've mentioned previously, in the BioRegion there is a growing group of digital health companies, which cut across several subsectors: software and digital-platform developers grouped under the heading *Suppliers and engineering firms*, specialized consulting firms and biotechnology companies offering bioinformatics services. In total there are 40 companies, nearly all of which are micro-enterprises, which generate annual revenue of approximately €16 millions and employ roughly 200 people. In another chapter of this report we will delve deeper into our analysis of the latest developments in digital technology for health.

As a whole, the companies in the life sciences sector employ **42,133 workers**, which is 8,444 more than in the previous report (up 25%). Biotechnology companies, with a total of 9,989 workers, saw the lowest growth —up 18% compared to growth of 42% in people employed by medtech companies (11,244 employees) and 30% in the number of people working at consulting firms and specialized services, suppliers and engineers (6,622 employees grouped under the heading *Other*). Once again, it must be noted that the growth in biotechnology firms was organic and not the result of expanding the analysis pool, as happened in other groups. This is therefore a positive indicator of the progressive consolidation of Catalan biotech firms.

We don't have any data on the number of R&D workers in any of the subsectors, but according to the Spanish National Institute of Statistics (INE) survey on the use of biotechnology in 2013, **Catalan biotechnology companies have nearly 2,200 people working in R&D**, 56% of which are researchers and the rest, technicians. This figure is surely lower than the real situation, however, as the random methodology used for the INE survey yields a smaller number of biotech companies than those really operating in Catalonia.

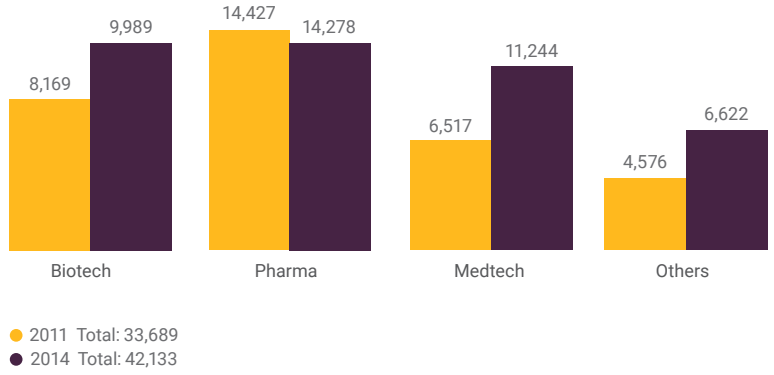
According to data from the INE, the Spanish pharmaceutical industry employs 4,449 R&D workers (full-time equivalent, FTE). Based on the weight of Catalonia in the total number of pharmaceutical employees, **R&D personnel at Catalan pharma companies is approximately 1,700 FTE positions**.

Graph 12
Evolution of revenue of the BioRegion companies (2011-2014)
(million €)



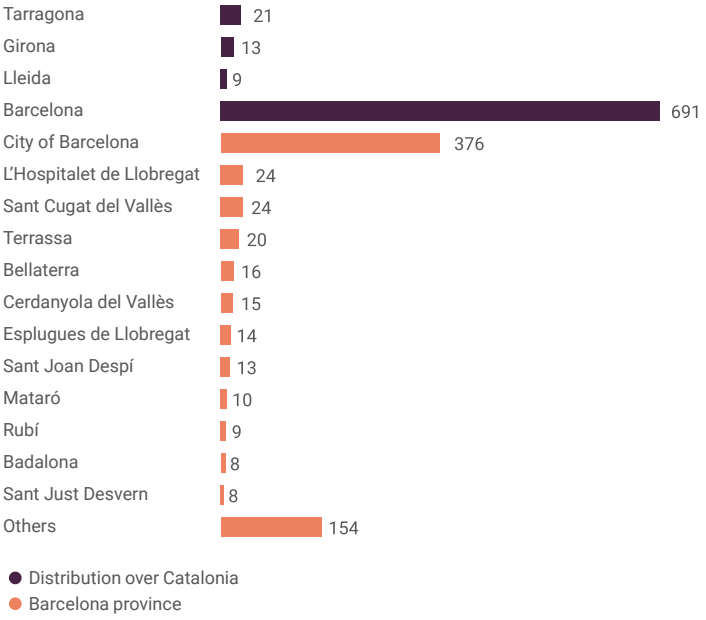
Source: Directori Biocat / SABI

Graph 13
Number of workers in the BioRegion companies (2011-2014)



Source: Biocat Directory / SABI

Graph 14
Geographic distribution of companies in the BioRegion



Source: Biocat Directory

Barcelona, epicenter of the BioRegion

Barcelona is home to 95% of the business fabric in the life sciences sector in Catalonia. As shown in graph 14, the province of Barcelona (94%) and especially the Catalan capital (51%) make up the bulk of the sector.

Within the capital, the greatest concentration of companies is found in the neighborhoods of Les Corts and Sarrià - Sant Gervasi —which have a total of 169 companies, 45% of all those in the city of Barcelona, with a noteworthy hub at the Barcelona Science Park— and Eixample (28%). The third area of concentration is the neighborhood of Sant Martí (22@), where 13% of all companies in the city of Barcelona are located.

Graph 15 shows the type of companies located in the city of Barcelona, which is home to the majority of investors (81%) and consulting and professional services firms, approximately half of all biotechnology and pharmaceutical companies, but only 39% of suppliers and engineering firms and 36% of medical technology companies.

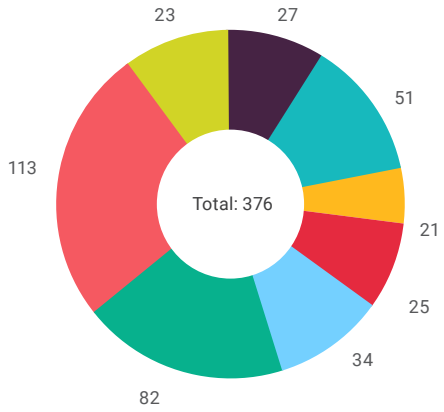
Technology platforms and scientific services provided by universities and research centers, connections —in terms of logistics but also professional networking— access to highly trained personnel, and proximity to sources of funding and the government are just some of the factors that encourage companies to group together in the city of Barcelona and its metropolitan region. Nor should we forget, in this regard, that **85 of the companies active in the BioRegion are spin-offs of universities, hospitals and research centers**, and the majority of public research bodies are also located in the metropolitan area.

Internationalization of companies in the BioRegion

Europe is the destination for most foreign sales of companies in the

BioRegion that have products or services on the market. In fact, the main destination of sales for Catalan life sciences companies continues to be

Graph 15
Companies in Barcelona (city) by sector



Source: Biocat Directory

Spain, but Germany, Italy, France and the United States are the top international destinations for exports (or where services are marketed). If we broaden our focus to look at which countries are involved in R&D collaborations or that companies expect to enter in the near future (graph 16), the USA is by far the top priority for internationalization in the sector, and Great Britain joins the three European countries mentioned previously as a preferred market, although in terms of sales destination it is surpassed by Mexico.

These data come from the survey on internationalization Biocat conducted between March and June 2015, with responses from approximately 100 companies, mostly biotechnology firms (48%). 80% of companies that responded to the survey have products or services on the market and 58% conduct sales activity in international markets. The number of markets where these companies say they are present varies widely (from 1 to more than 100 countries), and although the average is 26 countries per company, only 25% of companies have products in more than 20 markets.

Graph 16 cross responses on the top five markets by volume of sales, the top five countries where organizations have scientific or technological development agreements, and the top five countries companies would like to move into or start collaborations in over the next two years.

Some of the most relevant countries in terms of sales —like Portugal, which 9% of companies list among their top markets, or Switzerland, which is a priority sales destination for 6% of companies— didn't make it onto the graph because their presence in terms of scientific/technological collaborations or potential future markets is low or non-existent.

Despite the weight of global markets in the sales strategy of these companies, only 40% currently have a department or team specializing in internationalization. 62% of companies with international sales activity have subsidiaries or local branches —in 7 countries on average— but most use local or Spanish distributors to expand their commercial reach.

26% of companies with international sales activity indicate that the income from sales in foreign markets makes up between 80% and 100% of their total turnover, while for 38% of companies foreign sales account for 40% to 79% of their income.

International presence in manufacturing is scarce. Only seven companies out of the hundred that responded to the survey say they have production plants abroad. Of the 10 production centers identified, half are located in Europe, 3 in Latin America and 2 in Asia (India and China). Some companies say only part of production takes place there, specifically for the local market.

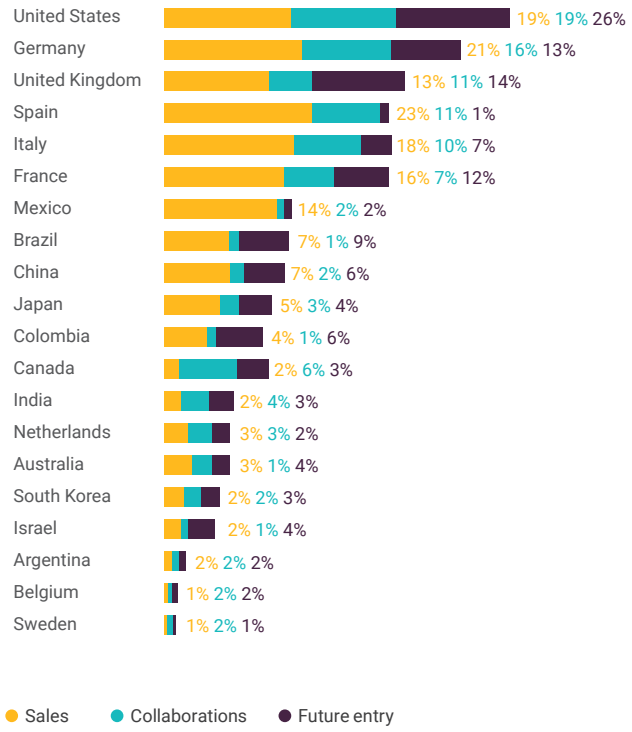
41% of the companies surveyed say they have scientific/technological development agreements with organizations in 29 different countries, with an average of two international agreements per company. Additionally, 21% of companies have licensed out their products and 20% have acquired licenses on products from other organizations. The partners in these licensing agreements are mainly other companies (89%), research centers (45%), universities (34%) and hospitals (19%).

This data on internationalization must be put into context in terms of the wide variety of business models found in the life sciences sector. Only some types of companies —pharmaceutical, medical device manufacturers, CMOs, etc.— have industrial production activities and seek out foreign markets to export products. Most biotechnology firms, whether they focus on research into new therapies and diagnostics, providing R&D services or working in fields such as food, the environment or cosmetics, work mainly in the pre-production stages and their business models focus on providing services or licensing their products —often a patent for innovative technology— to larger companies, which then produce and market the final product.

Funding companies in the BioRegion

Companies in the BioRegion attracted more than €100 millions in investment over the 2013-2015 period, more than half (€55.16 millions) over the past year (see graph 17 and table 1). In 2015, companies attracted 66% more funds than in 2013, when €33.12 millions were raised and the previous record since recording began in 2003. In 2014, however, there were "only" 16

Graph 16
Main markets for BioRegion companies



Source: Biocat Internationalization Survey 2015

investment operations for a total of €11 millions –one third of that seen in 2013. Although the figures for that year also include the capital increase by InKemia IUCT Group on the Spanish Alternative Stock Market (MAB) for €3.4 millions.

Despite this drop in direct investment in companies in the BioRegion, **2014 was an extremely positive year** given the importance of the operations in the sector. Specifically, **Oryzon Genomics** signed the largest deal ever reached by a Catalan or Spanish biotechnology firm, selling the rights to exploit its experimental drug ORY-1001 for acute myeloid leukemia —with orphan drug status— to pharmaceutical corporation **Roche** for a total of $500 millions, including an initial payment of $21 millions and an additional $50 millions in research milestones, $4 millions of which has already been paid out for successful completion of the first stage of phase I clinical trials.[21] The agreement between Oryzon and Roche covered only two of the 16 patents held by this Catalan biotechnology firm, which was founded in 2000 by Carlos Buesa and Tamara Maes as a spin-off of the University of Barcelona and began its international expansion by opening a subsidiary in Boston (USA) in October 2014, now focusing on research into diseases with a high social impact, like Alzheimer.

Beyond its financial impact, the importance of the Oryzon-Roche agreement lies in the fact that it confirms the great potential of research being conducted in Catalonia and has drawn the attention of international investors to companies in the BioRegion, which has helped attract funds for other important operations.

Oryzon was also one of the companies that fuelled the **high capitalization in the sector in 2015**, with a round for €16.5 millions that it used to fund its IPO on the Madrid Continuous Market in December 2015.

The other large operation in 2015 in the BioRegion was carried out by **Minoryx Therapeutics**, a company doing research into rare neurodegenerative diseases that closed a €19.4-millions round to fund clinical validation of MIN-102. This drug is a candidate to treat X-linked adrenoleukodystrophy (X-ALD), a rare disease that causes motor dysfunction and can lead to death for which there is currently no treatment available. This round, led by **Ysios Capital**,[22] was in addition to two operations closed by Minoryx in early 2015: €1.6 millions invested mainly by **Caixa Capital Risc** and €750,000 from the **HealthEquity** fund (promoted by the Barcelona Medical Association and the Riva y García financial group). These funds are in addition to the €700,000 in grants and loans from public entities from 2013 to 2015.

In addition to the aforementioned operations, 2015 saw seven more over the million-euro mark (see Table 1). Noteworthy among these, as it is a new area of interest on an upward trend, are the four funding agreements signed by digital health start-ups: two of which are online platforms to give patients direct access to medical services (**TopDoctors** and **Clinic Point**), one to create personalized health plans (**Medtep**) and one medical imaging software company (**Galgo Medical**). One of these companies, Medtep, saw investment from a Mexican fund —Stella Maris Partners— and decided to move its headquarters to the United States to facilitate access to the North-American market, although its marketing and product-development teams remain in Barcelona. There are other similar cases of companies in the sector (**Avizorex, Neos Surgery, Palobiofarma**) that, although their registered business headquarters are not in Catalonia, carry out most of their activity here. As such, we have included them in our investment statistics.

Additionally, a Catalan investment manager, Ysios Capitals, led the most important round even seen in a Spanish biotechnology company. Specifically, it involved Sanifit, a company based in Mallorca, which obtained €36.6 millions to fund development of SNF472, a drug to treat cardiovascular disease linked to calcification in kidney dialysis patients.[23]

The importance of operations like those of Minoryx and Sanifit is clear when seen in the context of the European venture capital market. According to data from the EVCA, the European Venture Capital Association, this type of investment —seed, early-stage and later-stage venture— totaled €3.6 billions in Europe in 2014, funding projects in 3,209 companies. Countries in southern Europe —Portugal, Spain, Italy and Greece— and those in central and eastern Europe saw the lowest levels of investment: the EVCA estimates €200 millions in VC investment in southern countries compared to the €900 millions of venture capital invested in the three large hubs (Great Britain/Ireland, France/ Benelux and Germany/Austria/Switzerland). Operations in the life sciences sector made up only 13.1% of all venture capital and private equity investment in Europe in 2014, going to 15.8% of all companies that received investment.[24]

In Spain, the Spanish Association of Venture Capital Firms (ASCRI) puts venture capital investment higher, at €280 millions in 2014, with 10% going to the life sciences sector. Catalonia is home to 38% of the companies, in any sector, that received investment, and more importantly, received 60% of all capital invested. In the biosciences, the €10 millions attracted by Catalan companies in 2014, according to ASCRI, makes up 36% of all VC investment in Spain that year.

Over the 2013-2015 period, we also saw new funding options emerge for small innovative companies, which are also new ways to broaden the social base of R&D investment and give access to small investors. We mean **crowdequity**, a formula based on the idea of crowdfunding —a way of channeling donations to social and cultural projects through the Internet—that goes a bit further. Instead of just making a donation, with crowdequity investors get a share in the company's equity and can see return on their investment if the project turns a profit.

So, while bodies like FECYT promoted the creation of crowdfunding platforms, like Precipita (October 2014), geared towards raising funds for research and scientific dissemination projects, other private crowdequity initiatives were also launched. In Catalonia, specifically, there are three active initiatives: **Capital Cell**, founded in 2013, has carried out operations with several companies in the biotech sector, including Iproteos, ZeClinics and SM Genomics; **Crowdcube**, created in Great Britain in 2011, opened a subsidiary in Barcelona in mid-2014 and closed the largest crowdequity operation ever seen in the Spanish biotech sector in October 2015, raising €234,000 for Mind the Byte; and **Funds4Science**, the latest of this type of initiative launched in early 2015.

Companies in the BioRegion attracted more than €100 millions in investment over the 2013-2015 period, more than half (€55.16 millions) over the past year

The financial panorama in the sector over the past two years also includes Catalan biopharmaceutical company **Reig Jofre** going public in June 2014, through a merger with Natraceutical, a company specializing in nutritional supplements. With a joint turnover of €150 millions, this made Reig Jofre the fifth pharmaceutical company to be traded on the Spanish Continuous Market (Madrid Stock Exchange) after Grifols, Almirall, Rovi and Faes Farma. Since then, the company has closed several significant deals, including one to move into the Japanese market with Kern Pharma and other distribution contracts with Catalan biotechnology firms, and closed 2015 with a turnover of €157 milion, 2.9% higher than previous year.

Furthermore, in July 2014, pharmaceutical company **Almirall** closed an agreement with British-based **AstraZeneca** to transfer its respiratory line in an operation valued at €1.56 billions, €910 millions of which are in research milestones. This led to the opening of a new AstraZeneca R&D center in Barcelona in June 2015 and the company announcing it will invest €540 millions in research in Spain over the coming three years. In late 2015, Almirall acquired 100% of the **Poli Group** —a holding company made up of Taurus Pharma GbmH, Polichem, SA, and Polichem S.r.l.— for €365 millions to complement its shift towards dermatology.

2015 saw another significant licensing agreement: biotechnology firm **Palobiofarma** —which continues to do the bulk of its work in Catalonia despite having moved its registered headquarters to Navarra in 2013 after receiving an injection of capital from Sodena, the financial instrument of the government of Navarra— licensed the rights to its drug PBF-509 to treat lung cancer to Novartis for €13 millions, a figure that will increase if research milestones are met.

The investment activity of Catalan multinational corporation **Grifols** deserves special mention, increasing its portfolio of stakes in companies and strengthening its position as a key stakeholder in the global biotechnology and biomedical sector. In addition to its stake in Nanotherapix (51%), Araclon (51%), VCN Biosciences (40%), Progenika (60%) and Aradigm (35%) —which we covered in the *2013 Biocat Report*— the

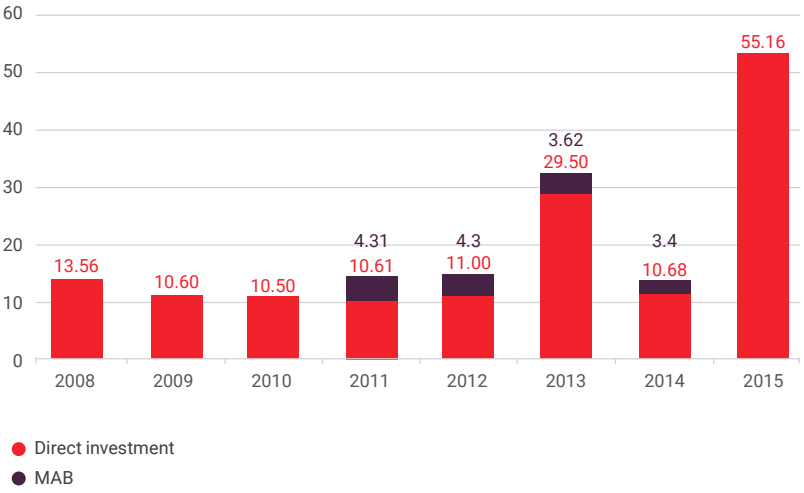
company acquired 21.3% of TiGenix in November 2013. This Belgian company conducts research in Madrid after acquiring Cellerix, whose founders included former minister of Science and Innovation Cristina Garmendia. Grifols expects to take on up to 40% of TiGenix by 2018.

Just a few weeks later, Grifols announced its purchase of the Novartis hematology diagnostic division, based in California (USA). The operation was valued at $1.67 billions and strengthened Grifols' presence in the United States, where the company has 120 plasma collection plants, among other assets. In 2014 and 2015, the company expanded its investment portfolio with two additional operations: in September 2014 Grifols paid €21 millions for a 50% stake in Kiro Robotics, a spin-off of the Mondragón Corporation that specializes in producing technology to automatize hospital processes; in March 2015 it acquired 45% of the shares of Alkahest, with an investment of $37.5 millions and an additional $12.5 millions for marketing rights. Alkahest is a spin-off of Stanford University and its researchers have shown that some factors in the blood of young animals can help older animals recover cognitive and mental faculties.

In addition to these investments in companies with innovative projects, Grifols, which closed 2015 with global income of €3.93 billions, devoted more than 6% of its turnover to R&D. Specifically, in 2015 the company invested €236 millions in R&D —5.9% of turnover— up 30% from 2014.

The Biocat Directory shows **26 investment bodies active in Catalonia**, including seven associations of business angels, four corporate investors, one institutional investor (Catalan Institute of Finance, ICF) and eight venture capital firms, as well as the crowdfunding and crowdequity initiatives discussed above. All of these organizations invest or have invested in the life sciences sector, but only four specialize in this area and invest a significant volume: **Caixa Capital Risc**, **Ysios Capital**, **Inveready** and **HealthEquity**.

Graph 17
Capitalization of companies in the BioRegion (2008-2015)
(in million Euros)



Source: BiotechGate / Biocat Directory

Caixa Capital Risc led or co-led 26 of the operations in table 1, for a value of nearly €24 millions. It has several investment vehicles, two of which focus exclusively on the biosciences sector: Caixa Capital Biomed (€17 millions) and Caixa Invierte Biomed (€35 millions). It also has a fund for new technology —Caixa Capital TIC, with €20 millions— which could be of interest to digital health companies.

Ysios set up its first fund in 2008, with €69 millions, from which it has invested in 11 biotechnology companies, four of which were Catalan. In 2014, it set up a new fund with €100 millions, also geared towards the bio sector. Of the investment registered in Catalonia, Ysios has led or co-led four operations for a total value of €28.4 millions.

Inveready manages more than €50 millions. Specifically, the Inveready Biotech II fund created in 2012 is endowed with €15 millions. In the BioRegion, this firm has led or co-led 10 investment agreements for a total of €9 millions.

HealthEquity is the newest specialized fund here in the BioRegion. It was promoted by the Barcelona Medical Association and is managed by Riva y García. The fund is endowed with €7 millions, which may be expanded to €15 millions, and so far has participated in two of the rounds closed in 2015 by Minoryx Therapeutics.

Table 1. List of investment operations

Year	Company	Stage / Type of financing	Investment (in milions €)	Main investor/s	Coinvestors
2003	Oryzon Genomics	Participation loan	0.4	ENISA	
2004	AB-Biotics	Equity - Seed	0.05		
2005	Inkemia IUCT Group	Capital increase	0.29	Founders	Private investors
2006	ERA Biotech*	Participation loan	1.4	Uninvest	Invertec, Reus Capital Riesgo, Talde Capital II
2007	Genmedica Therapeutics	Equity - Start up	3.5	BCN Emprèn	Caixa Capital, Unifondo, Innova 31
2008	Agrasys	Equity - Seed	0.36	Uninvest	
2008	Anaxomics Biotech	Equity - Seed	1	Private Investors	
2008	ERA Biotech*	Equity - Start up	2.8	Axis	Highgrowth, Uninvest
2008	Genmedica Therapeutics	Participation loan	0.8	ENISA	
2008	Oryzon Genomics	Equity - Start up	8.6	CORSABE	2 family offices(Inversiones Costex, S.L. y G3T, S.L.), other investors
2009	AB-Biotics	Participation loan	0.4	ENISA	
2009	Ability Pharmaceuticals	Capital increase	0.36	Founders	
2009	ERA Biotech*	Equity - Start up	3.75	Crédit Agricole Private Equity	HighGrowth, Axis, Uninvest and other Spanish entities
2009	ERA Biotech*	Participation loan	0.8	ENISA	
2009	Gem-Med	Capital increase	1.4	BCN Emprèn	Uninvest, family offices (Alduero, DyF 2000
2009	Inkemia IUCT Group	Capital increase	0.1	Private Investors	
2009	Neurotec Pharma*	Participation loan	0.15	ENISA	
2009	Omnia Molecular	Equity - Seed	1.5	Caixa Capital Risc	Business angels
2009	Oryzon Genomics	Equity - Start up	0.3	BCN Emprèn	Najeti
2009	Sepmag Tecnologies	Participation loan	0.28	ENISA	
2009	SOM Biotech SL	Equity - Seed	0.11	Founders	3 private investors
2009	Thrombotargets Europe	Equity - Start up	1.3	*Undisclosed*	
2009	Thrombotargets Europe	Equity - Start up	0.15	*Undisclosed*	
2010	Ability Pharmaceuticals	Equity - Seed	0.4		
2010	Ability Pharmaceuticals	Equity - Seed	1.1	Founders	Government subvention
2010	Inkemia IUCT Group	Capital increase	0.07	Private Investors	
2010	NEOS Surgery	Participation loan	0.6	ENISA	
2010	Omnia Molecular	Equity - Start up	2.1	Caixa Capital Risc	ENISA
2010	Oryzon Genomics	Participation loan	0.75	ENISA	
2010	Palobiofarma	Participation loan	0.3	ENISA	
2010	Sabirmedical	Equity - Seed	5	Ysios Capital, Caixa Capital Risc	
2010	Sagetis	Equity - Seed	0.08	Caixa Capital Risc	Founders
2010	SOM Biotech SL	Equity - Seed	0.1	*Undisclosed*	
2011	AB-Biotics	Participation loan	0.25	ENISA	
2011	AB-Biotics	Capital increase	4.31	MAB	
2011	Genmedica Therapeutics	Equity - First stage	3	Caixa Capital Risc	BCN Emprèn, Uninvest, VentureCap, family offices, private investors
2011	ImicroQ	Participation loan	0.05	Caixa Capital Risc	
2011	Inkemia IUCT Group	Capital increase	0.11	Private Investors	
2011	Inkemia IUCT Group	Capital increase	0.06	Private Investors	

Year	Company	Stage / Type of financing	Investment (in milions €)	Main investor/s	Coinvestors
2011	Minoryx Therapetutics	Participation loan	0.05	Caixa Capital Risc	
2011	Neurotec Pharma*	Equity - Start up	0.5	Inveready, Caixa Capital Risc	
2011	Sabirmedical	Equity - Seed	1	Axis-ICO	
2011	Sagetis	Equity - Start up	0.5	Caixa Capital Risc	Business Angels
2011	SOM Biotech SL	Equity - Seed	0.75	INNOVA31	6 private investors, ACCIÓ, MSSSI, MCYT
2011	STAT-Diagnostica & Innovation	Participation loan	0.035	ENISA	
2011	STAT-Diagnostica & Innovation	Equity - Seed	2	Ysios Capital, Axis	
2011	Transbiomed	Equity - Start up	1.2	Inveready	Business angels, participation loan
2011	VCN Biosciences	Government subvention	1.1	Genoma, CDTI, ACCIÓ	
2012	AB-Biotics	Capital increase	4.3	MAB	Capital MAB (ICF), Almirall, other investors
2012	AB-Biotics	Debt leverage	0.7	Several bank entities	
2012	Ability Pharmaceuticals	Equity - Seed	1	Inveready, Genoma Espanya	Partners, private investors, business angels
2012	BCN-Innova	Participation loan	0.1	ENISA	
2012	BCN-Innova	Participation loan	0.15	ICF	Family offices, Business Angels Network Catalunya (BANC)
2012	DBS Screening	Equity - Start up	0.12	Caixa Capital Risc	Business angels
2012	Genmedica Therapeutics	Participation loan	0.9	ENISA	
2012	Genocosmetics	Equity - Start up	0.14	Caixa Capital Risc	Business angels
2012	Inbiomotion SL	Equity - Start up	2	Ysios Capital	Fundació Vila Casas, JVRisk Technologies, and other investors
2012	Inkemia IUCT Group	Capital increase	1.3	Pre-MAB investors	
2012	Iproteos	Equity - Start up	0.11	Private investors	
2012	Mind the Byte	Participation loan	0.05	ENISA	
2012	Minoryx Therapeutics	Participation loan	0.05	ENISA	
2012	Palobiofarma	Equity - Start up	1	Inveready, Fitalent	Genoma España
2012	Phyture Biotech	Capital increase	0.27	IUCT Emprèn	
2012	Plasmia Biotech	Capital increase	2.3	*Undisclosed*	
2012	SOM Biotech SL	Equity - Start up	0.41	*Undisclosed*	Institutional Pharma, business angels
2012	VCN Biosciences	Equity - Start up	0.4	Gri-Cel (Grifols)	
2013	AB-Biotics	Capital increase	1.12	MAB	
2013	Ability Pharmaceuticals	Participation loan	0.25	ENISA	
2013	Ability Pharmaceuticals	Participation loan	1.2	MINECO (INNPACTO-2012)	
2013	Bionure	Equity - Start up	1.5	Technomark	Founders, ENISA
2013	ClinicPoint	Equity - First stage	0.5	Cabiedes & Partners	
2013	Gem-Mad	Equity - Seed	0.4	Caixa Capital Risc	Promoters
2013	ImicroQ	Equity - First stage	1.1	Caixa Capital Risc	Business angels
2013	Inbiomotion SL	Participation loan	0.3	ENISA	
2013	Inkemia IUCT Group	Capital increase	2.5	MAB	
2013	Minoryx Therapeutics	Equity - Seed	1.5	Caixa Capital Risc, Inveready	MINECO, ACCIÓ
2013	Minoryx Therapeutics	Participation loan	0.1	ENISA	
2013	Palobiofarma	Equity - First stage	4.5	Sodena	Inveready, Fitalent, Development Society of Navarre

Year	Company	Stage / Type of financing	Investment (in milions €)	Main investor/s	Coinvestors
2013	Phyture Biotech	Participation loan	0.1	ENISA	
2013	Plasmia Biotech	Capital increase	0.25	*Undisclosed*	
2013	RobSurgical	Equity - Seed	0.1	Caixa Capital Risc	Founders
2013	Sagetis	Equity - First stage	0.5	Caixa Capital Risc	Business Angels
2013	SpecificPig	Equity - Seed	0.2	Caixa Capital Risc	Business Angels
2013	STAT-Diagnostica & Innovation	Equity - Start up	17	Kurma Life Sciences Partners	Idinvest, Boehringer Ingelheim Venture Fund, Caixa Capital Risc, Ysios Capital, Axis
2014	Agrasys	Equity - First stage	0.5	Inveready	
2014	Aniling	Equity - Seed	0.6	Caixa Capital Risc	Promoters
2014	Avizorex Pharma	Equity - First stage	2.5	Inveready	Government subvention
2014	Braingaze	Equity - Seed	0.336	NEOTEC program, Across Business Partners	
2014	Devicare	Equity - Seed	0.3	Caixa Capital Risc	Promoters
2014	Galgo Medical	Government subvention	0.065	Crédit d'impôt recherche (CIR)	
2014	Galgo Medical	Participation loan	0.11	ENISA	
2014	Genmedica Therapeutics	Equity - Second stage	1.7	Caixa Capital Risc, Ferrer	ICF
2014	Inkemia IUCT Group	Equity - Second stage	3.4	MAB	
2014	Iproteos	Capital increase	0.1	Equity crowdfunding campaign [Creoentuproyecto.com], 41 private investors	
2014	Mind the Byte	Crowdfunding	0.2	InKemia IUCT Group	
2014	Mint Labs	Capital increase	0.24	ENISA, ICF, Wayra	
2014	Phyture Biotech	Participation loan	0.95	*Undisclosed*	
2014	ProteoDesign	Capital increase	0.7	Caixa Capital Risc	Business angels
2014	Reva Health	Equity - Seed	*Undisclosed*	Inveready	
2014	Subtilis Biomaterials	Equity - First stage	0.28	Caixa Capital Risc, Banc Sabadell	
2014	*Undisclosed*	Equity - First stage	1.1	*Undisclosed*	Caixa Capital Risc, other investors
2015	Cebiotex	Equity - Seed	0.25	Caixa Capital Risc	Promoters
2015	ClinicPoint	Equity - Seed	1	Faraday Venture Partners	Cabiedes & Partners
2015	Foodterapia	Equity - Second stage	0.5	Faraday Venture Partners	Cabiedes & Partners
2015	Galgo Medical	Equity - First stage	1	Inveready	Government subvention
2015	GoodGut	Equity - Start up	0.15	IFEM	Private investors
2015	Greenaltech	Participation loan	2	NutraQ AS	
2015	Iproteos	Equity - Start up	0.15	IFEM	Private investors
2015	Medtep	Participation loan	1.83	Stella Maris Partners	CG Health Ventures, other private investors

Year	Company	Stage / Type of financing	Investment (in milions €)	Main investor/s	Coinvestors
2015	Mind the Byte	Crowdfunding	0.234	Equity crowdfunding campaign [Crowdcube], 115 private investors	
2015	Mind the Byte	Government subvention	0.05	SME Instrument - European Commission	
2015	Minoryx Therapeutics	Equity - First stage	1.6	Caixa Capital Risc	Sanfilippo Foundation Switzerland
2015	Minoryx Therapeutics	Equity - First stage	0.75	Healthequity	
2015	Minoryx Therapeutics	Government subvention	0.7	ACCIÓ, MINECO, MINETUR	
2015	Minoryx Therapeutics	Equity - First stage	19.4	Ysios Capital	Kurma Partners,Roche Venture Fund, Idinvest Partners, Chiesi Ventures
2015	Mint Labs	Crowdfunding	0.15	Equity crowdfunding campaign [Capital Cell], 34 private investors	
2015	NEOS Surgery	Government subvention	1.94	SME Instrument - European Commission	
2015	Oryzon Genomics	Equity - First stage	16.5	J. Fernandez and other private investors	Capital MAB (ICF)
2015	Psious	Equity - Start up	0.956	Rothenberg Ventures	Other investors from Singapore and Spain
2015	SpecificPig	Participation loan	0.2	IFEM	Private investors
2015	Top Doctors	Equity - Second stage	1.1	Castle Connolly Medical	Inveready, Fons d'Enginyers, business angels
2015	Transmural Biotech	Participation loan	0.2	IFEM	Private investors
2015	Transplant Biomedicals	Equity - Start up	1.5	Kereon Partners	Caixa Capital Risc, IFEM, private investors
2015	*Undisclosed*	Equity - Seed	2.5	*Undisclosed*	Caixa Capital Risc
2015	usMIMA	Equity - Seed	0.403	Caixa Capital Risc	Eix Technova, Banc de Sabadell, ICF, private investors
2015	ZeClinics	Crowdfunding	0.1	Equity crowdfunding campaign [Capital Cell], 64 private investors	

* Liquidated companies

Source: BiotechGate / Biocat Directory

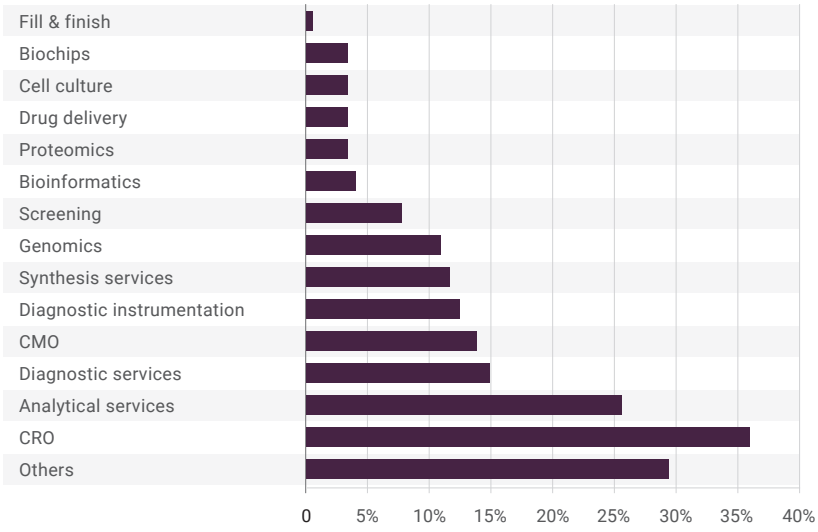
COMPANIES – ANALYSIS BY SUBSECTOR

Biotechnology and pharmaceutical companies

Of the 221 biotechnology companies listed in the Biocat Directory, 45 produce new therapies and diagnostic tools, 92 specialize in R&D services and 84 develop products and services in various areas, such as veterinary medicine, agriculture, food, cosmetics and industrial processes.

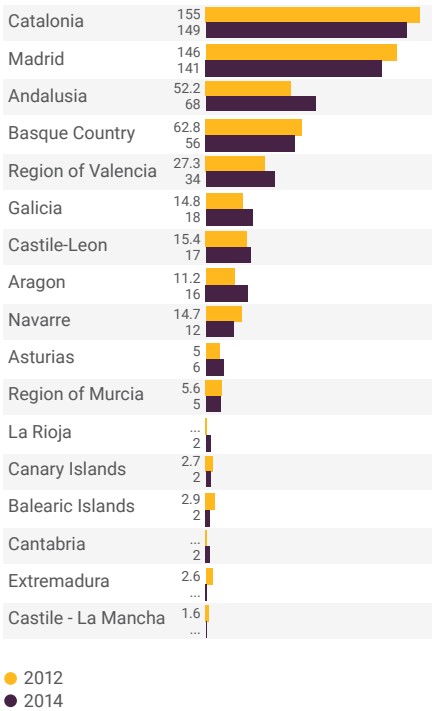
Over the 2013-2015 period, 27 new biotechnology companies were created (see graphs 5 and 6), which is nearly 14% more than in the previous report. More than half of the new biotech firms provide R&D services (14), among which projects focusing on genetics and bioinformatics abound.

Graph 19
Areas of activity of biotech companies in the BioRegion that offer R&D Services



Source: Biocat Directory
Each company may be included in more than one category

Graph 18
R&D investment of Spanish biotech companies by region (2012-2014)
(in million Euros)



Source: INE

Catalonia leads the biotechnology sector in Spain, both in terms of number of companies and R&D investment. Despite the difference in the figures as a result of the methodology used by the INE,[26] Catalonia is ranked first both in number of biotechnology companies and businesses that use biotechnology as well as in R&D investment. The latest data from the INE published in the *Asebio Report*, for 2013, shows that Catalonia has 14.89% of all companies that use biotechnology and 19.43% of all biotechnology firms, followed by Madrid (12.13% and 17.53% respectively) and Andalusia (9.27% and 15.49%, respectively).[27]

With joint expenditure of €416 millions (28.7% of the total) in 2014, Catalonia maintains its position of leadership in R&D investment in biotechnology. In terms of Catalan biotechnology companies, R&D spending dropped from 2012 to 2013 and then recovered slightly in 2014 (Graph 18).

Graph 19 shows the type of activity conducted by biotechnology firms that provide R&D services —the largest group of biotech firms, which went from 73 to 92 companies. If we compare the current catalog of services provided by these companies with those offered in 2013, what stands out is the growth in **CRO** (contract research organizations) — services now offered by 36% of companies, versus 23% two years ago— and **genomics**, services that 11% of these biotech firms offer, compared to 4% in 2013. The number of companies developing **diagnostic instruments** also increased, up from 8% to 13%.

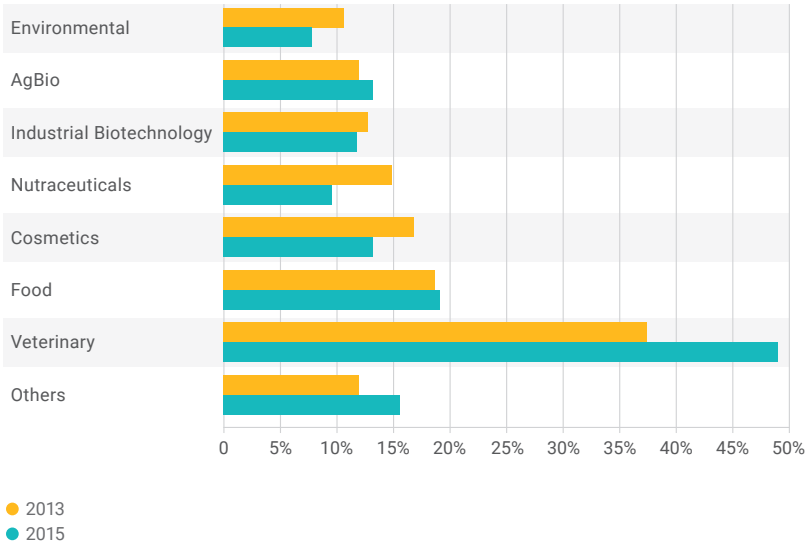
In the group of *Other* biotechnology companies, which has 11 businesses more than in 2013, the majority still focus on health and animal feed, although the relative weight of this group has fallen due to growth in other areas, including the production of **nutraceutics**[28] —which went from 9% of companies in 2013 to 15%— biotechnology to conserve and recover the **environment** —from 6% to 11%— and **cosmetics** —from 12% to 17%— as shown in graph 20.

The group of biotechnology companies that produce therapies and diagnostic tools is the only one to have shrunk since 2013 —down from 48 to 45 companies— although 9 new companies have also been created in this area. Often, although they see positive results in the initial stages of research and receive support from private and institutional investors, further work ends up revealing the projects are unviable or not attractive enough to obtain the investment and collaborators needed to scale up to market. Drug development requires considerable investment and many years of clinical trials. Every molecule and new therapeutic approach competes with other research being done at the same time, each trying to prove it is the best solution to a specific condition, and this isn't easy. As a result, this segment is the most fragile and over this period it has seen great successes —Oryzon Genomics, Palobiofarma— but also several other projects forced to fold —like Argon Pharma, Advancell, Era Biotech and Neurotec Pharma, among others— some of which had been around for more than 10 years.

As in the *2013 Biocat Report*, we analyzed the activities of the 45 biotech companies working in therapies and diagnostic tools along with that of the 46 pharmaceutical corporations that do R&D in Catalonia.[29] Graph 21 shows the weight of generics, production of small molecules and anti-infective agents, which are the main activities of the pharmaceutical companies —linked to manufacturing classical, chemical-based drugs— although researching and producing molecular diagnostic products is slowly gaining ground. Research into peptides and proteins, often linked with more efficient, precise drug-delivery solutions, stands out among the activities in biotechnology companies, along with the production of antibodies.

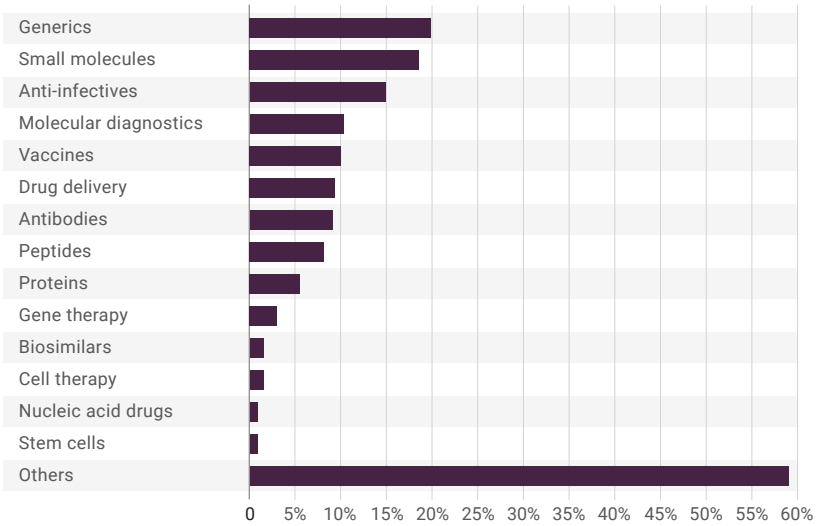
As Graph 22 shows, neoplasms (cancer) are the priority therapeutic area for Catalan biotech and pharma companies. 38% of all companies work in this field, with research often geared

Graph 20
Arees of activity of BioRegion companies included in the Biotech - Other category (2013-2015)



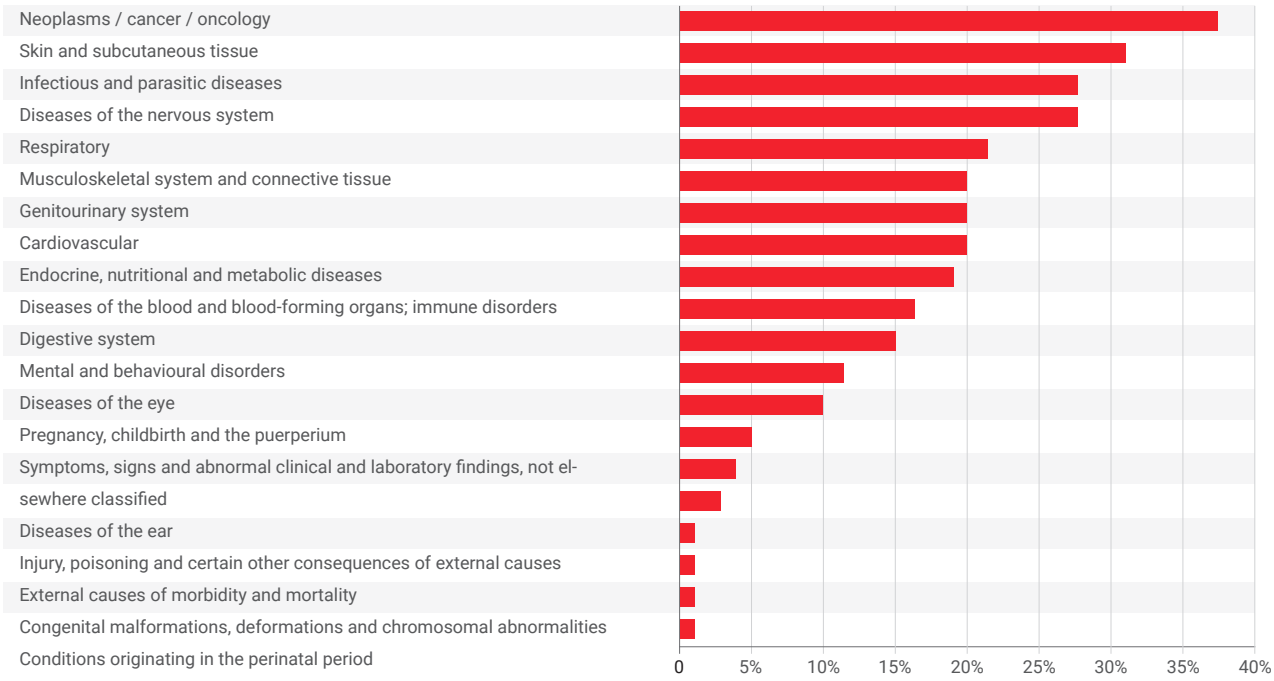
Source: Biocat Directory
Each company may be included in more than one category

Graph 21
Areas of activity of companies working in therapeutics and diagnostics in the BioRegion (biotech and pharma)



Source: Biocat Directory
Each company can be included in more than one category

Graph 22
Therapeutic areas of pharma and biotech companies in the BioRegion



Source: BiotechGate / Biocat Directory
Each company can be included in more than one category

towards types of cancer classified as rare diseases. In this regard, it must be noted that both the experimental drug Oryzon licensed to Roche in 2014 in an operation valued at more than €350 millions and that being developed by Minoryx, which received more than €19 millions in funding in 2015, have orphan drug designation.

Drugs for rare disease are driving many of the large acquisitions of companies on the global market. The extinction of patents —with exclusivity of 7 (USA) to 10 years (Europe)— the high price of these drugs and the total patient loyalty —as they are diseases without any other therapeutic alternative— have made orphan drugs a top priority for big pharma.[30] Rare diseases are mainly genetic, which means biotechnology can contribute therapeutic approaches and treatments that aren't within the scope of traditional pharmacology.

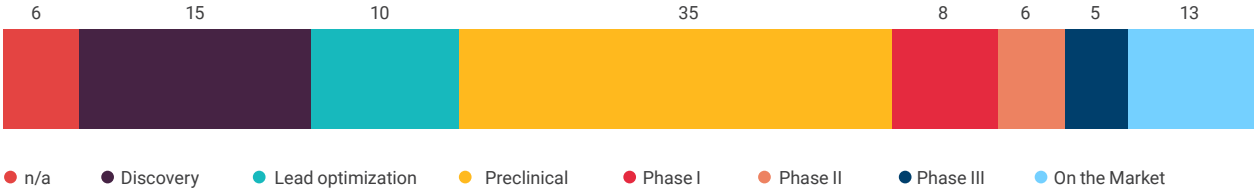
Dermatological conditions (31%), infectious diseases (28%) and the central nervous system (28%) are, in that order, the main therapeutic areas, after cancer, that Catalan biotechnology and pharmaceutical companies are working on, in a panorama that is highly diversified.

Biotechnology companies devoted to producing therapies and diagnostics in the BioRegion of Catalonia have a **pipeline of 98 products** in various stages of development (graph 23), 13 of which are already on the market, according to data provided by the companies themselves. Two thirds of these new drugs are in the early stages of research and, specifically, preclinical trials are being done with 35 of them.

One third of these drugs (31) are indicated to treat **cancer and neoplasms**, followed by those for diseases of the **central nervous system** (13) and infectious diseases (13). Dermatology, which is the second highest area of interest on Graph 22, is mainly the territory of pharmaceutical companies; biotechnology firms only have one product for this indication in their pipeline and only 3 companies are doing research in this area. The same is true of cardiovascular conditions, which have practically no presence in the pipeline of biotechnology companies, despite pharma's interest in this therapeutic area. Biotech firms, however, are interested in the area of **endocrine, nutritional and metabolic disorders**, with 8 products in different stages of development.

The **46 pharmaceutical** companies registered have 30 products in various stages of preclinical and clinical development, and 124 products on the market. The **biotechnology** firms that work in areas like **veterinary health**, **cosmetics** and **nutrition** have 85 products on the market, most of which (65) are for health and animal feed, with a dozen nutritional products and probiotics and the rest, cosmetics and dermatology products.

Graph 23
Pipeline of therapeutics & diagnostics biotech companies in the BioRegion
(Number of products)



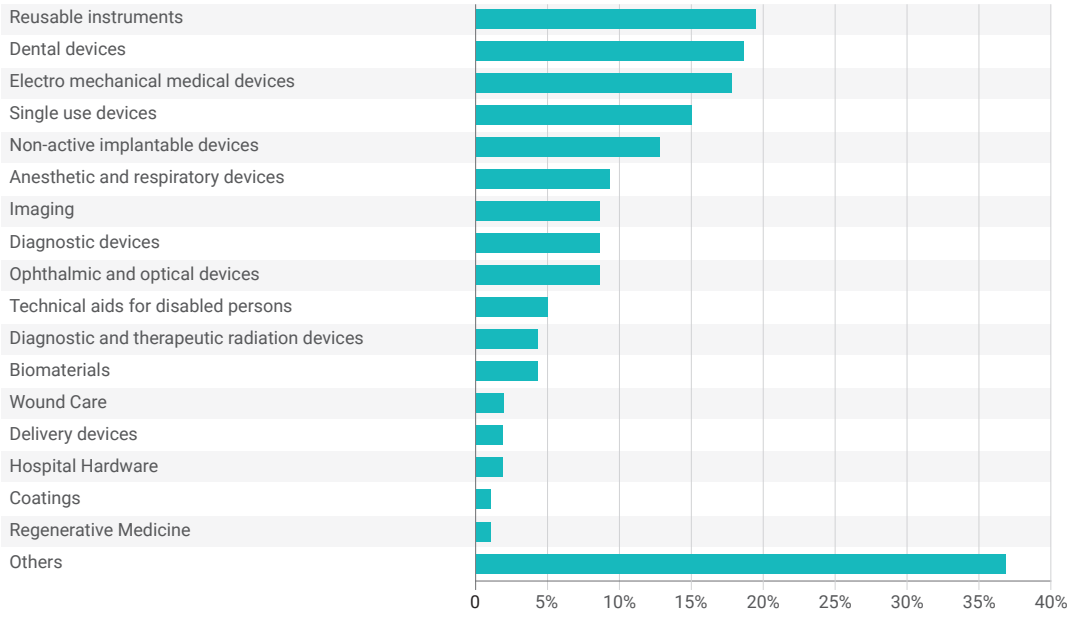
Source: BiotechGate / Biocat Directory

Medical technology and digital health

As we've mentioned previously, the BioRegion has a group of 94 companies that research, develop, produce and market medical devices and systems, included in the *medical technology* group. However activity in medical technology also extends to 93 companies in the category of suppliers and engineering firms (distributors, manufacturers of medical instruments and laboratory fungibles, engineering firms and electronics companies), 11 biotechnology companies —which produce or distribute in vitro diagnostic devices (IVD)— and two information technology services companies classified in the professional services and consulting category. Therefore, there are a total of **200 companies active in the medtech arena**.

Regarding companies in the medical technology category, graph 24 shows their main areas of activity, with the production of reusable instruments (often surgical material) leading the way, as it did in the previous report, with 19% of all registered companies. The production of dental devices has gained ground (second, with 18% of companies) as a result of several existing companies in this area of activity being included in the Biocat Directory for the first time. The third most common area is the production of electromechanical devices (17%).

Graph 24
Areas of activity of medtech (R&D) companies in the BioRegion



Source: BiotechGate / Biocat Directory
Each company can be included in more than one category

Despite the wide variety of activities, giving each one a low percentage of companies working in the area, growth has been particularly noteworthy in the number of companies active in diagnostic devices –mainly in vitro diagnostic (IVD)— which accounted for less than 2% of the total in 2013 and is now 8%. Although there are still relatively few companies working in this area, the ones doing so are researching innovative fields like biomaterials and regenerative medicine.

Regarding the companies in the category of suppliers and engineering firms that are active in medical technology, more than half (51) distribute products, one third manufacture production or lab instruments, and a similar number produce lab materials or fungibles (each company counts different activities).

Furthermore, the BioRegion has **40 companies active in digital health**, meaning they apply digital technology to address challenges in health, to discover new mechanisms that make diseases work or design new drugs using bioinformatics, to create new online platforms providing medical services or to design software to monitor health or for neurorehabilitation, among many other possible examples.

Specifically, this group of 40 companies includes 8 that offer **bioinformatics and computational research** services (Acellera, Anaxomics, aScidea Computational Biology Solutions, Chemotargets, Intelligent Pharma, Mind the Byte, Molomics Biotech and Sequentia Biotech). There are several platforms designed to make it easier for patients to request **medical visits or appointments** (Clinic Point, Doctoralia, Doctux, Medtep, Online Medicus, Top Doctors), services to help professionals work as a team or to **monitor and follow up with patients** (Bettercare, Bioaccez, Hesoff Group, Linkcare), companies specializing in **medical imaging** (Alma, Visió Mèdica Virtual, Galgo Medical), **virtual reality** solutions to treat psychological disorders (Psious, Sinaptiks), platforms for **personalized cognitive services** (BrainHealth Solutions), **communities of patients** (Social Diabetis) and even a series of companies that design customized applications or software solutions for hospitals or other healthcare providers.

Experts and analysts believe that in the coming years we will see growth in this segment of companies devoted to finding solutions to health challenges using digital technology. In this regard, a highly interesting initiative kicked off in 2015: the BIB (Bioinformatics Barcelona), an association that aims to act as a catalyst for advanced research and technology and knowledge transfer initiatives in the field of biomedicine that will help better understand diseases and move towards personalized medicine. Big data and bioinformatics, on one hand, and the convergence of disciplines –biotechnology, nanotechnology, photonics, electronics, robotics, etc.— on the other, are transforming research and development of new therapies. It is highly likely that business models will also continue to change, making room for innovative new entrepreneurial initiatives that will make Catalonia even more competitive in the life sciences arena.

RESEARCH BODIES AND SUPPORT FACILITIES

The Catalan life sciences research system hasn't changed much since the publication of the *2013 Biocat Report*, although the process of grouping several bodies together has begun, in order to gain critical mass and take advantage of synergies and complementarities at the different research institutes.

The Catalan research model, based on autonomous centers, results-based contracts, independent assessment of national and international experts and a firm commitment to attracting talent (through ICREA programs), has been proven effective and put a whole slough of institutes with just under 10 years of history among the top bodies in the world in their respective disciplines. Nevertheless, by number of publications and volume of projects and researchers, they are still far from the large international benchmarks, which is a hurdle in competing for resources and the best teams.

While entrepreneurship is one of Catalonia's strengths, as shown by the large number of spin-offs to come out of bodies in our research system, generating patents and, above all, their transfer to the business arena through licensing agreements is the big issue pending. Spain continues to hold one of lowest positions in Europe in number of patents applied for and granted, and although Catalonia generates a considerable percentage (more than 20% of all those granted in Spain), it's only a medium-sized piece of a very small pie.

Facilities, in figures

The BioRegion of Catalonia, as of the end of 2015, has 41 research centers working in the healthcare and life sciences or related subjects, such as nanotechnology, photonics, chemistry, etc. (table 2). Most of these centers (32) are part of CERCA, which brings together Catalan research centers. Three of these, the Center for Research in Agricultural Genomics (CRAG), Catalan Institute of Cardiovascular Sciences (ICCC) and Catalan Institute of Nanoscience and Nanotechnology (ICN2), also belong to the Spanish National Research Council (CSIC), which has nine other centers working in the biosciences or related fields in Catalonia.[31]

It must be noted, furthermore, that Catalonia has two large research facilities, the **Barcelona Supercomputing Center (BSC)** and the **Alba-CELLS Synchrotron**, which in addition to serving the national and international scientific community also have research groups carrying out their own lines of research. There is also the **National Center for Genomic Analysis (CNAG)**,

which was integrated into the Center for Genomic Regulation in July 2015, and is now known as CNAG-CRG.

Since publication of the previous report, the **Centre de Recerca en Sanitat Animal (CReSA)** has been integrated into the **Institute of Agrifood Research and Technology (IRTA)** and the **CRESIB** (Barcelona Center for International Health Research) has joined **ISGlobal**, which was recognized as a CERCA center in October 2015.[32]

However more fusion and convergence processes are underway, destined to reduce the number of active centers, in order to facilitate economies of scale in terms of management and facilities while increasing critical mass and research resources. Thus, ISGlobal is expected to absorb **CREAL** (Center for Research in Environmental Epidemiology), which has been coordinating with the previous center for some time now. The **Catalan Institute of Cardiovascular Sciences** (ICCC) is expected to merge with the **Research Institute of the Sant Pau Hospital**, and work is being done on a merger of the **Institute of Predictive and Personalized Medicine of Cancer** (IMPPC), **Josep Carreras Leukemia Research Institute** (IJC) and **Health Sciences Research Institute of the Germans Trias i Pujol Foundation** (IGTP).

Additionally, in mid-2015 the **Barcelona Center of Science and Technology (BIST)** was created, bringing together six large Catalan research centers: the Center for Genomic Regulation (CRG), Institute of Chemical Research of Catalonia (ICIQ), Catalan Institute of Nanoscience and Nanotechnology (ICN2), Institute of Photonic Sciences (ICFO), Institute for High Energy Physics (IFAE) and Biomedical Research Institute of Barcelona (IRB Barcelona). BIST aims to create the conditions necessary to promote top-notch research and boost the international visibility of member centers, as well as fostering collaboration in areas like postgraduate training, knowledge

Table 2. Research centers working in biosciences and related fields in the BioRegion

Center	Dependence
Centre de Medicina Regenerativa de Barcelona (CMRB)	CERCA
Centre de Recerca en Epidemiologia Ambiental (CREAL)	CERCA
Centre de Recerca Matemàtica (CRM)	CERCA
Centre de Regulació Genòmica (CRG)	CERCA
Centre de Visió per Computador (CVC)	CERCA
Centre Internacional de Mètodes Numèrics en Enginyeria (CIMNE)	CERCA
Institut Català de Recerca de l'Aigua (ICRA)	CERCA
Institut Català d'Investigació Química (ICIQ)	CERCA
Institut de Bioenginyeria de Catalunya (IBEC)	CERCA
Institut de Ciències Fotòniques (ICFO)	CERCA
Institut de Física d'Altes Energies (IFAE)	CERCA
Institut de Medicina Predictiva i Personalitzada del Càncer (IMPPC)	CERCA
Institut de Recerca Biomèdica de Barcelona (IRB Barcelona)	CERCA
Institut de Recerca Biomèdica de Lleida (IRB Lleida)	CERCA
Institut de Recerca Contra la Leucèmia Josep Carreras (IJC)	CERCA
Institut de Recerca de la Sida (Irsi-Caixa)	CERCA
Institut de Recerca en Energia de Catalunya (IREC)	CERCA
Institut de Recerca i Tecnologia Agroalimentàries (IRTA)	CERCA
Institut de Salut Global de Barcelona (ISGlobal)	CERCA
Institut d'Investigació Biomèdica de Bellvitge (IDIBELL)	CERCA
Institut d'Investigació Biomèdica de Girona Dr. Josep Trueta (IdiBGi)	CERCA
Institut d'Investigació Biomèdica Sant Pau (IIB Sant Pau)	CERCA
Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol (IGTP)	CERCA
Institut d'Investigació Sanitària Pere Virgili (IISPV)	CERCA
Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)	CERCA
Institut Hospital del Mar d'Investigacions Mèdiques (IMIM)	CERCA
Vall d'Hebron Institut de Recerca (VHIR)	CERCA
Vall d'Hebron Institut d'Oncologia (VHIO)	CERCA
Centre de Recerca en Agrotecnologia (Agrotecnio)	CERCA/UdL
Centre de Recerca en Agrigenòmica (CRAG)	CERCA/CSIC
Institut Català de Ciències Cardiovasculars (ICCC)	CERCA/CSIC
Institut Català de Nanociència i Nanotecnologia (ICN2)	CERCA/CSIC
Institut de Biologia Evolutiva (IBE-CSIC-UPF)	CSIC
Institut de Biologia Molecular de Barcelona (IBMB-CSIC)	CSIC
Institut de Ciència de Materials de Barcelona (ICMAB-CISC)	CSIC
Institut de Diagnòstic Ambiental i Estudis de l'Aigua (IDAEA-CSIC)	CSIC
Institut de Microelectrònica de Barcelona. Centre Nacional de Microelectrònica (IMB-CNM-CSIC)	CSIC
Institut de Química Avançada de Catalunya (IQAC-CSIC)	CSIC
Institut de Robòtica i Informàtica Industrial (IRII-CSIC)	CSIC
Institut d'Investigació en Intel·ligència Artificial (IIIA-CSIC)	CSIC
Institut d'Investigacions Biomèdiques de Barcelona (IIBB-CSIC)	CSIC

Source: Own elaboration

transfer, developing and managing science and technology platforms and attracting talent.

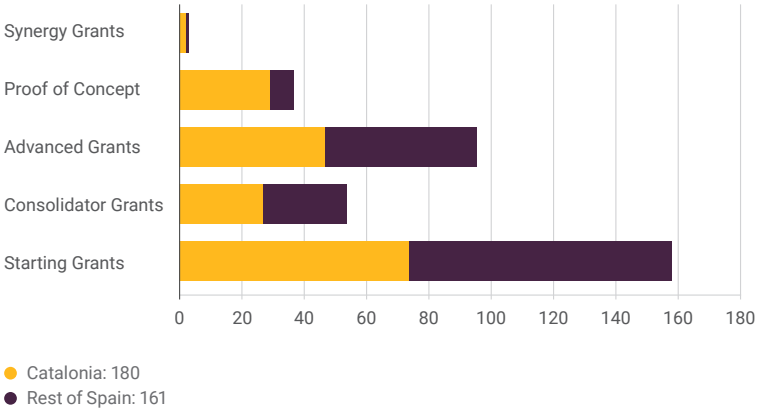
The six BIST centers, all with Severo Ochoa recognition, have a joint total of 1,700 researchers in 150 research groups, more than 500 students and an average of 75 PhD dissertations each year. BIST members generate around 1,000 scientific publications per year –more specifically, researchers at these centers published 144 articles in journals like Nature and Science between 2008 and 2012— and have received a total of 49 grants from the European Research Council (ERC).

BIST is mirroring global benchmarks like the Weizmann Institute of Science, in Israel, and the California Institute of Technology (Caltech). Although not far off in some indicators, like number of PhD students or research groups for example, the difference lies in private funding and publications. The goal of BIST is, in short, to strengthen research of excellence that Catalan researchers have proven they can do by boosting the impact of their results.

According to the latest figures published by the INE for 2014, **there are 43,898 people working in R&D in Catalonia**, of which **25,474 are researchers**,[33] 21% of all of those in Spain. Their weight, however, is more pronounced in terms of results of research: Catalonia produces **27% of all scientific publications**[34] and obtained **53% of all ERC grants** between 2007 and 2015 to go to scientists in Spain (graph 25).

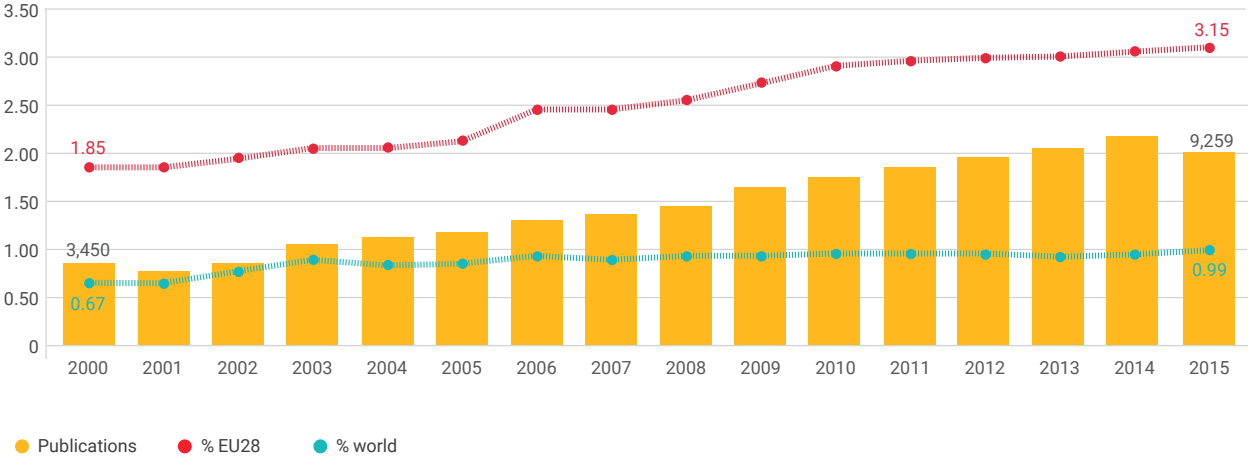
Of the 180 ERC grants obtained by scientists working in Catalonia, 78 are in the physical sciences and engineering and **62 in the life sciences**, while the other 40 went to research in social sciences and humanities. By number of ERC grants received, within the scope of this report, ICFO and CRG are tied

Graph 25
ERC Grants awarded (2007-2015)



Source: AGAUR

Graph 26
Scientific production in life sciences in Catalonia



Source: Scopus / Observatori de la Recerca (OR-IEC), Institut d'Estudis Catalans

for first, with 18 grants each. ICIQ and IRB Barcelona follow on the ranking, with 10 ERC grants each.

Regarding scientific production in the healthcare and life sciences, **the number of publications rose 168% from 2000 to 2015, going from 1.85% of all scientific production in Europe in these areas to 3.15%, and contributing 29% of publications in Spain**. As graph 26 shows, Catalonia contributes 0.99% of all scientific production in the world in the life sciences.

Catalan research in the life sciences also stands out in terms of national indicators. Catalonia is home to **11 institutes with accreditation as Severo Ochoa centers of excellence**, of the 23 currently recognized around the country, and nine of these eleven work in the life sciences or related disciplines. 6 out of the 10 units recognized as Maria de Maeztu units of excellence are also Catalan, three of which do research in the life sciences.[36]

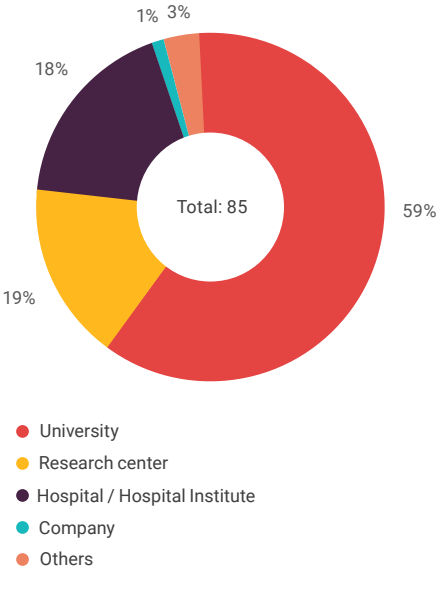
If we focus on the 41 research centers working in the biosciences and related subjects, there is a total staff of **8,716 employees**, including **5,499 researchers**.[37] Approximately 47% of these researchers are women, a percentage that is notably lower than that of the overall gender balance in these centers, where women make up 54% of the staff. Female presence is particularly scarce in centers associated with physical sciences or mathematics, where women make up roughly 25% of the staff but only 20% of researchers. On the other end of the spectrum, the number of female researchers is particularly noteworthy at hospital research institutes, where women make up more than 70% in many cases.

According to figures from the CERCA institution, Catalan research centers as a whole have a joint annual budge of **€400 millions**.[38] Contributions from the Government of Catalonia make up approximately 40% of these resources and, despite the crisis and financial difficulties of recent years, this has held relatively steady since 2009: R&D&i expenditure that year was €171 millions, while the 2015 budget earmarked €165 millions for investment in this area.[39]

Universities

The 11 Catalan universities that offer degrees in the biosciences graduate roughly 5,500 students each year in the health and life sciences. According to data from the Catalan Secretariat for Universities, in the 2013-2014 school year there were 6,491 students registered in undergraduate programs in the life sciences (biology, biomedical engineering, bioinformatics and various environmental sciences degree programs) and 996 in masters programs. Furthermore, there were an additional 2,287 undergraduate students and 607 masters students in various programs categorized under the heading Food/Nutrition, and nearly one thousand doing an undergraduate degree (964) or masters programs (34) in **veterinary science**. Finally, in the **health sciences** (medical sciences, nursing, dentistry, optics and optometry) there were more than 15,700 undergraduate students and 1,175 masters students.

Graph 27
Active spin-off companies in the BioRegion by origin
(2005)



Source: Biocat Directory

Predoc and postdoc students make up 18.22% of all **research personnel at Catalan public universities**, which in 2013 totaled **18,285 people**.[40] There aren't any studies focusing specifically on the weight of the health and life sciences in university research, but if we extrapolate the percentage of students studying life sciences degrees (12%) to the number of researchers, we calculate more than 2,100 researchers in the life sciences and related disciplines at Catalan universities. In any case, more than half of all dissertations read at Catalan public universities in 2013 were from the life sciences and science in general.[41]

According to calculations from the ACUP (Catalan Association of Public Universities), Catalan public universities were responsible for 51% of all Catalan scientific production from 2007 to 2011, with nearly 58,000 publications and an average impact of 1.38.[42]

Catalan universities attracted €187 millions for R&D&i in 2013. This figure, unfortunately, dropped between 16% and 20% per year since 2010.[43] 65% of these resources (2013) were from competitive calls, with a progressive decrease in national funds (47%), and growing weight of European calls (53%).

In technology transfer, Catalan universities —like the region in general— are far from their European or North American counterparts. At the beginning of this article we quoted a report published in *Nature Biotechnology*, which states that the top 11 universities in the United States licensed more than 1,500 patents in 2014, 1,072 in the life sciences arena.[44] In Catalonia, according to data from the

ACUP, in 2013 universities submitted 84 patent applications to the Spanish Patent and Trademark Office (OEPM), 15 of which were for inventions in the life sciences. So, although there has been a decrease in the number of new patent applications (113 were submitted in 2012), the number of applications in the biosciences rose slightly, from 14 in 2012 (see more information on patents in graphs 29 and 30).

The indicators on the creation of spin-offs, however, are more significant. According to data from the ACUP, in 2012 Catalan universities had 118 active spin-offs. In the life sciences arena, **92 spin-offs were created between 1992 and 2015, 85 of which were still active** in late 2015. As shown in graph 27, 59% of these companies (50) came out of universities.

Hospitals

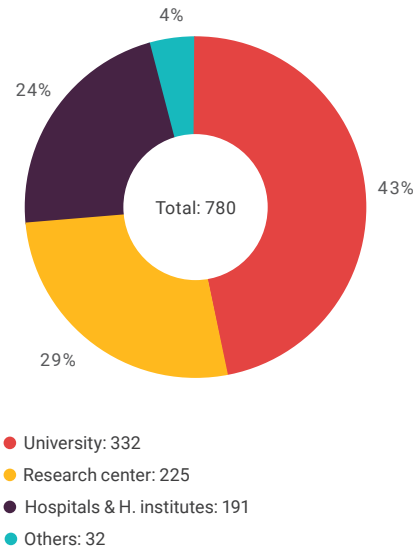
The 15 Catalan university hospitals and their research institutes —nine as of late 2015— **account for 32% of all scientific publications** (2007-2011), are home to 24% of the accredited research groups in the life sciences (graph 28) and generate between 4% and 7% of all patent applications submitted to the OEPM (see graph 30).

As a whole, the Catalan hospital system is made up of 195 establishments: 65 publicly owned (13 of which, university hospitals), 36 private (2 of which, university hospitals), 62 social health centers (government subsidized), 17 psychiatric and/or social health centers (with or without government subsidies) and 15 psychiatric centers (subsidized). These centers employ more than 89,000 workers,[45] approximately one third of which work at the 15 university hospitals. In total, these hospitals and the 9 associated research institutes have some **5,000 researchers**.

New in the period this report focuses on is the **Barcelona Clinical Trials Platform** (www.barcelonaclinicaltrials.org), promoted by the Catalan Ministry of Health and Biocat, bringing together the most important centers in Catalonia in terms of volume of clinical trials, in order to improve coordination, integration, quality and speed of research. The goal is to make Catalonia one of the top five European regions for clinical trials.

As of January 2015, the centers that belong to the platform totaled 2,740 participations in trials, with 13,498 patients recruited. The vast majority of the patients were involved in phase III trials (44%), followed by those in phase IV (25%).

Graph 28
Research groups working in life sciences or related disciplines (SGR 2014-2016)



Source: AGAUR

Also new this period, a new hospital research center was announced in March 2015: **Parc Taulí Institute of Health Research and Innovation (I3PT)**. This is a joint initiative of the Parc Taulí Health Corporation, Sabadell Service Centre for the Elderly, UDIAT Diagnostics Centre, the Parc Taulí Foundation and the Autonomous University of Barcelona that aspires to gain recognition as a CERCA center and accreditation under the Institute of Health Carlos III.

Research groups

Catalonia has 1,652 consolidated research groups, according to the results of the 2014-2016 call from the Government of Catalonia. Of these, a total of **780 groups (47%) do research in the areas covered in this report, whether in health and life sciences or physical sciences and engineering applied to these fields.**

As shown in graph 28, the majority of research groups in the life sciences and related disciplines work at universities (43%), research centers (29%) and hospitals or hospital research institutes (24%). There are also a small number of groups at other organizations, like large-scale research facilities (Barcelona Supercomputer Center, Alba-CELLS Synchrotron), technology centers or bodies in the health system.

Patents

Research in health and life sciences in Catalonia generated 286 patent applications submitted to the OEPM (Spanish Patent and Trademark Office) over the past 5 years (graph 29). The number of patents granted in this same period (301) was slightly higher, although we must take into account that the review and analysis process prior to granting a patent can take several years, which explains the peak in patents granted in 2011 seen in the graph. The majority of these applications come from companies (46% in 2014), while universities stand out as the main applicant on patents at public bodies (22% in 2014), as shown in graph 30. A significant number of applications —between 20% and 25% over the past 5 years— list an individual as the main applicant.

Life sciences patents on which the main applicant is Catalan make up 17%

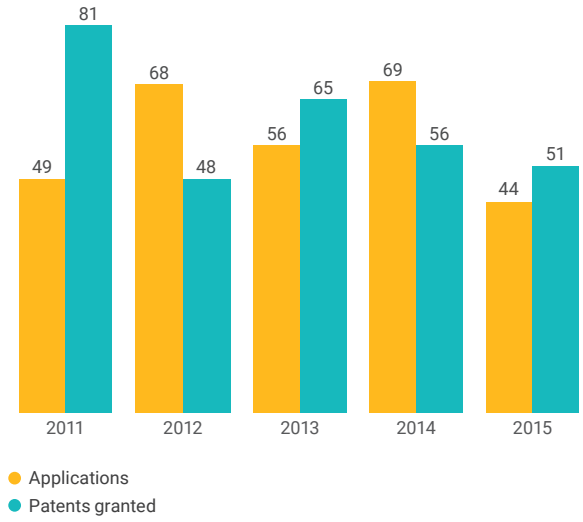
of all those submitted to the OEPM in the biosciences. This figure is slightly lower than Catalan participation in the total patents granted by the Spanish office, which was 21% in the 2009-2014 period (3,246 in Catalonia compared to a total of 15,560), while Catalan applicants received 27% of all utility models granted. Catalonia's participation in the number of patents granted by the EPO (European Patents Office) to applicants in Spain is much more significant, making up 51% of the total in 2014 (650 of 1,280).

The number of patent applications in the life sciences submitted to the national office from Catalonia has held quite steady, although Spain as a whole is still far behind other nearby European countries. In this regard, it must be noted that, according to the latest report from the World Intellectual Property Organization (WIPO)[46], in 2014 Spain submitted 1,456 patent applications to the EPO, while nearly twenty times as many were submitted from Germany (25,621), seven times more from France (10,557), and even twice as many from Italy (3,613).

It is worth remembering, however, that biotechnology, with a total of 5,905 patent applications submitted to the European Office in 2014 —12% more than the previous year— is one of the fields of technology showing the most growth currently. Patent applications submitted to the EPO for medical technology in 2014 totaled 11,124 —up 3.2% from 2013— while patent applications for pharmaceutical products (5,270) dropped 5.4%.

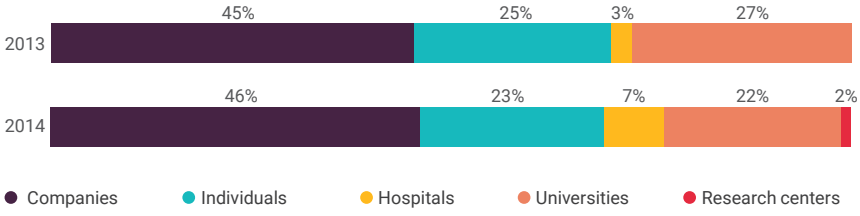
The number of international patent extensions under the PCT (Patent Cooperation Treaty) submitted from Spain and applications to the United States Patent Office in 2014 —1,705 and 1,707, respectively— are slightly higher than the number of EPO applications. However IP protection in markets like China and Japan is practically anecdotal: in 2014 Spain applied for just 340 patents in China, out of a total of more than 928,000 applications received in that country. The most recent data from Japan, for 2012, shows that Spain submitted 264 patent applications out of a total of 342,796.[47]

Graph 29
Life sciences patents from applicants in Catalonia processed by the OEPM (2011-2015)



Source: OEPM

Graph 30
Percentage of life sciences patent applications processed by the OEPM
(first applicant from Catalonia)



Source: OEPM

The birth of Eurecat

The merger of five large technology centers to form Eurecat shows the urgent need for innovations to reach the market, which this body hopes to drive by rationalizing support structures and making them more competitive. Eurecat, which was launched in late 2014 and completed its structure in July 2015, initially included the Ascamm centers, Barcelona Media, BDigital, Cetemmsa and CTM, allowing it to provide technology services in a wide range of sectors including aeronautics, food, automobile, construction, health, energy, rail transport, textiles, ICT and cultural industries, among others. In late 2015, the Reus-based Technological Center of Nutrition and Health (CTNS) joined Eurecat and, according to the directors of Eurecat, the number of

member centers is expected to double over the coming two years. However, Leitat, which was initially part of the Eurecat project, decided not to join in September 2015.[48]

Eurecat, which has a total staff of 450 professionals and expects to see turnover of €40 millions for 2015 and €60 millions in 2016, provides services for nearly one thousand companies, mostly SMEs. It is currently conducting 160 R&D projects —in 2015 it received €7.5 millions in EU funds for projects— has 73 patents and has generated 7 spin-offs. The Government of Catalonia, through the Ministry of Enterprise and Employment, is supporting Eurecat with €10 millions in 2015 and €20 millions in 2016. Despite these resources, the management structure of the new center is mainly private, with a board of trustees made up of representatives from 14 companies, including pharmaceutical firm Reig Jofre and veterinary company Hipra.[49] Biotechnology is one of the areas of technology that Eurecat hopes to bolster over the coming years.

With this operation, **the number of technology centers in Catalonia dropped to seven**. This, however, wasn't the only change aimed at driving business innovation in the period covered in this report. The **TECNIO** program has also been transformed; it is no longer a network of technology-services centers, it has now become a seal to "identify innovation stakeholders". In short, it is an effort to expand and diversify the offering of outstanding technology geared mainly towards SMEs. With this change, the program has opened itself up to companies and private institutions, and to services associated with knowledge transfer, from intellectual property managers to investment funds.

METHODOLOGY AND NOTES

The bulk of the data on which the analyses in this chapter are based comes from the Biocat Directory. This database of companies and organizations in the BioRegion of Catalonia is managed in collaboration with Venture Valuation, the company that owns the international Biotechgate database, with which the Biocat Directory shares technological support and classification criteria.

All of the companies and organizations in the BioRegion are classified under one of the following headings, corresponding to their main sector of activity:

- *Biotechnology - Therapeutics and diagnostics*
- *Biotechnology / R&D services*
- *Biotechnology - Other*
- *Pharma*
- *Medical Technology*
- *Supplier & Engineering*
- *Professional Services and Consulting*
- *Investors*
- *Public / Non-Profit Organizations / Medical Facilities*

Some companies could potentially be classified under more than one heading given their activities but the criteria established requires them to select the one they consider their main focus. Although this may make analysis a bit less flexible, the system makes it possible to better evaluate the weight and progress of each of these sectors of activity.

Regarding pharmaceutical companies, the classification differentiates between companies that research, develop, produce and market drugs —which are in the *Pharma* category— and those that only distribute or provide specialized services for pharmaceutical companies, even if these are R&D services, which go in either the *Supplier & Engineering or Biotechnology / R&D Services* group, depending on their specific activities.

Something similar occurs with medical technology companies. The Medical Technology category includes companies that research, develop, produce and market systems or devices for medical applications in humans or animals, while other activities often included in a broader view of this sector —distribution of medical devices, production of laboratory materials and medical instruments, electronics companies and those that develop e-health software and apps, among others—are included in the *Supplier & Engineering* group in the Biocat Directory.

The analysis takes into account this classification and, when necessary, cross references data from different categories to provide a fuller view of the sector (for example, to identify digital health companies). For more information on classification, see: http://biocat.biotechgate.com/app/info/definitions.php.

The data on therapeutic indications (graph 22) and the pipeline (graph 23) of Catalan biotechnology companies comes from Biotechgate and was provided by the companies themselves.

The financial and personnel data is from the SABI database (Iberian Balance Sheet Analysis System), which gets its information from the business registry.

The information on rounds of investment (Table 1) was taken from the company files in the Biocat Directory and reports published by the companies themselves, by the investment funds, in press release, articles on specialized platforms, and ASCRI. The table includes companies that were active in Catalonia at the time of the transaction even though some have later moved their headquarters out of the area. When the company did not specify the type of round, an approximation was made based on the maturity of the company or product being developed and what the investment will be used for.

The patent information comes from the database of the OEPM (Spanish Patent and Trademark Office) and the tax address of the main applicant was

used to identify patents from Catalonia. We also received support from the University of Barcelona Patents Center, which provided data from the other international offices mentioned.

1 *Beyond Borders. Reaching new heights*, Ernst & Young, 2015, p. 5.

2 "The top 15 pharma companies by 2014 revenue", *FiercePharma*, 18 March 2015.

3 "Will Wall Street Volatility Dampen The Sizzling Biotech IPO Market?", www.forbes.com, 25 August 2015; "Biotech IPOs Grind to a Halt as Stock Rout Rattles Investors", www.bloomberg.com, 8 October 2015.

4 *Idem*, Ernst & Young, 2015, p. 9.

5 *Global Use of Medicines in 2020*, IMS Institute for Healthcare Informatics, 2015.

6 European Federation of Pharmaceutical Industries and Associations (EFPIA), *The Pharmaceutical Industry in Figures. Key Data 2015*.

7 Pharmaceutical Research and Manufacturers of America (PhRMA), *PhRMA Annual Membership Survey*, Washington DC, 2015.

8 However 2013 was a step back, with only 27 new drugs approved from 36 applications submitted, far from the 39 approved in 2012.

9 *EMA recommends 81 medicines for marketing authorisation in 2013* (20/01/2014) and *Record number of medicines for rare diseases recommended for approval in 2014* (09/01/2015), News & Press releases, http://www.ema.europa.eu/

10 *Pulse of the industry. Medical technology report 2015*, Ernst & Young. This report is compiled with data from publicly traded companies in Europe and the United States, specifically 414 companies in 2014.

11 *Idem*, p. 33.

12 "Top US universities, institutes for life sciences in 2014", Bioentrepreneur by *Nature Biotechnology*.

13 See *Methodology*.

14 In this regard, it must be noted that at the time the 2013 Biocat Report was published, only two of the 38 companies created in 2013 had been registered.

15 *La situación de la I+D en España y su incidencia sobre la competitividad y el empleo*, CES, July 2015, p. 51.

16 Idescat, from data collected through INE Survey on Innovation in Companies. http://www.idescat.cat/pub/?id=aec&n=496

17 See *Methodology*.

18 This includes €599 millions to pharmaceutical distribution companies classified under the heading of *Suppliers and engineering firms*.

19 This figure includes 11 biotechnology companies working in in vitro diagnostics. To avoid duplications, these companies weren't included in the calculation of income for the medtech segment.

20 As noted in the *Methodology*, the financial data was taken from SABI, which has hardly any information on companies created between 2013 and 2015.

21 *ORYZON achieves milestone in the clinical development of ORY-1001*, press release dated 7 September 2015.

22 *Minoryx Therapeutics completes Series A funding of €19.4M ($21.7M)*, press release dated 14 October 2015.

23 *Sanifit raises €36.6M*, press release dated 8 September 2015.

24 *2014 European Private Equity Activity. Statistics on Fundraising, Investments & Divestments*, EVCA – European Private Equity and Venture Capital Association, May 2015.

25 *2015 Informe de Actividad Capital Riesgo en España*, ASCRI, Madrid, 2015, p. 22-25.

26 The INE does a yearly *Survey on the use of biotechnology*, as part of its *Survey on innovation in companies*, however the data received isn't analyzed as a whole but in a random sample. As a result, even though the Biocat registry shows the number of biotechnology companies in Catalonia has grown year after year since 2005, the INE attributes fewer biotech firms to Catalonia for 2013 than for 2012.

27 *Informe Asebio 2014*, Madrid, July 2015, p. 39.

28 Term coined by combining 'nutrition' and 'pharmaceutical' to define food products created to address specific consumer health needs.

29 Distributors and commercial offices without R&D activity are classified in the *Supplier & Engineering* category.

30 "Los huérfanos seguirán propiciando las compras y fusiones en el sector", *Correo Farmacèutico*, 8 June 2015, p. 16.

31 The CSIC has a total of 21 centers in Catalonia: http://www.dicat.csic.es/dicat/ca/centros-csic-en-cataluna

32 RESOLUCIÓ ECO/2405/2015, of 21 October, on the recognition of several CERCA centers in Catalonia.

33 All the personnel figures are in FTE (full-time equivalent).

34 Data for the 2005-2010 period was compiled by the Consorci de Serveis Universitaris de Catalonia (CSUC) in the presentation *El Portal de la Recerca de Catalonia: agregant informació de procedència i institucions diverses*, Quartes Jornades sobre Gestió de la Informació Científica (JGIC-2015), Barcelona, 21-22 May 2015.

35 Barcelona Supercomputing Center (BSC-CNS), CRAG, CRG, IBEC, ICFO, ICIQ, ICN2, IFAE and IRB Barcelona.

36 The IBMB-CSIC Structural Biology Department, the Pompeu Fabra University Department of Experimental and Health Sciences (UPF), and the Autonomous University of Barcelona Institute of Environmental Science and Technology (UAB).

37 The figures on CERCA centers are from the document *Pla d'igualtat d'oportunitats i gestió de la diversitat*. Institució CERCA, April 2014. The CSIC figures are from the document Datos 2014, available on the CSIC website: http://www.csic.es/datos-sobre-el-csic#.

38 Institució dels Centres de Recerca de Catalonia, *Memòria d'activitats 2014*, p. 15.

39 Government of Catalonia. Budget site. http://aplicacions.economia.gencat.cat/wpres/2015/02_llei.htm

40 *Indicadors de recerca i innovació de les universitats públiques catalanes. Informe ACUP 2015*, p. 96.

41 *Idem*, p. 32.

42 *Indicadors de recerca i innovació de les universitats públiques catalanes. Informe ACUP 2014*, p. 36-37.

43 According to figures from ACUP, R&D&i attracted €224 millions in 2012, €277 millions in 2011, and €347 millions in 2010. *Informe ACUP 2014*, p. 11, and *Informe ACUP 2015*, p. 14.

44 See note 11.

45 *Informe EESRI. Estadística dels centres hospitalaris de Catalonia, 2013*, Government of Catalonia Ministry of Health, February 2015.

46 *World Intellectual Property Indicators*, World International Property Organization (WIPO), 2014.

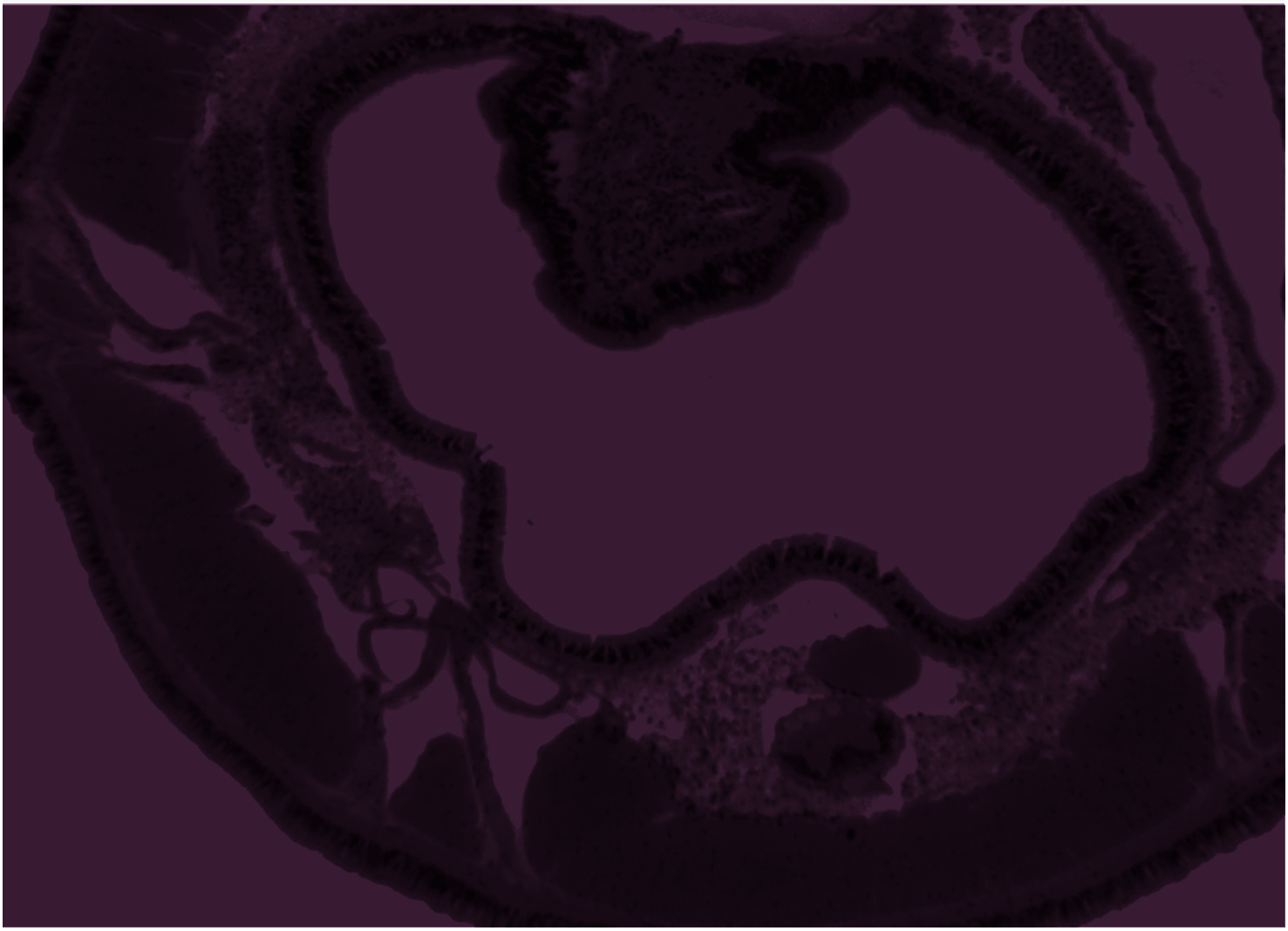
47 Data provided by UB Patent Center.

48 "Xavier Torra preveu que Eurecat doblarà el nombre de centres tecnològics durant els pròxims dos anys", *Vilaweb*, 17 August 2015 and "Eurecat becará a 100 universitarios para aportarles experiencia laboral", *La Vanguardia*, 20 October 2015.

49 *Eurecat completa l'estructura del seu patronat i es marca l'objectiu de facturar 60 milions d'euros el 2016*, ACCIÓ and Government of Catalonia press release dated 20 July 2015.

The future of healthcare and pharma

Bertalan Meskó
Medical Futurist



Enormous technological changes are heading our way. If they hit us unprepared, which we are now, they will wash away the medical system we know and leave it a purely technology–based service without personal interaction. Such a complicated system should not be washed away. Rather, it should be consciously and purposefully redesigned piece by piece. If we are unprepared for the future, then we lose this opportunity. I think we are still in time and it is still possible if an easily digestible and practical guide becomes available.

Discovering and understanding the latest trends and technologies that will shape the future of healthcare help us in this challenge. Some of these trends include:

1) Health sensors - Portable diagnostics

Smartphones being used as biosensors and wearable devices enabling patients to measure almost any health parameter at home would mean that information and health variables would finally not only be available in the ivory tower of medicine, but at home. This way, patients would have a chance for a better health management. Lifestyle could also be gamified with these devices to make it more healthy. There are smartforks currently available that teach us how to eat properly; we can soon measure the number of calories in our food with Tellspec; can measure oxygen saturation; pulse variability, ECG, EEG and even more.

2) Artificial intelligence in decision making

Even the most acclaimed professors can only keep a few studies in mind, but there are actually 23 million papers in the database of PubMed.com. It is humanly impossible now to keep up with these. But help is coming. IBM's supercomputer named Watson has been tested at several clinics in the decision making process. While the doctor talks with the patient, Watson checks the medical records and the global literature, then makes suggestions. Every time, the doctor makes the final call with all the required information being available.

3) The end of human experiments

Even in the 2010 years, we are still testing new drugs and molecules on patients. Some of them get the actual drug, others get placebo to see the difference. Several research groups are working on the creation of the first virtual physiological model of the human

Smartphones being used as biosensors and wearable devices give patients a chance for a better health management

body. This way, thousands of new molecules could be tested on billions of patients models looking for side effects or toxic outcomes with a supercomputer. HumMod is the most famous example.

4) Augmented reality

Rafael Grossmann, MD uses Google Glass to stream operations to his medical students to teach them in an entirely new way. Moreover, now when the patient comes in and they discuss symptoms, he can still look into the patient's eye, instead of immediately looking at the monitor while inputting data. The Evena glasses let nurses see the actual veins while taking blood. The opportunities are almost endless.

5) Social media and its effects

It is not a real and unique technology, but the whole social media era played a huge role in the initiation of the so-called Empowered Patient or the Participatory Healthcare movement. Now, patients get access to all the information that were only available for medical professionals before. Moreover, they can get connected to other patients dealing with similar problems. See Smart Patients as the example.

6) Direct-to-consumer genomics

With the advances genomic companies have made, now anyone can get access to their own genome sequences. While the cost of this was about 3 billion dollars more than tey years ago, now it is getting close to $1-2,000, and eventually, sequencing will be cheaper than the shipping cost of the sample. Although we cannot make many medical decisions based on the pure data, the analysis of our DNA will soon give us the power of make better decisions about our future. This way, the era of personalized medicine when we only get drugs that are designed to our own genomic background will finally arrive.

7) Surgical and android robots

There are about a thousand da Vinci surgical robots around the world. Medical schools such as the on in Washington started to teach skills to future surgeons which are needed to control the robot instead of manually performing the operation. They are getting more complicated and more intuitive at the same time. Soon, they will be so precise, an intermediary robot will be needed not to translate the lousy vibrations of the human hand into the robot's laser-precise movements. It might make it possible in regions with doctor shortages to perform simpler tasks by physicians who control the robot from continents away. InTouch Health develops acute care telemedical robots to let the physician be where it is needed at least half virtually.

What if we can jump higher, run faster, or be smarter just because we can afford to use technologies in and on our bodies?

8) Augmenting human features

If we can repair lost limbs or diseased tissue, only one step is needed to actually augment human capabilities and features. State-of-the-art prosthetic devices such as Touch Bionics i-limb ultra is getting closer to mimicking the human hand. Ekso Bionics has been teaching over 3,000 patients how to learn to walk again with exoskeletons while being paralyzed from the waist down. In a ship factory in South Korea, some workers now work with exoskeletons on a daily basis. What if we can jump higher, run faster, or be smarter just because we can afford to use technologies in and on our bodies? Such issues will have to be discussed on a public level.

9) Nanorobots living in our bloodstream

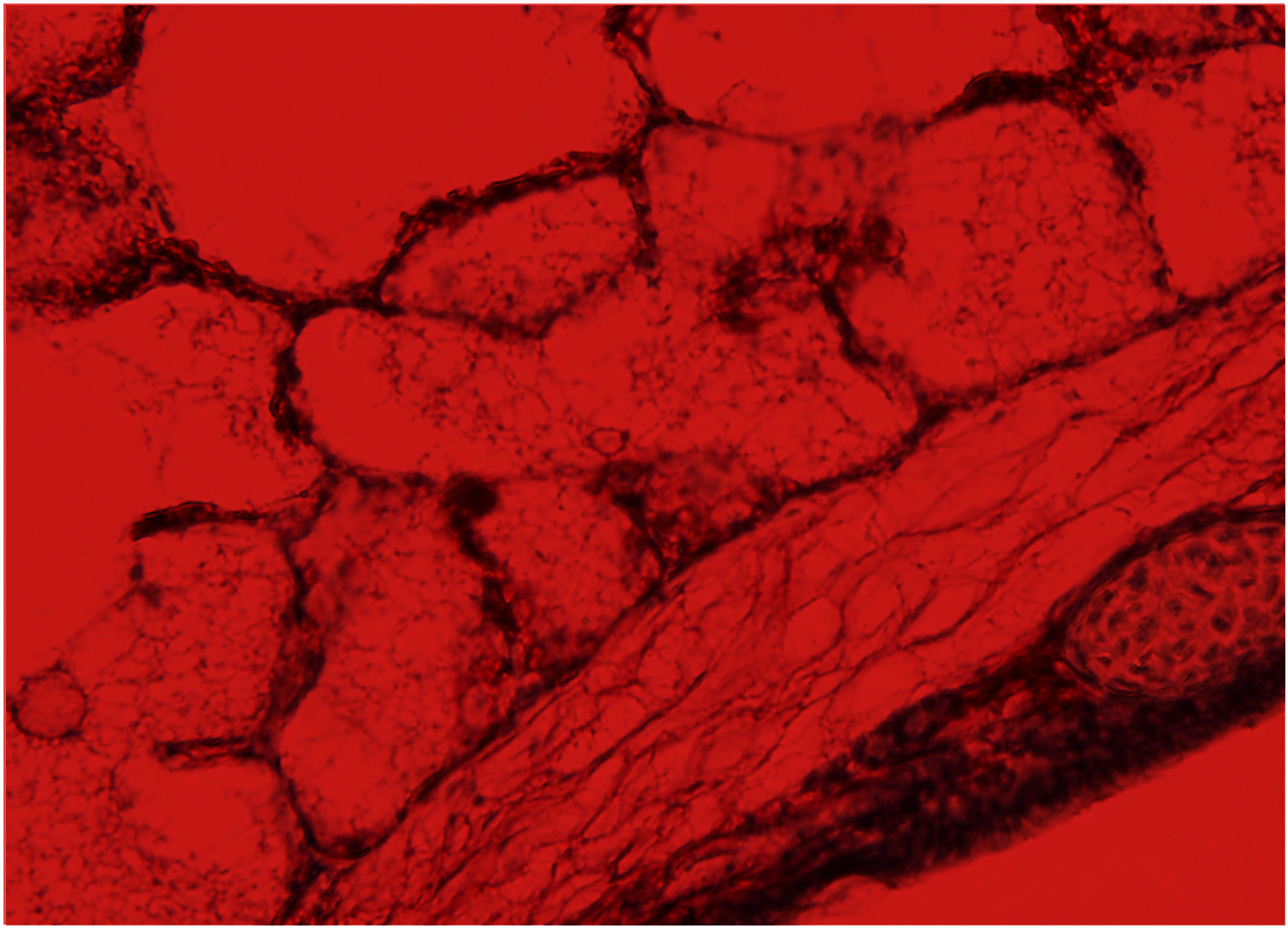
In the far future, robots on the nanoscale could live in our bloodstream and prevent any diseases by alerting the patient when a condition is about to develop. They could interact with our organs, measure every health parameter and intervene when needed. From the other side, imagine how many changes it would give to bioterrorism and how our privacy could be hurt. We will have to find the right balance between these before the technology becomes available.New technologies will finally help medical professionals focus more on the patient as a human being instead of spending time hunting down pertinent information. They will be able to do what they do best: provide care with expertise. In turn, patients will get the chance to be equal partners in this process taking matters into their own hands. But only if we are prepared.

The future of healthcare is only going to be positive if we prepare for using disruptive technologies in everyday medicine in a way that we don't just keep the human touch but further improve it.

*Bertalan Meskó, PhD in Genomics, is a medical futurist who has given more than 500 presentations to institutions including Yale, Stanford, and Harvard universities; the center of the World Health Organization; and the Singularity University. He is the founder of Medicalfuturist.com, a website that provides daily news about the future of medicine, and Webicina.com, the first service to curate medical and health-related social media resources for patients and medical professionals. He is the author of My Health: Upgraded and The Guide to the Future of Medicine books; as well as the Social Media in Clinical Practice handbook. He is the founder of the award-winning medical blog Scienceroll.com; and the founder and lecturer of the Social Media in Medicine online and offline university course.

How attractive is the BioRegion of Catalonia for foreign investment?

Guy Nohra
Co-Founder and Managing Director of Alta Partners



Most US investors don't know that Catalonia has a thriving life sciences cluster. With no "signature" deals in the news, investors who are already deluged with local deal flow are not aware of the possibilities in Barcelona. European investors are better informed but have not dedicated much time or energy to sourcing deals in Catalonia because of the small number of visible companies.

How could this situation change? In order to attract the attention of a foreign investor, Catalan biosciences companies basically need two attributes: world-class science and an excellent well-rounded entrepreneurial management team.

The BioRegion needs tangible "wins" at all stages. We need to see successful early stage funding of startups. Then, most importantly, there should be substantive mezzanine rounds raised for later-stage companies so that entrepreneurs can stay home. Finally, investors are attracted by exits, whether by Initial Public Offering (IPO) or Mergers and acquisitions (M&A). So we need multi-stage success at all points of the spectrum. Money attracts money. That is why I believe that the BioRegion of Catalonia is ripe for larger venture capital funds that can invest across all stages. In recent months, some of these necessary tangible "wins" have already hit the headlines.

In October 2015, Minoryx Therapeutics, a Catalan drug development company specialized in the discovery of new drugs for orphan diseases, announced it had completed a Series-A round of funding for €19.4 millions led by Ysios Capital, a Catalan investment fund, with the support of new foreign investors such as Kurma Partners, Roche Venture Fund, Idinvest Partners and Chiesi Ventures.

Local life sciences investment funds -such as Ysios Capital in this case- are a crucial component in attracting foreign investors. They are the feet on the ground and they have the best knowledge of the ecosystem. They know the entrepreneurs best; they are most qualified to vet investments; and they will be the most important board members in the companies due to their geographic proximity.

Catalonia counts on 26 investors in the life sciences, including 8 venture capital organizations, 7 networks of business angels and 5 corporate funds and investment banks. There are 6 specialized investors (Ysios, Caixa Capital Risc, Goodgrower, Healthequity, Inverready, and IUCT), all them created in the last 10 years. The biggest ones

I believe the BioRegion of Catalonia is ripe for larger venture capital funds that can invest across all stages

are Caixa Capital Risc –which currently manages €160M for life sciences and other emerging sectors- and Ysios Capital, which currently has over €125M in assets under management and provides private equity financing to early and mid-stage human healthcare and life science companies with a special focus on pharmaceuticals, diagnostics and medical devices (more information of both investors at the end of the chapter).

Also in October 2015, Palobiofarma, another Catalan biotech company (currently based in Navarra), hit the headlines again to announce they have entered into a $15 millions licensing agreement with Novartis. This deal illustrates that the biotech company Oryzon Genomics was not an isolated case when it signed the most important deal so far involving a Catalan company , receiving $21 millions from Roche to develop epigenetics drugs (2014).

At the time of writing this article, Oryzon Genomics, valued at €95 millions, was preparing to be listed on the Spanish Continuous Market as a first step towards the Nasdaq, becoming the first biotechnology firm to be traded on the Spanish Continuous Market, although there are some Catalan biotech firms traded on the Alternative Stock Market. Undertaking a successful IPO is considered an important step in achieving credibility for small companies. Fully developed capital markets are the key to successful IPOs. When preparing an IPO strategy, European biotech companies have an important decision to make: whether to pursue a US listing or one in Europe, closer to home. Until the EU has a Nasdaq type of exchange, I would recommend a serial approach: first undertake a successful IPO in your home country or in the EU, then follow that up with a Nasdaq listing. If a dual listing is possible, that would also be advisable.

I believe that being listed on the Spanish Continuous Market is a very positive development for companies like Oryzon, but it will also be very important for the company to successfully achieve its operational goals. This will ensure its stock performs well, which will make a dual listing easier and encourage other firms to follow suit. French companies have been very successful in doing home-turf IPOs and my hope would be for Catalan companies to follow suit.

If the life sciences ecosystem continues to develop, and the players in the market keep hitting positive milestones, then venture capital will move into the BioRegion. When foreign investors see success they will be more attracted to Catalan biosciences companies. Catalan companies need to continue succeeding scientifically, clinically, and commercially, when applicable, securing large strategic investment from big pharma and in fundraising.

Local Catalan life sciences investment funds are a crucial component in attracting foreign investors, as they have the best knowledge of the ecosystem

At the end of the day, success breeds success. Money follows success, and new money will follow existing money.

*Guy Nohra is a co-founder of Alta Partners, and was also a partner at Burr, Egan, Deleage & Co., which he joined in 1989. He has been involved in the funding and development of notable medical technology and life science companies including AcelRx, ATS Medical, Cutera, Innerdyne, R2 Technology, deCODE genetics, and Vesica. Previously, Guy was Product Manager of Medical Products with Security Pacific Trading Corporation. Currently, he serves on the board of directors of several companies including Bioventus, Carbylan Biosurgery, USGI Medical, Vertiflex, and ZS Pharma, and is the Chairman of the Board of USGI Medical and ZS Pharma. He has been named to the Forbes "Midas List" of dealmakers in high-tech and life sciences.

Venture Capital

Caixa Capital Risc

José Antonio Mesa
Head of Investment

2004
Year founded

30
Employees

34M€
Turnover

Number of operations

44

www.caixacapitalrisc.com

What type of investments do you look for? What characteristics does a project have to have for you to consider it has potential and decide to invest?

The companies in our portfolio are all led by entrepreneurs that are highly committed to the project and have the technical and managerial skills necessary to see it through. They operate in large or growing markets and are global, with technology that has been validated by the market and an innovative, profitable value proposition.

Science-based companies are known for their long development processes and need for important injections of capital. Caixa Capital Risc is aware of these characteristics of the sector and can offer start-ups long-term guidance, investing throughout the process, from the early stages through Caixa Innvierte Start, to series A and B funding through other specialized vehicles.

Which projects or type of investments have been the most profitable?

The growth and development stages of life sciences companies are long, which means that results and return on investment takes time. Business projects focusing on drug development, if all goes well, have the best return for investors. However they are also the riskiest.

Life sciences operations are up compared to previous years, but what does the ecosystem of the BioRegion need to continue attracting new venture capital funds and investment?

We have good universities and a very high level of research. We need success stories and researchers with a track record in business, serial entrepreneurs that give both national and international investors confidence.

Venture Capital

Ysios Capital

Josep Ll. Sanfeliu
Soci i cofundador

2008
Year founded

11
Employees

48.5M€
Turnover

Number of operations

16 Investments

5 Divestments

www.ysioscapital.com

What type of investments do you look for? What characteristics does a project have to have for you to consider it has potential and decide to invest?

We invest in early and mid-stage biotechnology companies that focus on therapeutic and diagnostic products or medical devices. Above all, we focus on companies developing innovative, disruptive products, mainly geared towards unmet medical needs, that have a clear benefit for patients and potential savings for healthcare systems.

We also value industry interest in forging partnerships or agreements to bring the innovations we invest in to market.

Which projects or type of investments have been the most profitable?

We have seen significant return through our divestment of Biovex, Endosense and Am-Pharma, which was the result of financial and human efforts in the form of investment and direct participation in day-to-day supervision of the companies through their administrative boards. Amgen acquired Biovex for €1 billion, seeing more than fourfold return on investment. Endosense, in the medical technology sector, yielded IRR over 40% and Am-Pharma has validated its potential by signing a structured acquisition agreement with Pfizer that could mean up to sevenfold return.

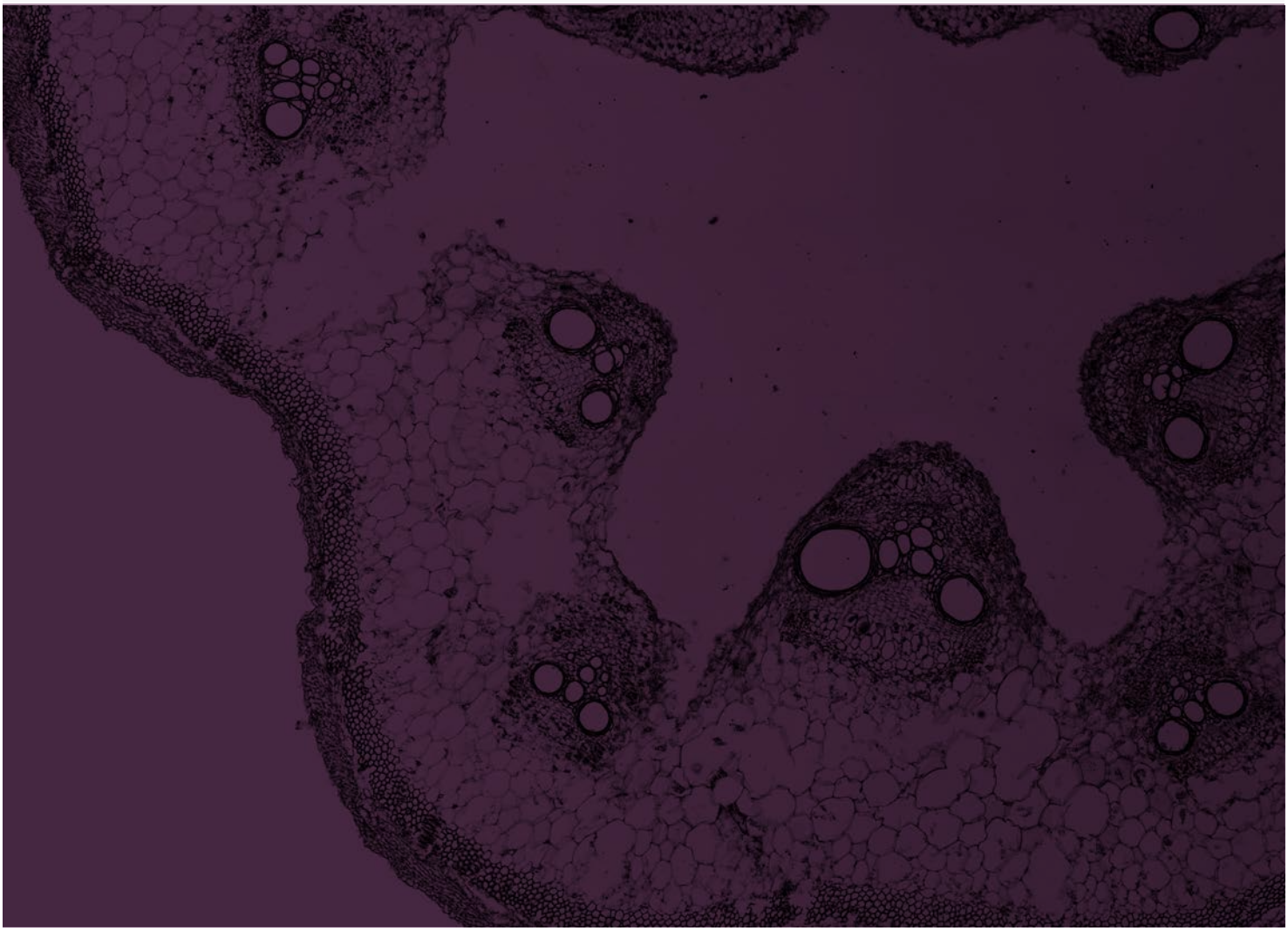
The key is a combination of innovation, an unmet medical need, potential market and interest from potential partners. However we must also take into account that these are risky innovations that always depend on the clinical results. The risk is often what determines return, which is why the return on medical device companies tends to be lower than for therapeutic devices.
In our case, we try to maintain a balanced portfolio of very early stage companies and more developed ones, as well as a proportional distribution of sectors, to compensate risk and return.

Life sciences operations are up compared to previous years, but what does the ecosystem of the BioRegion need to continue attracting new venture capital funds and investment?

We believe more private investment is needed, above all in the early stages, and we must facilitate the arrival of foreign capital. Global efforts and transparent entrepreneurs are also key in achieving this support.

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 BioRegion 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 fuelling 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 do it the other way around.

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

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 worldwide 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 reactives 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.

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.

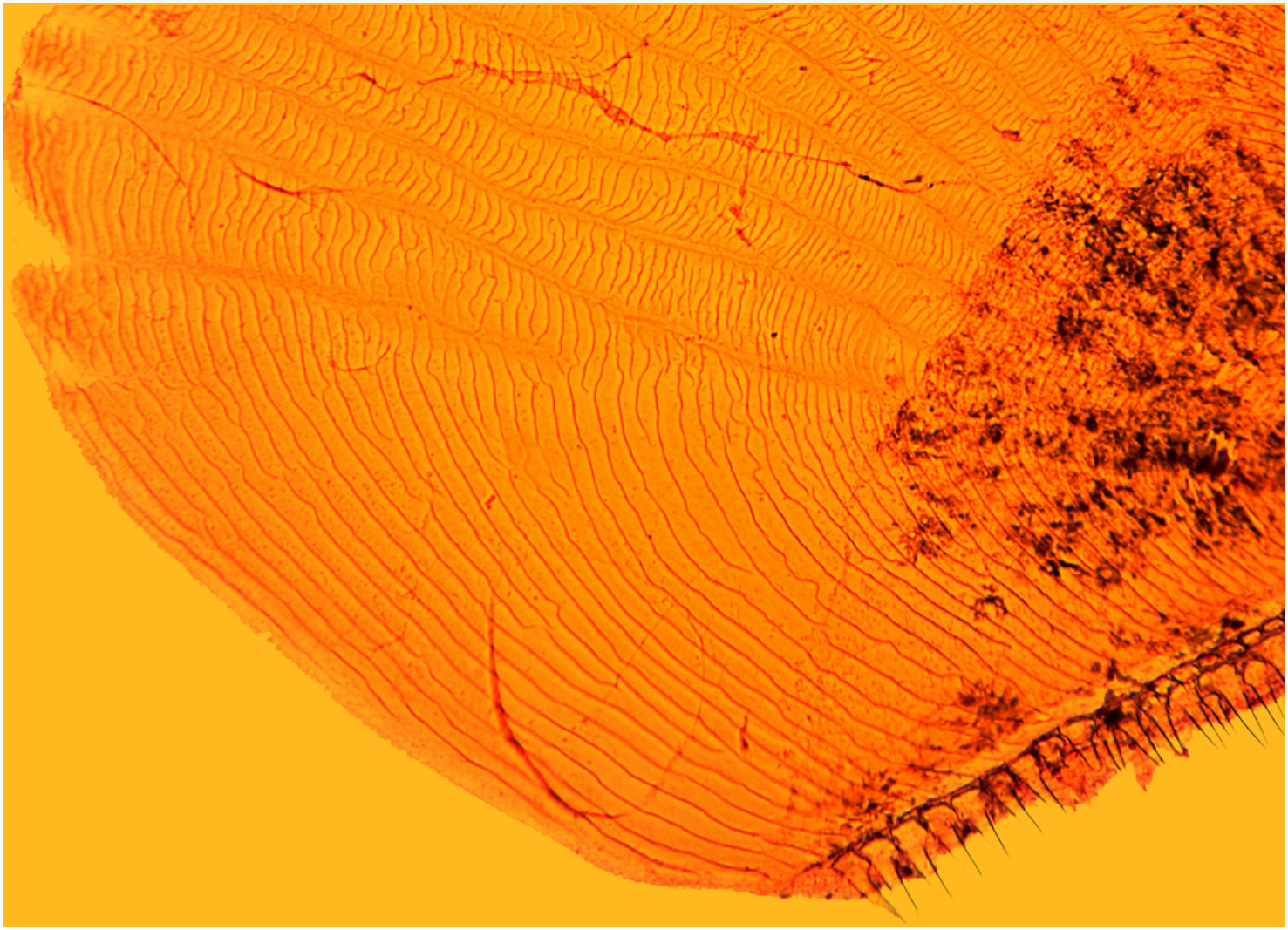
We believe that companies working in health must strike a balance and act as a nexus between these two forms of medicine to foster holistic health. In this regard, integrating Forté Pharma has also been an important move strategically.

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.

Clinical research as a tool to seize value

Gemma Estrada
Head of Clinical Research at Ferrer and Former Director
of the Barcelona Clinical Trials Platform (BCTP)



The universal challenge facing all modern healthcare systems is to reach a high overall level of health with an accessible, integrated, quality care model that is also sustainable. This means healthcare systems must be made more efficient, freeing up available resources to allow people to live longer, healthier lives.

In Catalonia, this task of freeing up resources comes up against the fact that the demand for healthcare is increasing due to the ageing population and an increasingly complex morbidity profile. On one hand, life expectancy is nearly two years above the European average (1.9 years above the EU-15) and, on the other, the number of patients with chronic illnesses (heart failure, obstructive pulmonary disease, diabetes, mental disorders, depression, dementia and cancer) and associated comorbidities is rapidly growing and putting increasing pressure on the healthcare system, which already has financial problems and overworked healthcare professionals.

Faced with this situation, which is the same to some extent in all developed countries, Catalonia must seek out new healthcare, economic, social and technological paradigms to address these needs. Efficiency can be boosted incrementally by rationalizing prescriptions, promoting good healthcare practices, educating patients on consumption, speeding up the administrative processes and cutting down on fraud, but this isn't enough. A wholesale transformation of the healthcare system is needed. And it may be necessary to transform hospitals into integrated service units where patients can receive comprehensive care, as Michael E. Porter and Thomas H. Lee propose in their article

The demand for healthcare is increasing due to the ageing population and an increasingly complex morbidity profile

The Strategy That Will Fix Healthcare, (HBR, October 2013). These authors argue that the only way to boost value for patients is to achieve "desired health results" at a lower cost, and that means structuring healthcare around patient needs, which is a "whole" and not a "series of different conditions" that different specialists deal with from independents departments. These authors also insinuate that payment for healthcare should be based on what the patient gets out of it, not volume. This implies using powerful IT systems that can handle all life and health information at once, and also having tools to measure the individual cost of care for each person.

Although Catalonia, unlike other countries, has not yet begun the shift from public hospitals towards integrated service units (like, for example, Norway at the new Oslo University Hospital), it has begun down the path towards the sustainability and progress of the healthcare

system by reinforcing protection and promotion of health, disease prevention, food safety and clinical research.

Promoting research is in line with one of the main messages of the World Health Report (WHO 2013), which says all countries must both produce and consume research. Beyond investing in new technology, the report says we must invest in making better use of existing knowledge. This means transforming it into practical applications that address real health problems. The WHO proposes increasing collaboration between governments, universities, research centers, international organizations, hospitals and private companies in order to bridge the gap between these different parties.

To take the path the WHO recommends, in Catalonia we must move towards integrating clinical research into medical practice, which will lead us to redefine the role of healthcare professionals, pharmacists, academic researchers, patients, family members and caregivers. Likewise, to move towards personalizing treatment as a service, more than as a product, as Porter and Lee recommend, in Catalonia we must push forward in recognizing the complementarities of the public healthcare system and private initiatives.

This article covers current trends in clinical research, the reach of clinical trials in hospital centers in Barcelona and the initiatives of the Government of Catalonia Department of Health to promote transversal actions that make clinical research in Catalonia more efficient and have a greater impact. In particular, it will discuss the creation of the Barcelona Clinical Trials Platform (BCTP), an instrument to attract more clinical research to Catalonia with the aim of seizing value for patients and the healthcare system itself.

Current trends in clinical research

The pressure to do trials quickly and efficiently has increased exponentially over the past ten years. It could be said that this increase has been proportional to society's recognition of the value trials contribute in terms of health and wellbeing, to patients' expectations of making fatal diseases into chronic conditions, and to companies' desire to make the most of drugs before patents expire.

The Barcelona Clinical Trials Platform is an instrument to attract more clinical research to Catalonia with the aim of seizing value for patients and the healthcare system itself

In recent years, despite the slowness of the main regulatory agencies (the United States Food and Drug Administration and the European Medicines Agency) in incorporating technological advances into clinical trials, there have been interesting changes like decreased use of printed paper for collecting data and a move towards electronic trials, even electronic storage of clinical trial archives, which is a great savings logistically, reducing the space required and improving access without sacrificing security. Progress has also been made in moving towards electronic signatures, although there isn't yet a universally accepted, fully compatible solution that both pharmaceutical laboratories and hospital researchers can adopt.

Information and communication technology (ICT) has evolved so quickly, and has such potential when applied to clinical research, that current debate focuses on how to boost ICT to make the development of therapeutic molecules and medical devices faster and cheaper.

Real-time data capture in clinical trials improves transparency (as does registering and publishing all clinical trials). At the same time, this also makes it possible to decentralize trials, which means studies can be done far from the hospital, expanding the sphere of recruitment and making patients more comfortable and more likely to adhere to treatment.

ICT also allows clinical trial data to be integrated with real-world data, not only regarding health but also socioeconomic aspects, etc., and to build a joint system of big data that, once integrated and analyzed, makes it possible to take strategic decisions at the right time. These decisions may be to continue developing a molecule or be epidemiological in nature.

Social networks make it easier for patients to participate in the drug-development process and are a tool to maintain patient centricity.

In addition to the contributions of ICT, there have been other scientific evolutions applied to medicine that have enriched the debate on how to make clinical development more efficient. Three good examples are precision medicine, adaptive design and collaborative initiatives:

- Precision medicine means each patient can be assigned the most appropriate treatment at the right dose, making clinical trials faster and with fewer participants (example 1: ASCO's Targeted Agent and Profiling Utilization Registry- TAPUR study; example 2: the National Cancer Institute – MATCH study: Molecular Analysis for Therapy Choice trial).

- Adaptive design, which tests multiple hypotheses in the same study and allows the design to change over the course of the study, based on the results, also allows doctors to move patients from one branch of a trial with an ineffective treatment to one in which the treatment works (for example, European Prevention of Alzheimer's Dementia -EPAD project).

- Collaborative initiatives from consortia of companies, governments, regulatory bodies, preclinical and post-clinical researchers, patients' associations, etc., that create open repositories of data and share methodology, structures, standards and training to benefit the whole community (for example, Transcelerate).

With all of these changes to how clinical trials are designed (adaptive protocols), how data is collected (real time), how it is integrated and analyzed (big data) and how trials are funded (public-private partnerships), we are living in a time of great changes in the world of clinical research. Two books that discuss this are *The Guide to the Future of Medicine: Technology and the Human Touch*, by Bertalan Meskó, and *The Patient Will See You Now*, by Eric Topol.

We are moving from paying service providers (like CROs) to working to make them partners in the process and compensating them for the value received. A transition is underway from "one-size-fits-all" studies to studies based on "precision medicine" (more adapted to the target population) and from mainframe clinical trials (those conducted right around the hospital) to hand-held clinical trials (remote studies) thanks to mobile apps and home devices like smart clothing (for example, Hexoskin) and digitals tattoos (for example, Someya Organic Transistor Lab) that control patient health, diet, activity, etc. These advances continuously monitor patients, replacing sporadic medical care (doctors visits) with ongoing patient care.

Barcelona Clinical Trials Platform

With the aim of positioning Catalonia among the leading European regions in conducting clinical trials, Barcelona Clinical Trials Platform (BCTP) brings together the most important institutes in Catalonia by volume of clinical trials into a single platform to improve the coordination, integration, quality, inclusivity and speed of clinical research.

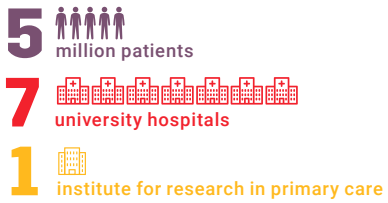
BCTP was created by the Department of Health and Biocat in the final quarter of 2014 to position Catalonia among the top five European regions for conducting clinical trials

BCTP was created by the Department of Health and Biocat in the final quarter of 2014. The strategic line of the Catalonia Health Plan 2016-2020 dealing with research and innovation promotes the consolidation of the BCTP with the aim of increasing the number, quality and importance of clinical trials conducted in Catalonia. By having different centers join forces and take advantage of synergies in clinical research, it will be possible to attract innovative therapies in the early stages of development to Catalonia.

As of January 2015, the centers that belong to the platform totaled 2,740 participations in trials, with 13,498 patients recruited. BCTP kicked off as a pilot program but it is expected to expand in the middle term to include other research institutes and hospitals in Catalonia. This initiative is inclusive and provides a joint structure covering the whole region so that hospitals in Catalonia may act as a sort of metacenter that is a benchmark in developing new drugs, medical devices and biological products.

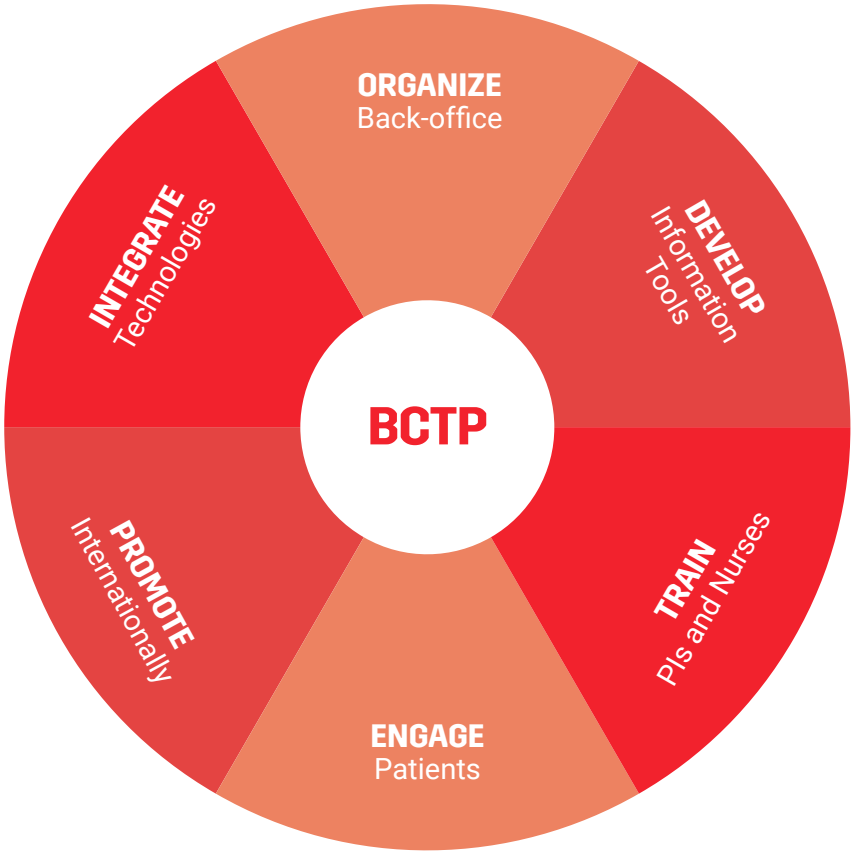
The greatest challenge facing the founding members of the BCTP is to align patients' needs with researchers' expertise and industry's aims in order to speed up the arrival of innovative treatments and improve the results of public health policies and interventions.

BCTP is a gateway for clinical trials, with access to 5 million patients.



Source: BCTP

BCTP areas of action to achieve collective excellence in clinical trials in order to attract and develop innovative treatments in Catalonia.



Source: BCTP

1. Simplified bureaucracy to cut negotiation and authorization times for clinical trials and facilitate the transfer of patients between centers to give patients access to therapies being developed.

2. Centralized information to enable integrated, cohesive, efficient running of its member institutes by creating collaborative computer tools.

3. Lifelong learning for clinical trial staff to ensure researchers and nurses are trained, certified and up-to-date with best clinical practices (BCP).

4. Commitment to patients to make the general public more aware of clinical trials and inform potential patients of the trials conducted in Catalonia.

5. Joint promotion of members to boost the collective international visibility of the member institutes at fairs, congresses and events in the sector.

6. Integrating research into clinical practice to channel the research expertise and technology present in Catalonia towards clinical development of targeted therapies and a move towards personalized healthcare.

Metrics for clinical research in Catalonia

The BCTP's main asset is its concentration of key opinion leaders with significant scientific leadership in many therapeutic areas, who can provide insight into the impact and feasibility of emerging therapies, participate in designing clinical trials and analyze results. Nevertheless, collective excellence in clinical trials must be measured with specific indicators aligned with the industry's interests (metrics: volume of studies initiated, time to regulatory authorization, length of contract negotiations, recruitment index, etc.) and these metrics must be measured in the same way at all institutes.

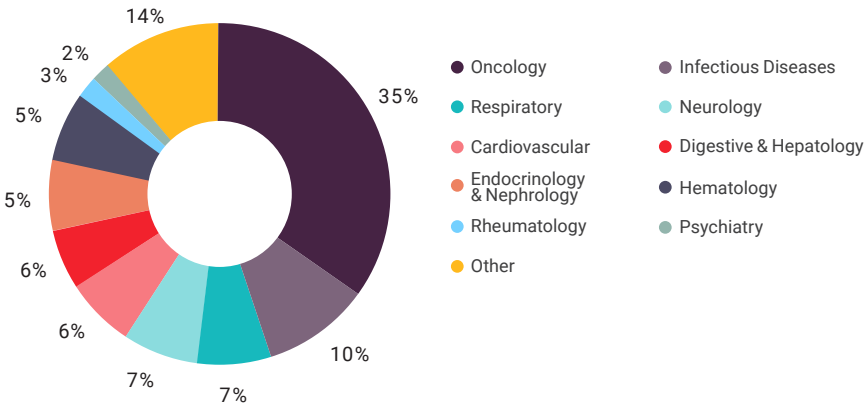
The BCTP has retrospectively collected metrics for the 2012-2014 period from each of the member institutes. So, the current benchmarks for the BCTP come from compiling the clinical trials conducted individually by each member. With the bureaucratic simplification implemented by the BCTP and the integration of clinical trials and medical practice, more studies will be attracted to the region and, presumably, there will be a positive evolution of these base metrics, which appear below.

Newly initiated clinical trials (2012 - 2014)

2,515
sites participating in clinical trials initiated between 2012 and 2014

78%
participations in pre-registration phases (Phases I, II and III)

New clinical trials (2012-2014) by therapeutic areas:

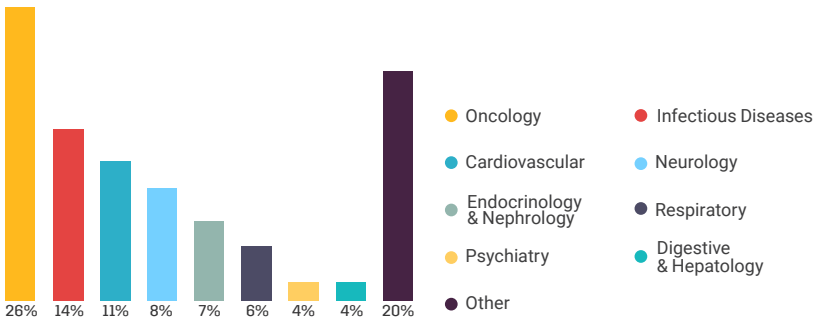


Completed clinical trials (2012-2014)

1,487
sites participating in clinical trials completed between 2012 and 2014

13,287
patients recruited

Patients recruited into completed clinical trials (2012-2014) by therapeutic area:

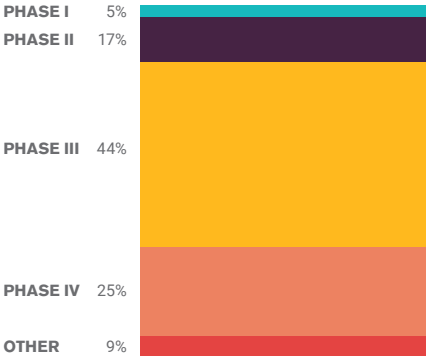


Ongoing clinical trials (as of January 2015)

2,740
sites participating in ongoing clinical trials

13,498
patients recruited

Patients recruited into ongoing clinical trials by phase:



Oncology

Completed trials (2012-2014):

467 Sites participating

3,503 Patients recruited

Ongoing trials as of January 2015:

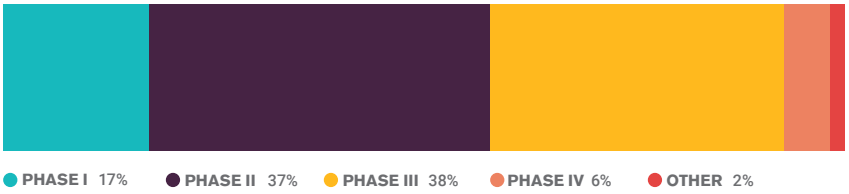
935 Sites participating

3,635 Patients recruited

Source: BCTP

Newly initiated trials (2012-2014):
(% of sites participating by phase)

TOTAL 886 centers



Infectious Diseases

Completed trials (2012-2014):

151 Sites participating

1,864 Patients recruited

Ongoing trials as of January 2015:

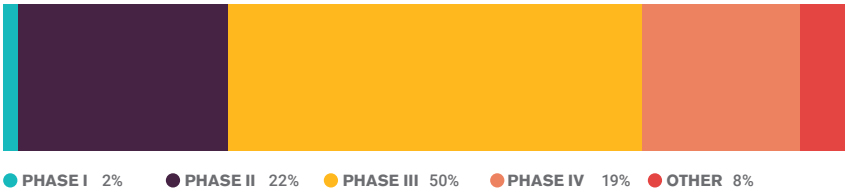
277 Sites participating

1,533 Patients recruited

Source: BCTP

Newly initiated trials (2012-2014):
(% of sites participating by phase)

TOTAL 245 centers



Digestive & Hepatology

Completed trials (2012-2014):

102 Sites participating

452 Patients recruited

Ongoing trials as of January 2015:

138 Sites participating

572 Patients recruited

Source: BCTP

Newly initiated trials (2012-2014):
(% of sites participating by phase)

TOTAL 140 centers

Respiratory

Completed trials (2012-2014):

110 Sites participating

815 Patients recruited

Ongoing trials as of January 2015:

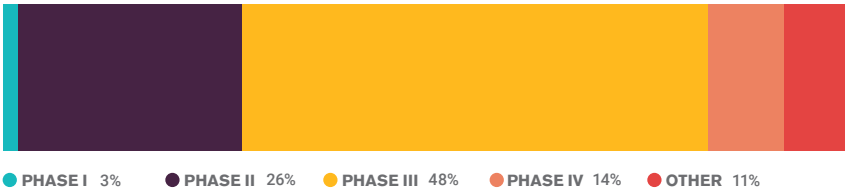
130 Sites participating

556 Patients recruited

Source: BCTP

Newly initiated trials (2012-2014):
(% of sites participating by phase)

TOTAL 189 centers



Cardiovascular

Completed trials (2012-2014):

95 Sites participating

1,452 Patients recruited

Ongoing trials as of January 2015:

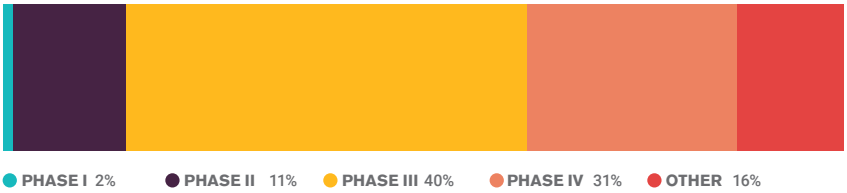
226 Sites participating

2,325 Patients recruited

Source: BCTP

Newly initiated trials (2012-2014):
(% of sites participating by phase)

TOTAL 156 centers



Neurology

Completed trials (2012-2014):

147 Sites participating

1,023 Patients recruited

Ongoing trials as of January 2015:

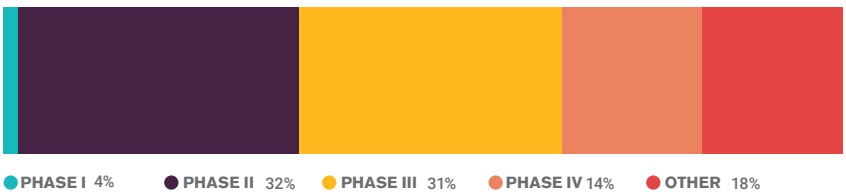
241 Sites participating

867 Patients recruited

Source: BCTP

Newly initiated trials (2012-2014):
(% of sites participating by phase)

TOTAL 185 centers



Endocrinology & Nephrology

Completed trials (2012-2014):

85 Sites participating

953 Patients recruited

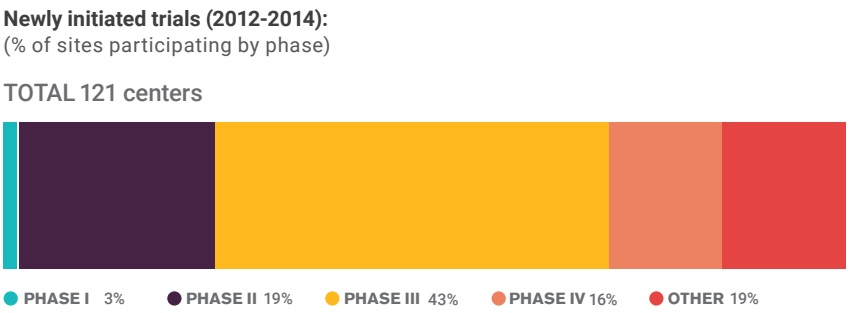
Ongoing trials as of January 2015:

167 Sites participating

1,247 Patients recruited

Source: BCTP

Newly initiated trials (2012-2014):
(% of sites participating by phase)



Like what is happening in other developed countries, Catalonia is preparing to address the challenge of growing demand for healthcare on a large scale with unique characteristics, which include ageing and chronic diseases with associated comorbidities. Diagnostic, therapeutic and technological advances, as well as transforming hospitals into integrated service units for patients, are the way to tackle this challenge, as is integrating clinical research into medical practice.

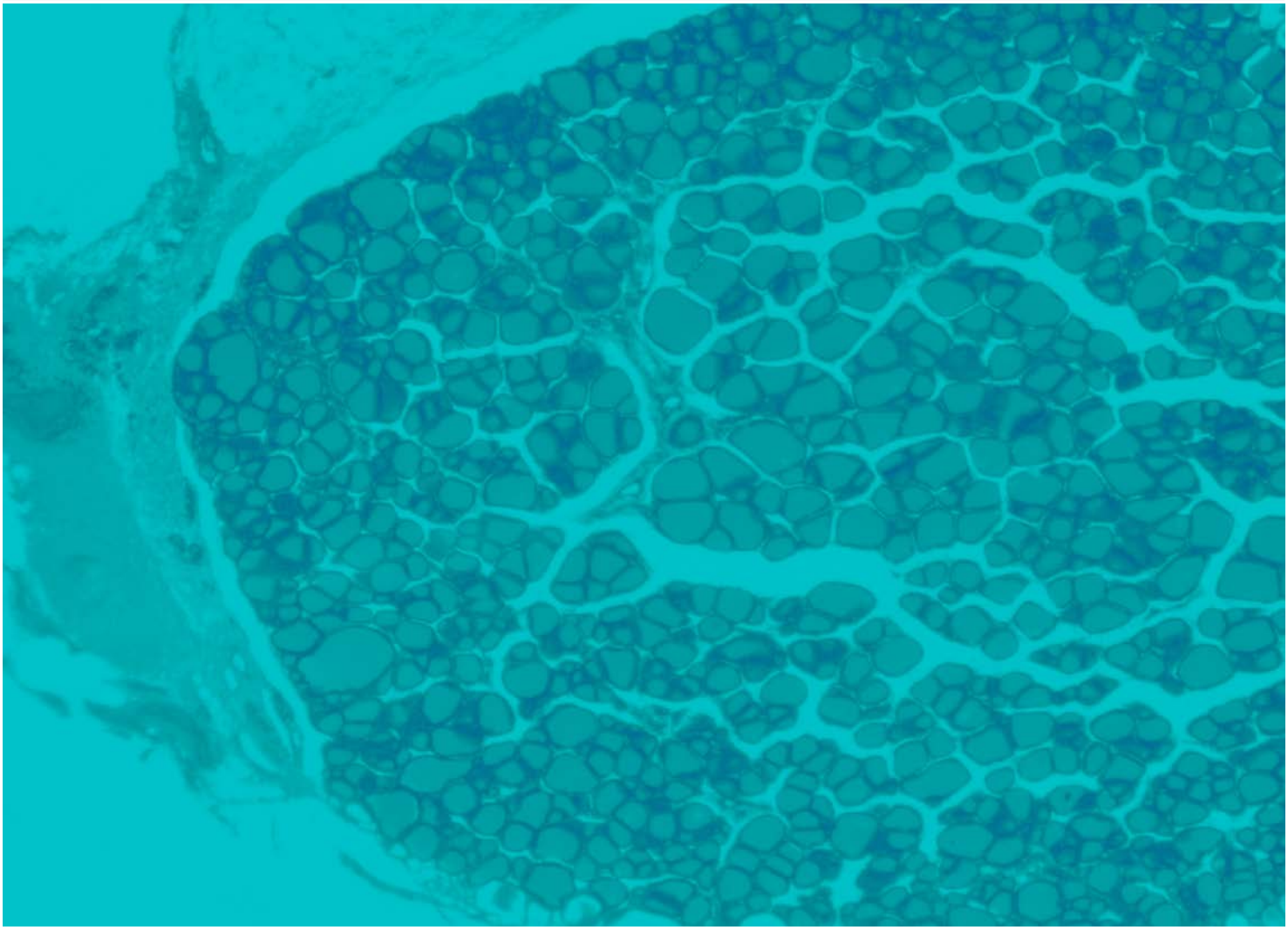
In this context, it makes sense that the Department of Health and Biocat decided to create a clinical trials platform (BCTP) to forge new pathways for collaboration between hospitals and pharmaceutical companies, contract research organizations (CRO), governmental agencies and medical societies to attract large clinical trials to Catalonia. If all hospitals work within the platform, we will create a critical mass, foster repetition of opportunities and cross-pollination between similar programs.

Finally, the efforts of the BCTP to integrate clinical research into medical practice will allow us to offer patients innovative treatments. Through clinical research we bring the talent and technology from Catalonia's research institutes and hospitals to the patients, thus seizing the value we generate through research.

With the bureaucratic simplification implemented by the BCTP and the integration of clinical trials and medical practice, more studies will be attracted to the region

The medtech revolution: the European medical technology industry

Thomas Klein
Specialist journalist



Most people use at least one medical device every day. Ranging from high-tech MRI machines and surgical robots to contact lenses or condoms, there are currently over 500,000 products available that fall under this category, according to the European industry association Eucomed.

According to MedTech Europe, around 7.5% of the total healthcare expenditure is spent on medical technology in Europe. The largest segment within medical technology in 2013 was in vitro diagnostics with global sales of $ 47.4 billion followed by cardiology ($39.9 billion), diagnostic imaging ($35.5 billion), and orthopaedics (33.8 billion), according to the statistic portal Statista.

The medical technology sector is known to be one of the most innovative industries. Eucomed says that the industry's products usually only have a lifecycle of 18-24 months before they are replaced by an improved device. Medical technology is regularly at the top of the list of technology fields with the most patent applications. According to the European Patent Office, more patent applications were filed for medical technology in 2014 (11,124 applications) than for any other type of technology, including digital communication (10,018), biotechnology (5,905) and pharmaceuticals (5,270).

Many of the industry's heavyweights, such as Johnson & Johnson and Baxter, are based in the US, but some of them could be interested in relocating their headquarters in Europe to take advantage of the considerably lower corporate taxes: Medtronic have already done it, moving to Ireland.

Across Europe, there are roughly 25,000 medical technology companies employing more than 575,000 people. In the US, about 520,000 people work for 6,500 medical device companies. This shows how the industrial structure differs between the two continents. The European industry is dominated by small and medium-sized companies (SME). In 2014, only five of the top 20 global medical device companies by revenue were based in Europe (Siemens AG, Fresenius, Koninklijke Philips, Novartis, Essilor). Many of those European medtech champions are part of big industrial conglomerates, such as Siemens or Philips, or pharmaceutical companies, such as Novartis and Roche. While there are a number of global players in Europe, almost 95% of the European medtech companies can be counted as SMEs.

The medical technology sector is known to be one of the most innovative industries. More patent applications were filed for this field in 2014 than for any other type of technology

European medical device industry and markets

With roughly 40% of global expenditure on medical devices, the US are the biggest single market for medical technology. Europe comes in second with 30% of worldwide expenditure or about €100 billion per year. But emerging countries, such as China or Brazil, are catching up fast with growing middle classes demanding better healthcare. While the Western markets are pretty mature by now, in the future most of the growth for medical device companies will probably come from emerging countries.

The biggest single market in Europe is **Germany** with sales of about $26.8 billion per year, according to the market research firm Business Monitor International (BMI). Despite the fact that many hospitals are running deficits, the demand for medical equipment is comparable stable in Germany.

The second largest European market is **France** with sales of $15.0 billion. Over the last few years, the French government has implemented a number of cost-cutting measures including more demanding requirements for reimbursement for medical devices. The so-called Responsible Hospital Procurement (PHARE) Program is intended to save French hospitals €120 million annually in procurement costs for disposable items and €36 million for medical imaging devices. Hospitals hope to reduce spending by pooling their procurement in big purchasing groups.

In 2014, the **British** medical device market was worth $11.3 billion. Despite the fact that the National Health Service (NHS) which accounts for about 80% of expenditure for medical technology in the country is expected to face a funding deficit of £ 30 billion by 2020, BMI forecasts annual growth of 6,8% until 2018.

Valued at $9.4 billion, the **Italian** medical device market is the fourth largest in Europe. Faced with a huge national deficit, the Italian government curbed public medical device expenditure in 2014. Since 70% of the Italian medtech market depends on public spending, experts expect slow growth in this sector in the following years. Additionally, companies currently struggle with delayed payments from public bodies.

The US are the biggest single market for medical technology. Europe comes in second with about €100 billion per year

A similar picture presents itself when looking at **Spain**, the fifth largest European market, which is worth about $5 billion. Here too, the Spanish National Health System had to cut spending significantly.

BMI assumes that most European markets will grow again in 2015 with the exception of some Southern states that have been hit hard by the ongoing economic crisis, such as Italy and Spain. The market research company expects Western European markets to increase at a compound annual growth rate (CAGR) of 3.7% in the period between 2014 and 2019. Since the global CAGR is expected to be around 6.6%, the importance of the region for medical technology industry will be in relative decline.

European medical technology clusters

While medical technology companies can be found all over Europe, a number of regional industrial clusters have emerged. Those regions have a high concentration of medical device companies, component suppliers, clinics and research facilities with focus on medical research. The companies in those clusters benefit not only from the opportunities of joint research and the proximity of experts in many medical areas, but often also from collaboration in areas, such as lobbying and purchasing of components.

At the center of such medical clusters are often global medical device companies or world-renowned universities attracting talent, capital and supply industries. For example, the area around the German cities Nürnberg and Erlangen was the cradle of Siemens' healthcare unit. Today, the area is home to 180 medical technology companies with over 16.000 employees. Additionally, 40 hospitals treating more than 500.000 patients per year and 20 research institutes provide plenty of opportunities for research collaboration.

One of the biggest clusters in Europe is the located around the small town Tuttlingen in the **Southwest of Germany**. With more than 400 medtech companies employing over 13.000 people, the region claims to be "world centre of medical technology." Centered around surgical instrument manufacturer Aesculap and the endoscopy maker Karl Storz, more than 90% of the companies in the cluster are SME.

After Ireland started in the 1970s to attract foreign companies with low corporate tax rates and research incentives, many of the big US companies settled in the area around **Galway**. After that, an indigenous medical technology industry quickly established itself followed by a highly innovative research landscape.

The **BioRegion of Catalonia**, in Spain, **is also increasingly becoming one of the hotspots for innovation in medical technology with its over 730 life science companies**. Out of these, over

Catalonia, accounting over 200 medtec companies, is becoming one of the hotspots for innovation in medical technology in Europe

200 work in the field of medical technology, employing more than 11,200 people.. The industry benefits from cooperation with 41 research centers, 15 university hospitals, 13 science and technology parks and eleven universities offering life sciences studies in the region. The high concentration of research institutions focusing on life science and healthcare in the area facilitates the emergence of medical technology start-ups.

The 360 medtech companies in the area around **Zürich** in Switzerland can draw on the outstanding research capabilities of the Zürich universities, such as Swiss Federal Institute of Technology Zurich or the University of Zurich.

Other important healthcare clusters are in the area between **Stockholm** and **Uppsala** in Sweden with 611 companies (including pharmaceutical and biotechnology firms) employing 20,852 people, and the **Alsace Biovalley** in France with over 150 medtech companies.

In the future, the so-called "golden triangle" between **London, Cambridge** and **Oxford** with world-class academic institutions will probably become another healthcare technology hub. The City of London started several initiatives to bring together medical researchers, hospitals, medtech and biotech companies, the NHS and venture capital firms.

Changes ahead

The medical technology industry is undergoing a period of fundamental change. On the one hand are changing demographics in most parts of the world and the increasing prevalence of chronic diseases driving the demand for high-quality medical devices, diagnostic and imaging equipment, and innovative eHealth solutions. On the other hand healthcare expenditure is increasingly curbed by strained public budgets and austerity measures, especially in Southern Europe.

Medical technology companies are trying to adapt to the changing conditions by introducing cost-saving technologies, such as mobile health solutions, and new business models

As a consequence, hospitals are often reluctant to invest in expensive medical equipment or pool their purchases in procurement groups in order to push prices down. Healthcare insurances increasingly require medical technology companies to prove that new treatments are not only medicinally effective but also help to take costs out of the system before agreeing to pay for them.

According to a report conducted by the consultancy Analysis Group, prices for implantable medical devices have fallen between 17% and 34% in the period from 2007 to 2011 depending on category.

Medical technology companies are trying to adapt to the changing conditions by introducing cost-saving technologies, such as mobile health solutions, and new business models. For example, some companies started to offer comprehensive services on a pay-per-procedure basis instead of just selling devices. The US giant Medtronic, for instance, operates entire cath laboratories for hospitals.

Consolidation and M&A

The rapidly changing market environment is partly responsible for the wave of mergers and acquisitions across the medical device industry. In 2014, the sector was shaken by the $42 billion jumbo merger of Medtronic and Covidien, two of the heavyweights of the industry. One of the motivations for the deal was probably to save corporate taxes by being able to move the company headquarter from the US to Ireland. But size in itself increasingly matters in the medical device industry. Companies

The changing market environment, saving costs, the power of purchasing groups, increasing cost pressures and access to emerging technologies are the main reasons of the wave of recent M&A

seek to increase their scale in order to counter the greater bargaining power of purchasing groups. Additionally, they hope that sizes helps to achieve synergy effects. After its $13 billion acquisition of Biomet, orthopedics company Zimmer said that it expects to gain yearly cost synergies of $270 million from the deal.

On the other hand, increasing cost pressures force companies to concentrate on their strategic core business and sell peripheral units. For instance, the German pharma giant Bayer sold its diabetes care business for €1 billion to Panasonic Healthcare in 2015 and its angiopathy device division to Boston Scientific for €300 million.

Another driver for M&A activity is the determination of companies to gain access to emerging technologies. The Swiss company Roche, for examples, has invested heavily over the last years to acquire molecular diagnostic companies which are important for both its medtech and its pharmaceutical arm. Covidien acquired the Israeli firm Given in 2013 for its minimally invasive capsule endoscopy technology.

Friends of foes?

A further reason for the current wave of M&A is the fact that IT and consumer goods companies are entering the medical device market. The ubiquity of mobile technology in addition to the desire of patients to have more say in the management in their own health could be indicators that the medtech industry

is ripe for digital disruption.

Google made the headlines with some of its moonshot projects, such as smart contact lenses for diabetics or swallowable pills that detect various illnesses at an early stage. Apple released its Healthkit app to improve patient doctor communication and facilitate clinical trials.

Tech giant IBM has started to find applications in healthcare for its big data com-puter system Watson. Watson initially became famous beating human contestants in the game show Jeopardy, demonstrating the ability to understand natural language. In several projects IBM tested Watson's ability to use its computational powers to support physicians in diagnostics and treatment decisions. IBM now established a new business unit to commercialize Watson for the healthcare market and agreed to cooperate with some of the traditional medtech companies such as Medtronic and J&J in that field. In August 2015, IBM announced that it bought the provider of medical imaging systems Merge Healthcare for $1 billion in order to use Watson's cognitive capabilities to interpret medical images.

In order to achieve its goal to become one of the world's leading medical equipment makers by 2020, the Korean electronics group Samsung bought several medical device companies since 2010, including the Boston-based medical imaging company NeuroLogica and ultrasound device maker Medison. Furthermore, Samsung has set up a $50 million investment fund to invest in innovative startups that develop sensors and software for mobile health solutions. In June 2015, the company announced that it would cooperate with Medtronic to develop mobile diabetes apps.

While the activities of those newcomers is unsettling for many of the traditional medtech companies given their track record of disruption and their vast resources, it is unlikely that the IT giants will sweep away their established competitors overnight. It takes long years of experience to bring new products to market in a sector as regulated as medical technology. Therefore, it is more probable that the IT companies will seek to cooperate with more experienced medtech firms to market their ideas. Google, for example, announced in 2014 that it teamed up with Swiss Novartis to develop their smart contact lenses to market maturity.

Changes in the regulatory landscape

Since the wellbeing and sometimes the lives of patients depend on the proper functioning of medical devices, a new device has to undergo a stringent regulatory process before it is ready to hit the market. While in the US a single regulatory body, the Food and Drug Administration (FDA), is responsible for the approval and monitoring of medical devices, this task is performed in Europe by the so-called notified bodies. Notified bodies are independent institutions accredited by national authorities of EU member states. They evaluate technical documentation and quality systems of manufactures and test if the devices operate as expected.

Medtech manufacturers fear that more stringent regulatory rules will drive up costs to market new products and discourage innovation

In 2011, after the French manufacturer of breast implants PIP fraudulently used cheap silicone instead of medical-grade material harming thousands of patients, the system came under fire and politicians argued for stricter regulation. The EU institutions and the member states are currently working on a new legislation that will overhaul the EU medical device directives. The main objective is to improve the quality of the work of notified bodies and the security of medical devices. Among the measures in discussion are stricter monitoring of notified bodies and the concept of 'special notified bodies (SNB)' for certain categories of devices. Medtech manufacturers fear that more stringent regulatory rules will drive up costs to market new products and discourage innovation. One new requirement that is already felt by the industry are unannounced audits. Notified bodies are required to conduct unpredictable audits at the manufacturer's, critical subcontractor's or component supplier's manufacturing sites.

Emerging and future technologies. Hardly any industry implements new technologies as fast in its manufacturing processes and products as the medical device industry. For example, medtech companies are among the pioneers in finding applications for 3D printing technology. Because of the need to tailor many medical products to individual patients, 3D printing has become the standard process already in the manufacturing of certain devices, such as hearing aids or dental implants. It is expected that 3D-printed hip and knee replacements will be in mainstream use within two to five years.

One major trend in healthcare is personalized medicine where physicians are able to suit treatments to the patient. In this context, molecular diagnostic systems are gaining importance that analyze the patient's genome and proteome to find biomarkers hinting at certain diseases and predict the person's reaction to treatments.

As mentioned above, the digitalization of healthcare is progressing. Patients use cell phones and wearable devices to monitor their health. Big Data applications, such as IBM's Watson, will be used to support diagnostics and treatment decisions and predict the outbreak of pandemics by analyzing disease patterns. Already, robotic systems, such as Intuitive Surgical's Da Vinci device,

assist doctors during surgery.

In the research labs, scientists are working on even more futuristic technologies. In the future, nano sized devices will travel through blood vessels searching for biomarkers of diseases, delivering drugs and attacking cancer cells. Researchers are also working on technologies that are able to interpret electrical currents in the brain. Such brain-device interfaces might one day help quadriplegic patients to operate motorized exoskeletons.

Public payers and health insurances will demand that new medical devices not only improve the treatment but also help to save money

Scientist are also trying to take 3D Printing to the next step. They are replicating human tissue with the help of 3D printers. In 2013, researchers at Chinese Hangzhou University even claimed to have produced a small kidney. Currently, the major challenge for Bioprinting is to supply the printed structures with blood so that they can survive. While it is still probably decades away that companies will be able to print fully functional replacement organs, the technology might in the nearer future be used to produce tissue for clinical trials.

Conclusion

The medical device industry faces challenges in many areas. Regulatory changes are looming, new contenders are entering the market, and public healthcare budgets are ever decreasing. However, the prospects for the industry are still promising. Ageing populations and a globally growing middle class are indicators that the demand for medical technology will only increase in the future.

Medical device companies will have to employ new technologies in order to adapt to changing conditions, as public payers and health insurances will demand that new medical devices not only improve the treatment but also help to save money.

*Thomas Klein, freelance journalist based in Germany, writes about the medical technology industry and was the managing editor of European Medical Device Technology (EMDT) until 2015. Before he had worked as an editor and project manager at the F.A.Z.-Institut, a full subsidiary of the Frankfurter Allgemeine Zeitung (F.A.Z.) publishing group, writing about various economic issues with a focus on innovation management and the ICT-sector. Thomas studied Political Science, Sociology and History at the University of Trier.

Medtech

Bcn Innova

Oriol Prat
CEO

2008
Year founded

4
Employees

210K€
Turnover (2015)

www.bcninnova.com

Company mission

To develop, manufacture and market medical devices to measure ocular mobility.

What innovation do you bring to the market?

We make a device that had never been seen before. Previously, ocular mobility was measured manually, in a very imprecise and subjective manner, which led to many errors and meant that surgery wasn't always effective. Our device measures ocular mobility precisely and objectively, facilitating diagnosis and monitoring of the condition and, indirectly, improving the results of surgery.

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

From a technological standpoint, preparing a device that has never been seen before and starting to market it. We began marketing the device in 2013 but 2015 has been the year of consolidating sales in countries like Spain, France and Italy, but also markets further afield like Denmark, Poland, Malaysia, Indonesia, Hong Kong, Macau, Mexico, Algeria and Estonia, directly or through distributors.

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

We aspire to become the industry standard in measuring strabismus and other conditions related to eye mobility, so all ophthalmologists have our device in their practice and all patients can benefit from it.

Medtech

Biokit

Pau Planas
CEO

1973
Year founded

340
Employees

124M€
Turnover (2015)

www.biokit.com

Company mission

To contribute to precision medicine by offering innovative immunoassays and in vitro diagnostic solutions (IVD) that clients consider to be of high clinical value, safe and easy to use.

What innovation do you bring to the market?

Biokit's innovation is twofold: in technology, constantly striving for new knowledge and skills to develop and manufacture biomaterials (antigens and antibodies) and reactives to obtain best-in-class immunoassays; and in business, offering solutions that have the potential to transform our clients' workflow, allowing them to create proposals of higher clinical value. For example, Biokit is a pioneer in marketing some diagnostic tests on the high-sensitivity BIO-FLASH platform, offering a completely automatized solution for these tests for the first time on the global in vitro diagnostic market.

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

Having been able to grow a totally international business based on knowledge and talent is highly satisfying. Many factors have contributed to this, but I think the most decisive was combining the acquisition of advanced diagnostic technology with business opportunities where this technology has the potential to transform or innovate. Thanks to this good decision, Biokit has become a world leader in some segments of the IVD market.

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

That Biokit has continued to innovate and generate wealth based on the same professional and human values that have guided us so far.

Medtech

NEOS Surgery

Lluís Chico
Managing Partner

2003
Year founded

13
Employees

1.3M€
Turnover (2015)

www.neosurgery.com

Company mission

The mission of NEOS Surgery is to develop, homologate, manufacture and market new implantable healthcare products that help improve quality of life by understanding market demands in surgery –in particular, neurosurgery– in order to boost the value of the company and foster growth in a high value-added industry.

What innovation do you bring to the market?

The NEOS philosophy is essentially to develop implantables based on innovative materials and designs. Plus, we always go one step further in processing these materials. This way, we create more ambitious designs for our products so that they better fit the needs we've detected among neurosurgeons, who we are in constant contact with.

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

Here at NEOS we've achieved a significant international presence for our Cranial LOOP line of products, which are currently sold in more than twenty countries around the world. We've achieved this goal thanks to several factors: ambitious product development and patent strategy, approval from several regulatory authorities (CE marking in Europe, FDA in the USA, CFDA in China and soon the PMDA in Japan, among others), and commercial alliances with proven local partners, like the KLS Martin group in the United States.

Also, we've recently been granted an SME Instrument by the European Union under the Horizon 2020 project. As one of only six companies in Spain to benefit from this instrument so far in the sector (nanotechnology, materials and advanced manufacturing), NEOS will receive funding for two years to complete development of a product to treat herniated discs.

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

Some time from now, we would like to read that NEOS has become a consolidated company and is growing steadily on all levels, above all with regard to (exclusive) implantables with significant value added for users. We would like to see us become a benchmark international implant manufacturer. We hope to achieve this goal with a wide range of patented products developed internally, although we don't discount the possibility of working with other external partners (third-party development), both in the field of neurosurgery as in other areas of surgery.

Medtech

Starlab

Ana Maiques
Co-Founder

2001
Year founded

37
Employees

4.2M€
Turnover (2015)

www.starlab.es

Company mission

To transform science into products and services with a huge impact on society.

What innovation do you bring to the market?

After fifteen years of field research in neuroscience, we've developed innovative wireless medical devices to monitor and stimulate the brain in order to help patients recover from a cerebrovascular accident, chronic pain or depression.

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

Our innovative devices have been sold in more than 35 countries by our spin-off, Neuroelectrics. Important centers and universities like MIT, Harvard, NASA, Yale, UCSF, Mont Sinai Hospital, Inserm, Oxford and veterans hospitals use our technology to learn more about the brain and, therefore, be able to help patients who need it.

We have CE marking and our Boston office is beginning the process to gain FDA approval.

Neuroelectrics technology has received numerous awards, the latest being the Wired UK Best Start-up for Health in Europe Award 2015.

What would you like to read about the company in the news a few years from now?
I would like to read that Starlab has been recognized for conducting high-quality research and for having made the long journey from research to market (which is very difficult). I would like to read that our technology, like what we now market through Neuroelectrics, has become a game changer, significantly changing how we diagnose and treat patients with brain conditions. I would like to see that our devices are being used for home treatment around the world.

Medtech

STAT-Diagnostica

Jordi Carrera
CEO

2010
Year founded

30
Employees

-
Turnover

www.stat-diagnostica.com

Company mission

To develop a diagnostic device that decentralizes molecular diagnosis and immunoassays for critical applications like infectious diseases, cardiology and oncology. It is a machine that takes fungible cartridges of reactives that can be used, for example, in an ICU or fast testing hospital laboratory to allow for near-patient testing.

What innovation do you bring to the market?

Our main innovation is that the test is automatized, with a usability level that allows both nurses and doctors to do the test, thus bringing it to the patient. With a highly affordable manufacturing price and laboratory-level analytical capability, the results of the test don't have to be confirmed later in a central laboratory. They can be used by doctors to make clinical decisions.

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

In 2013, the company closed the largest investment in the biotechnology and medical technology sector in Spain in recent years: €17 millions. In 2016, we hope to close another for between €20 millions and €30 millions. Funding is key to moving forward, but the most important is the state of technology we've reached, which is now ready for transfer to manufacturing and negotiations with distributors. Between late 2016 and early 2017 we expect to launch on the European market.

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

Now we have the technology and aspire to develop the business. We would like to read that STAT-Diagnostica is earning money, as an independent company or as a business unit of a large corporation that has acquired it, and that we market a leading product that can stay on the European and American markets for 15 or 20 years.

Medtech

Transmural Biotech

Roc Viñas
Chief Operating Officer

2009
Year founded

11
Employees

50K€-100K€
Turnover

www.transmuralbiotech.com

Company mission

To develop and market new medical technology based on image processing that enables effective, non-invasive, early diagnosis of complex pathologies.

What innovation do you bring to the market?

The technology Transmural Biotech develops is geared towards meeting a clear need identified by world-renowned specialists internationally. New diagnostic techniques are needed that use medial imaging for efficient, non-invasive diagnosis of various pathologies.

With this vision, in recent years we have worked to develop technology to interpret medial images (mainly ultrasound imaging) to identify parameters not visible to the human eye that are associated with the presence of certain pathologies.

Starting from this technology, we've created our first final product, quantusFLM. This software analyzes an ultrasound of a fetus's lungs to determine the risk of neonatal respiratory morbidity, replacing previous tests based on amniocentesis.

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

Starting to market our first product, quantusFLM, in late 2014.

Having developed a final product and starting to market it is undoubtedly the best proof of the company's capabilities, and a key milestone in ensuring its consolidation.

Currently, by applying an innovative business model for marketing this product, we have users in 40 different countries.

These facts motivate us to keep working just as hard, because we believe that our vision of becoming a global benchmark in image diagnostics is closer than ever.

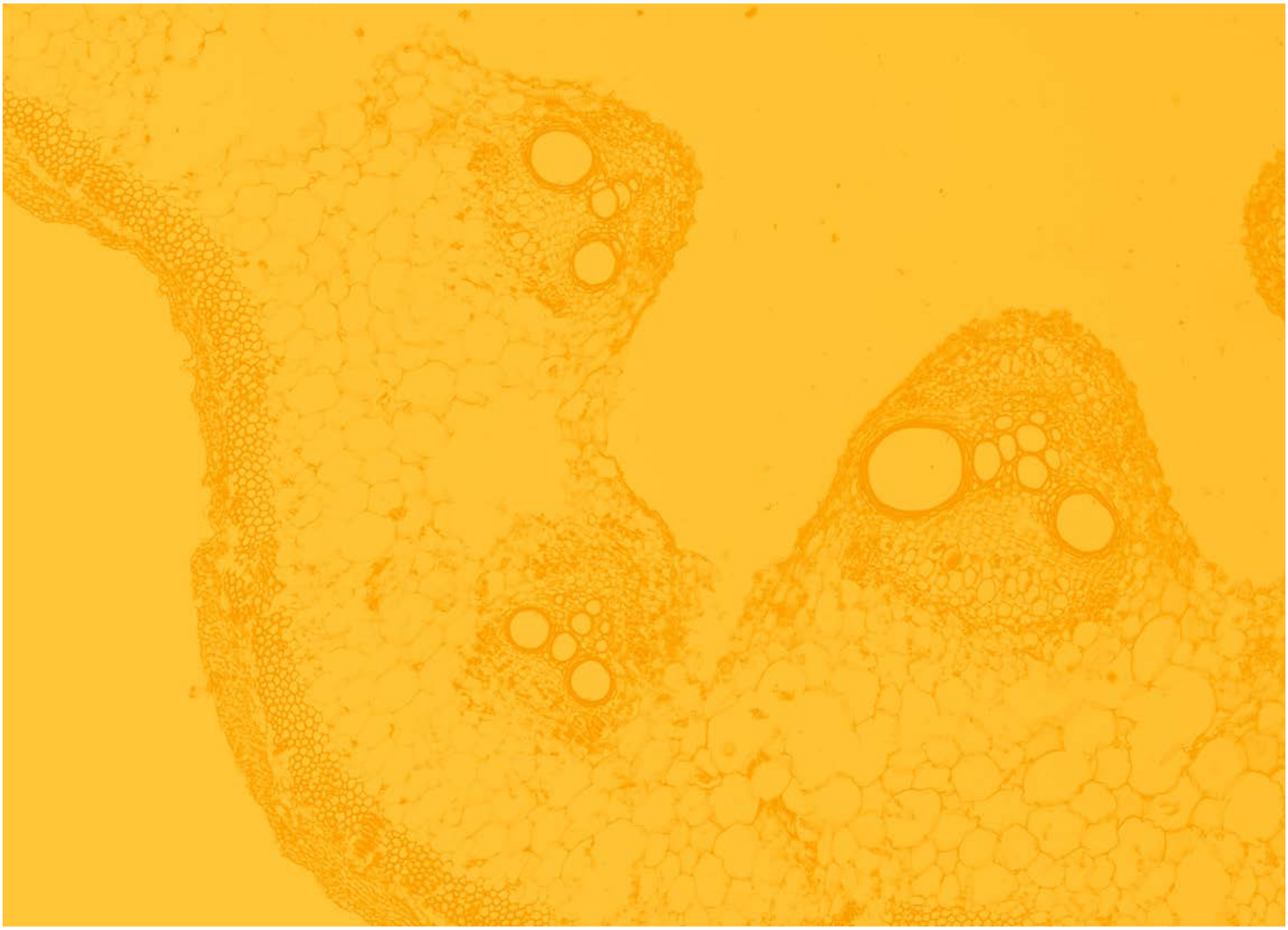
What would you like to read about the company in the news a few years from now?

That we've been able to develop and market new diagnostic tools that use our base technology to improve clinical capabilities to tackle pathologies that affect large parts of the population, like cancer, neurodegenerative diseases and premature birth, among others.

Also, that this has helped create jobs, consolidate the company internationally and generate profits for the partners that have believed in this project.

How data (and not technology) is reshaping the future of healthcare

Tamer Shahin
CEO of Nuviun



Although we frequently hear how the increased use of technology is changing the world of healthcare, the mounting power of this wave is really built upon that which resides within: data. It's the data which is derived from technology's increased use which drives such change, and it possesses massive potential to reshape the future of healthcare. Here, we examine a common term in relation to healthcare, data, and technology —Digital Health— to better understand its role in what lies ahead.

What is Digital Health?

Digital Health is the application of digital and genetic technologies to the delivery of health and healthcare. Digital Health reflects the merging of several fields: the Human Genome Project and genome sequencing technologies, Electronic Health Records (EHR) and Health Information Technology (Health IT), Big Data, Personalized Medicine, and Social Media.

Each field has developed quite independently and has enjoyed impressive and unique successes. However, as each field moves forward, their most promising and potentially fruitful expansion does not come from "business as usual" as in independent development, but instead by a mutual integration for a common purpose. This integration is called Digital Health. It seeks to form advantageous synergisms among disparate, yet complementary fields. Digital Health promises to change the way that physicians practice medicine and pharmaceutical companies develop therapies. It also encourages patients (people) to participate more in their own healthcare.

Digital Health encompasses two other recent movements in healthcare: eHealth and mHealth. eHealth is defined as the use of electronic processes to support the delivery of health care. This may include EHRs, consumer health informatics, provider health informatics, e-prescribing, and telemedicine. Similarly, mHealth stands for mobile health and refers to the use of mobile devices to deliver health care. mHealth may include the use of personalized computers, mobile smartphones, and tablets, but increasingly includes devices that collect personal health information, such as biological sensors and monitors. The World Health Organization and most other organizations consider

Digital Health reflects the merging of several fields: the Human Genome Project and genome sequencing technologies, Electronic Health Records and Health Information Technology, Big Data, Personalized Medicine and Social Media

mobile health as an extension of electronic health. Thus, mHealth is often discussed as a part of eHealth. By extension, Digital Health necessarily includes the concepts of eHealth and mHealth.

Digital Health embraces electronic and mobile technologies but also seeks to exploit salient developments in human genome sequencing and personalized medicine. Digital Health is considerably larger in scope than simply mHealth or eHealth because it seeks to incorporate concepts, information, and technologies from several rapidly advancing fields.

State of the art in Digital Health

Digital Health takes advantage of two major revolutions that matured in the late 20th century, the genetics revolution and the digital revolution. In the late 1990s, we unlocked the code to every human gene. At the same time, personal computers and the Internet became a welcome necessity and convenience in our daily lives. While the scientific underpinnings and technical developments were hard fought victories in the late 90s, the last decade was one of miniaturization, proliferation, and application. Our phones carry computing power and speed that could not be matched by room-sized computers of the past. The Internet is, or will soon be, a ubiquitous presence on the globe. Digital Health capitalizes on this unprecedented power, availability, and affordability to deliver a new form of personal and global health care. We are swiftly applying the technologies of the recent past and reaping the fruits of that scientific labor.

Perhaps the most salient feature of the last decade of advancement is that the technologies are not only more empowering and accessible, but also more affordable

Perhaps the most salient feature of the last decade of advancement is that the technologies are not only more empowering and accessible, but also more affordable. The Human Genome Project took more than a decade to complete. Then, an additional decade later, commercial entities now offer whole genome sequencing within a matter of weeks for under $100. The cost and time involved in this process has dropped so that it is conceivable for personal exome or whole-genome sequencing to become a part of standard healthcare screening, perhaps as early as birth.

Wearable sensors and real-time data acquisition (Personal Data Quantification)

The Digital Health complement to personalized genomes is the Quantified Self. The Quantified Self seeks to record and analyze the human experience using various sensors, monitors, and digital acquisition devices. The Quantified Self is self-awareness through self-monitoring; the assumption is that by tracking personal data, one can achieve better health, wellbeing, and longevity.

Putative mHealth devices include accelerometers that measure accelerations/decelerations and body/limb displacement, gyroscopes that sense angular velocity, and goniometers that measure joint range of motion, electromyography, GPS signaling and others. Some of these hardware components are found in typical smartphones, while others may be worn or (in the near future) implanted. As devices are miniaturized, they can be interwoven in fabrics or impregnated into ultrafine "second skins".

Big Data/Big Health

The amount of information that is created by just one "Quantified Self" is enormous. It almost boggles the mind to think of the data generated by a "Quantified Population." However, just as the cost of personal genome sequencing is dropping, so is the cost of digital data storage (and both are miniaturizing).

Big Data is not simply a concept for the future. Large collections of identified and de-identified health information exist in a nascent state already

It is therefore feasible to contain the data that makes up a "Quantified Self" or even data across a population. This concept of collecting massive amounts of data of organized and unorganized data is called Big Data.

When the data is collected in the health arena, it is often referred to as Big Health. Importantly, Big Health also refers to the unique advantages that emerge from the availability of large amounts of health data. Big Data and Big Health are core components of Digital Health. Big Data is not simply a concept for the future. Large collections of identified and de-identified health information exist in a nascent state already. For example, various government agencies have been collecting information from EHRs, pharmacy records, and related data sources for several years. These agencies use this data to track the delivery of health care, assess relevant disease endpoints, track outcomes, and reduce medical spending.

Conversely, several companies specialize in collecting, curating, and providing de-identified patient health information. They may also sell access rights to entities interested in various forms of research. Big Data/Big Health offers the ability to perform virtually limitless retrospective clinical studies. De-identified health data can be used to study epidemiology of diseases, health care economics, and comparative effectiveness. As with any dataset, the more points that you have, the higher the statistical power of the analysis. As Big Data becomes more manageable, searchable, and amenable to analysis, researchers will be able to ask questions that were formerly considered im-

possible to answer. Moreover, as the number of people who participate in personal data quantification increases, one could envision the use of Big Data in prospective studies as well.

Electronic Health Records

Most healthcare providers have used Electronic Health Records (EHR) or Electronic Medical Record (EMR) in their practices. Because of the flexibility and potential for growth, the preferred term is now EHR, as opposed to EMR, since it more accurately describes its scope as a repository for patient's health data. While the transition from paper records to EHR has been far from seamless, most would agree that a well-designed EHR is a powerful tool in the practice of medicine.

Current EHRs carry an electronic version of an array of records, including progress notes, allergies, laboratory reports, and medications. The digital EHR is no longer limited by the physical restraints of a paper chart. Data can be collected from various sources and collated into an intuitive, physician-directed interface.

A highly usable EHR is a critical component of Digital Health in the clinical arena. Physicians will require a central, portable repository of patient data that can be easily accessed and actionable. Just as the patient's paper chart has been the central repository of all clinical data in the past, present, and future, the EHR will house clinical and personal health data. By digitizing the record, however, the amount of searchable, usable data that can be contained in EHR far exceeds any paper chart.

The Cloud

The Cloud is an often discussed, but rarely defined concept. The Cloud is simply off-site data storage that is available through any internet-accessible device at any time. It only requires definition since the history of personal computing has been to store data locally, in hardware that was localized on the same site as the user. On-site or local data storage greatly limits the potential uses of the stored data. By uploading data to the Cloud, off-site servers can provide credential-verified and secure access to multiple users at the same time. Data files in a centralized server can be modified simultaneously and updated continuously, thereby ensuring constantly updated and up to date content. Moreover, access to the data is portable. It is not limited to a file in one doctor's office.

A highly usable EHR is a critical component of Digital Health in the clinical arena. Physicians will require a central, portable repository of patient data that can be easily accessed and actionable

Cloud computing is a necessary development for truly comprehensive EHRs and is thus important for the expansion of Digital Health. Telemedicine Cloud computing and Digital Health applications lend themselves to telemedicine which is the practice of medicine in which the clinician and the patient are physically separate but at the same time, connected by a digital interface.

Potential barriers to Digital Health

There are several barriers to widespread physician adoption of Digital Health. Most physicians are reluctant to adopt new healthcare strategies without significant proof that they are safe and effective. While it is common to choose therapies that have been tested in large-scale, blinded, controlled clinical trials and that have emerged from rigorous regulatory scrutiny, Digital Health applications are not scrutinized to the same degree.

In addition, it is unreasonable to expect physicians to personally evaluate or to even keep abreast of incremental developments in the field given the sheer number of mHealth technologies. In much the same way, there is a mismatch between the availability of personal genome sequencing (learning your personal DNA code) and applying that to the practice of medicine. The technology is ready and relatively inexpensive, but considerable work remains to make those findings clinically relevant. Physicians will require support through (likely years of) basic and clinical research studies in order to integrate genome sequencing into the physician-patient consultation.

While the benefits of EHRs/EMRs are becoming self-evident to most physicians, as the number of results and options within an EHR increases, so does the time and energy required to assess and manage those results. For any Digital Health enterprise to be successful in the hospital, it must be straightforward for the patient, but also for the physician. Digital Health software and EHRs will need to possess a sophistication such that large amounts of data are properly and rigorously analyzed before they are presented to the physician.

Any successful Digital Health technology must be user-friendly—bearing in mind that the user is both the patient and the physician. Patient privacy will be of paramount importance in the future of Digital Health. While users of social media products are notoriously free with personal information, they are generally more guarded with personal health information. Any developing Digital Health technology, especially EHRs and Big Data applications must assure users and regulators that personal health data is secure.

Another obstacle that is less often mentioned (but no less important) is the mechanism by which physicians will bill for Digital Health in the clinic. The long-term success of Digital Health in the clinic must include a mechanism for physicians to be reimbursed for their

time and effort. In one respect, increased access to patient data will help inform clinical decision-making and will improve outcomes. To get to that point will require significant physician involvement. Plainly said, without a financial incentive for physicians, Digital Health will not enjoy complete clinical integration.

The other issue that goes hand in hand with reimbursement/compensation is regulatory control of Digital Health. Regulatory bodies acknowledge the rapid advances of Digital Health technologies and provide guidance to an industry that is hungry to innovate. If regulatory guidance and approval lags, so lags the field as a whole and physician engagement.

Digital Health is growing rapidly, but is still in its early life stages. Many of the aspects described above are not fully developed and certainly not fully integrated. While one can have their genome sequenced for $99, they will receive little more than an unintelligible diary written with a four-letter alphabet. Likewise, just because someone can collect every joint position and theta brain wave and upload it directly to the Cloud does not necessarily mean that the data is useful, instructive, or that it can even be analyzed. At its heart, Digital Health is an awareness in which separate, powerful technologies are ripening at the same time. With proper integration, it can provide an unprecedented level of personal health care.

The future of Digital Health

Individualized Treatments. Because of the potential power of digital and genetic technologies, there have been dozens of possible future Digital Health applications proposed. However, some are more immediately relevant for the physician. Digital Health offers a completely re-conceptualized version of personalized or individualized medicine.

Truly Designer Drugs. Personalized genome sequencing has the potential to identify genetic susceptibilities early in life, in many cases at a point in which early intervention can make a difference. However, that is only the first promise. Why do pharmaceuticals work for some people and not others? Heterogeneous responses appear to be related to an individual's DNA sequence variants. In essence, knowledge of a person's genome not only predicts susceptibility to genetic diseases and disorders, but it also predicts response to available treatments.

Digital Health is an awareness in which separate, powerful technologies are ripening at the same time. With proper integration, it can provide an unprecedented level of personal health care

Rapid Response to Outbreaks. If you imagine a world in which most people use wearable sensors, possess and use medical apps, and have a portable EHR, it is not too hard to imagine a powerful epidemiological tool. Potential outbreaks could be identified and authorities could be dispatched immediately. This could shave several days off current response times. With outbreaks of highly contagious and virulent diseases, the time to respond is often the difference between containment and pandemic. Thus, widespread, voluntary, digital self-monitoring could have important public health implications.

The Digital Health landscape

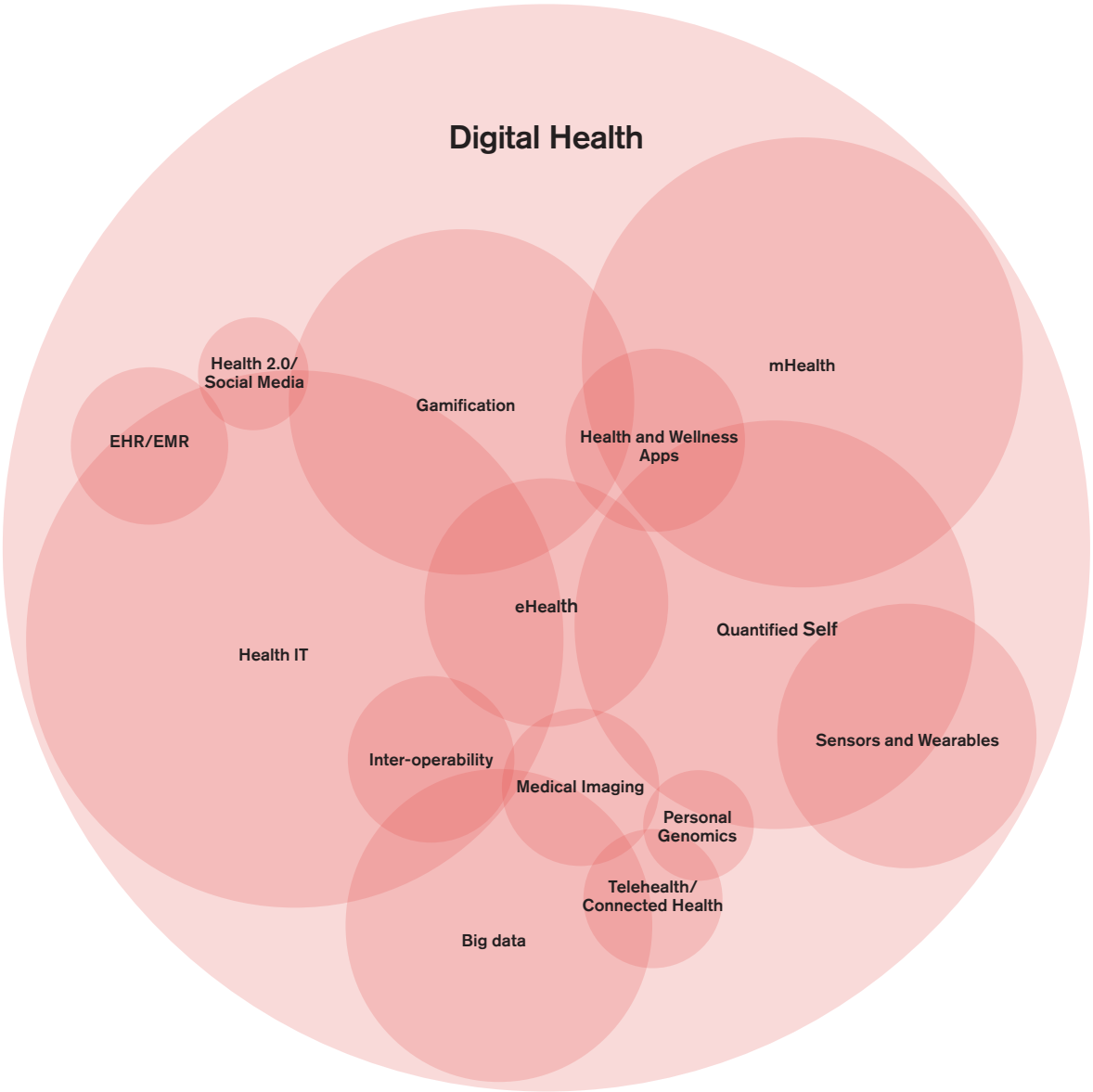
As has been noted, Digital Health is a broad term that covers a lot of territory—all healthcare-related applications, technologies and delivery systems that result from the confluence of medicine, genomics and the technologies that comprise the digital space.

It includes a variety of overlapping sectors such as Health IT, telehealth, eHealth, mHealth, EMR/EHR, personal genomics, quantified self, Big Data, gamification, Health 2.0/social media, medical imaging, sensors and wearables, and health and wellness apps. Interoperability is the final link in the chain that we strive for to put it all into play. In short, Digital Health is a big, interactive, and exciting world with massive potential to create great change.

Our Digital Health Landscape represents the connected nature of the digital health world—where one sector depends upon the other to produce best results. It's not to scale—and not meant to be. As the digital health revolution expands, so will the visibility and importance of various sectors.

*Tamer Shahin, PhD, is the CEO and chairman of the executive board at Nuviun, the leading emerging industries knowledge resource portal. Nuviun specializes in bringing emerging industries to the mainstream through a blend of cutting edge and traditional platforms such as an innovative collaborative online information portal, second-to-none industry conferences and exhibitions, roundtables and seminars, and business intelligence and partnering.

The Digital Health landscape
Source: Nuviun



Digital Health

Doctoralia

Frederic Llordachs
Co-founder

2007
Year founded

45
Employees

3M€
Turnover (2015)

www.doctoralia.com

Company mission

Doctoralia is the leading global platform connecting healthcare professionals and patients, transforming and improving relations between the two. It offers tools that help boost the online visibility of healthcare professionals, as well as helping them find more patients and better manage them. At the same time, it brings healthcare to users, giving them a place where they can ask questions, give opinions and find the best healthcare professionals for their needs.

What innovation do you bring to the market?

We started in 2007, the year the iPhone was launched, thinking that sooner or later people would end up looking for a doctor online. This allowed us to get out ahead of this phenomenon of the masses, as posting information about doctors is becoming more and more useful. The Doctoralia search engine, unlike others, allows users to search not just by the doctor's name or city, but also by medical specialization and sub-specialization, and even by a specific disease or insurance company, which aims to encourage more and more people to search for doctors and specialists online. What sets us apart is the number of doctors in our database, well above the competition, and the number of monthly users, which makes us an attractive tool for doctors and healthcare professionals to establish an online presence.

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

We've hit 120 million users a month, 3.5 million visits from registered medical centers and professionals, 2.5 million pages viewed monthly through our "Ask an Expert" service, and service in 20 countries around the world.

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

That a Catalan company, from Barcelona, is the leading platform in the world helping patients find doctors and giving healthcare professionals an online presence and digital tools.

Digital Health

Intelligent Pharma

Ignasi Belda
CEO

2007
Year founded

19
Employees

700K€ - 1.3M€
Turnover

www.intelligentpharma.com

Company mission

To conduct in silico research projects for the pharmaceutical, agrifood, cosmetics and petrochemical industries, as well as developing customized scientific software for these sectors.

What innovation do you bring to the market?

Here at Intelligent Pharma we reinvest a large part of our income in developing innovations in many different disciplines of science and technology that have an impact on our sector. Some of these disciplines include artificial intelligence, high-performance supercomputing, cloud computing, statistical modeling, physics/chemistry, etc. This makes us one of the most cutting-edge companies in our niche.

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

Having conducted more than 150 research projects for companies around the world. We currently have clients throughout America, Asia and, of course, Europe. So, more than a specific milestone, our satisfaction comes from contributing our grain of sand to all of these research projects, many of which have led to innovations that help improve patient quality of life and, in the best cases, save lives.

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

That a drug we have helped identify or optimize is saving thousands of lives.

Digital Health

Medtep

Pablo Pantaleoni
CEO i cofundador

2011
Year founded

30
Employees

500K€
Turnover

www.medtep.com

Company mission

For people who are concerned about their health, Medtep provides a digital platform that makes it easier to adopt behavioral changes by following clinically proven prevention and treatment plans.

What innovation do you bring to the market?

Nowadays, most platforms only focus on follow-up and collecting data using smartphones and third-party apps, without any other value added. Medtep adds value to these solutions with a validated, multidisciplinary, personalized ecosystem in which the doctor-patient relationship goes beyond the doctor's office. Plus, the Medtep treatment and prevention plans don't only aim to control the user's health, they also foster healthy life habits that improve quality of life.

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

On one hand, we've consolidated our internationalization process by opening offices in San Francisco (USA) and Mexico City (Mexico), and now have more than 120,000 users.

On the other, we've closed a round of funding for $2 millions, which has allowed us to expand the team and accelerate the pace of growth.

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

Obviously, we'd love to read about the company's growth and positive results. However, nothing would please us more than to learn that Medtep has led to a paradigm shift and helped improve quality of life for patients around the world. After that, success on other levels will surely follow.

Digital Health

Mint Labs

Paulo Rodrigues
CEO

2013
Year founded

6
Employees

12K€
Turnover (2015)

www.mint-labs.com

Company mission

Mint Labs' mission is to study the brain and develop tools to predict, detect and diagnose neurological disorders.

What innovation do you bring to the market?

Mint Labs is a cloud computing platform for advanced clinical research. We help specialists and researchers get the most from their data. We are an advanced image-processing and visualization company focusing on the brain; specifically, we use MRI technology.

There isn't any tool currently on the market that can match the analysis capabilities and performance of the Mint Labs platform. That makes us the latest generation of monitoring and diagnostic technology for brain disorders. Our competition's technology in the field is obsolete or much more basic. They simply provide storage on the cloud without our technology, which provides advanced image analysis and advanced imaging tools used exclusively by expert doctors.

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

After several pilot programs, our first revenue was a very significant milestone for us. It confirmed that, in addition to doing something that was technologically cutting edge and highly innovative in the field of brain research, we also have great business potential.

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

In a couple of years, I'd like to see how our understanding of the brain and brain disorders has significantly increased, and how Mint Labs and our unique collection of data on the brain has been key in accelerating research and development of new treatments for brain disorders. I'll be very proud to say that someone used Mint Labs to develop a new treatment for dementia or multiple sclerosis.

Digital Health

Social Diabetes

Victor Bautista
CTO - Product Development Manager

2012
Year founded

6
Employees

300K€
Turnover

www.socialdiabetes.com

Company mission

To allow diabetic patients to control their condition, leading a normal life and preventing complications, with the safety of a CE-certified medical device.

What innovation do you bring to the market?

The device adjusts a patient's insulin levels according to their real needs and habits, not the theoretical habits a book says they should follow. At the same time, as it learns from the patient's history, it helps avoid nighttime hypoglycemia, which can lead to a diabetic coma or death.

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

The most important milestone is undoubtedly the more than 90,000 downloads of our mobile app, due only to word of mouth, patient recommendations, without doing any sort of marketing or investment. We're very thankful and will always continue to listen and pay attention to the users' suggestions and ideas for improvement. We are also thankful for the numerous awards we've received, certifications and recognitions, and the confidence governments, hospitals, corporations, pharmaceutical laboratories, insurance companies and national and international bodies have shown in us.

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

That the device has saved thousands of lives.

Digital Health

Universal Doctor

Jordi Serrano
CEO and Founder

2008
Year founded

10
Employees

300K€
Turnover (2015)

www.universaldoctor.com

Company mission

To improve communication between healthcare professionals and patients who don't share a common language, and to become the multilingual healthcare system tool of the future.

What innovation do you bring to the market?

We develop medical translation applications that adapt to each user and technology.

So, on one hand, we've evolved with the changing technology, from CDs in the early days to flash websites, html, and multiplatform tools that allow users to access the information from any sort of device.

On the other, we tailor the service to each client, developing specific apps for pharmacies and developing smart dialogs that allow healthcare professionals to build their own repertoire of personalized questions for their patients to answer.

More than 150 universities, governments and hospitals, among others, are now using our technology.

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

International implementation of our technology in hospitals and healthcare institutions in countries like Spain, Belgium and Norway, as well as our mobile versions, which have been downloaded by more than 300,000 people. In 2014, Universal Doctor received the World Summit Award for medical applications from the United Nations.

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

We want to be a multilingual digital channel that can be adapted and customized by any healthcare location in the world. Hopefully one day you will be able to touch a wall in a hospital and see a Universal Doctor video in 72 languages. We aspire to be not only software, but a channel.

GRAPHS

TABLES

This bibliography, divided by topic corresponding to the articles that make up the 2015 Biocat Report, only includes the main official publications and reports used. The reports of organizations in the BioRegion are not included in this list but are cited in the body of the report where necessary. Other sources, mainly periodicals, websites, databases and press releases, are included as links in the online version of the Report.

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