

Scaling-up the BioRegion of Catalonia

BIOCAT REPORT 2017

A 2025 Vision for Catalonia

In collaboration with



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Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Foreword

INNOVATION, ENTREPRENEURSHIP AND NETWORK THINKING: A GROWTH MODEL FOR THE BIOREGION OF CATALONIA



Daria Tataj

Chairwoman of RISE High-Level Advisory Group to Carlos Moedas, European Commissioner for Research, Science and Innovation, Founder & CEO Tataj Innovation

INNOVATION, ENTREPRENEURSHIP AND NETWORK THINKING: A GROWTH MODEL FOR THE BIOREGION OF CATALONIA

The 2017 Biocat Report presents the innovation ecosystem and growth drivers of the life sciences and healthcare sector in Catalonia over the period 2015-2017. The data and findings of the report show an impressive picture. With 1,060 companies and 89 research institutions, including research centers, universities and university hospitals, the sector employs more than 223,000 people and generates over 7% of Catalonia's GDP.

The overall significant research and innovation potential of the region best describes its second position in the ranking of the ERC grants (per million inhabitants), 189 grants in the 'SME Instrument' and almost 5% of the Horizon 2020 FET Flagship funds, which matches the level of funding received by such countries as Austria, Denmark and Finland. The data presented in the report also show exponential growth of the region's overall entrepreneurial activity. The investment in startups grew threefold compared to the previous period, reaching almost 340 million EUR in 2015-2017 and 214 transactions attracting an increasing number international investors, which have increased from 6 to 41. In the first half of 2018, 17 foreign companies reportedly announced new research, technology or business centers in Barcelona or its surroundings. Regarding business creation, every week a new life-sciences company is created in Catalonia.

Over the last three decades, Catalonia has undoubtedly become one of the most innovative regions in Europe. With the focus on policies fostering better higher education, excellent research and collaboration between academia and companies, the Barcelona metropolitan area has become a magnet for talent and funding. In a fast-changing world where old economies have broken down, this part of Europe managed to reinvent itself in an emblematic way. From being an area once called 'the Catalan Manchester', in 2014 Barcelona proudly received the title of Innovation Capital conferred by the European Commission, and it has recently become the 4th city with most startups. This transformation has been strongly driven by the emergence of the life sciences and healthcare sector.

But the question is whether the growth of this sector can be maintained and then consolidated.

One can argue that the current growth model has a sound base with excellent research, solid higher education and vibrant entrepreneurial activity. Will that be enough to ensure prosperity and growth in the coming years and to scale it up? Should the Catalan government and the businesses located in the BioRegion expand the current base and explore new growth models?

I believe it is important to expand the current base. This means further strengthening the four pillars: research, education, innovation and entrepreneurship. It is also necessary to both consolidate the ecosystem and interconnect it better with global innovation networks. This can be done through Network Thinking. Network Thinking means developing the ability of all the stakeholders in the ecosystem to overcome the silo mentality and to embrace an open innovation culture and collaborative modes of innovating, coupled with an effort to become both tightly-knit locally and more loosely-coupled globally. In reality, both businesses and academia struggle to develop interfaces and collaborate in meaningful ways. Network Thinking helps co-create a deep, strategic shift at three levels: changing mindsets and building new skills; changing team dynamics through trust-based leadership; and introducing an organizational culture and governance which turn networks into creative communities.

In recent years, European research and innovation policies have evolved around the concept of openness. Open science, open innovation, open to the world: the '3 O's' as outlined by Carlos Moedas, the European Commissioner for R&I, have been one of the cornerstones of Horizon 2020. In June of this year, the European Commission announced its proposal for the next Framework Program: Horizon Europe (2021-2027). With a budget of 100 billion EUR, the scheme organizes existing policies and instruments and proposes new ones in three pillars: Open Science, Global Challenges and Industrial Competitiveness, and Open Innovation. The first pillar includes the European Research Council, Marie Skłodowska-Curie Actions and Infrastructures, with a budget expanded to 25.8 billion EUR. The second one, which has an overall budget of 52.7 billion EUR, proposes the novel mission-based approach, among others. The third one, earmarked 13.5 billion EUR, includes the European Institute of Innovation and Technology (3 billion EUR) as well as a new instrument: the European Innovation Council (10 billion EUR).

The missions and the European Innovation Council (EIC) are two important policy innovations. The missions-based policy means reorganizing investment in R&D about around more tangible, collec-

tively designed, clear and ambitious goals based on well-defined market and social needs. The move from the Grand Challenges approach to missions relies on bringing R&I closer to citizens, engaging them in co-defining it and selecting how to 'translate' such important challenges as the Millennial Development Goals, for example, into specific, measurable missions such as the fight against cancer. The EIC is supposed to focus on funding disruptive, market-creating ideas, technologies and applications and to help scale up the most innovative start-ups and small and mid-size companies to the global markets. It will focus on investing in people rather than institutions by providing direct support to innovators. Designed as a 'one-stop shop', the EIC will focus on the entire innovation process from the early development stages to market roll-out. Besides these new instruments, the Open Science approach will be taken to the next level by obliging open access to publications, data and research data management plans funded with Horizon Europe grants. The new Framework Program will also streamline co-funding partnerships with industry and, last but not least, further simplify legal and administrative procedures.

With its current position, the Catalan life sciences and healthcare sector will surely benefit from Horizon Europe. There will be more European funding for research and innovation, which is so sorely needed within the context of decreased public R&I funding in Spain. Catalonia is one of the main innovation hubs of the EIT with the EIT Health co-location center, and these activities for entrepreneurial education and business acceleration will be expanded. What is maybe the most relevant for existing businesses is the proposed scale-up in the ECI's funding. Last but not least, with Barcelona pioneering citizen engagement policies, there is a wealth of experience about how to establish meaningful 'missions'. Integration of these policies may help grow entrepreneurial firms, especially with the open data approach. The scaling up of an ecosystem is not a trivial issue, and the synergy between top-down policies and bottom-up projects, programs and activities will surely be a decisive factor which can make the Catalan life sciences and healthcare sector become the global, not only European, point of reference. New European policies should help it achieve this goal.

Introduction

A VISION 2025 FOR CATALONIA: SCALING-UP THE BIOREGION OF CATALONIA



Jordi Naval

CEO of Biocat

A VISION 2025 FOR CATALONIA: SCALING-UP THE BIOREGION OF CATALONIA

Biocat, The BioRegion of Catalonia Foundation, has been working over for the past 12 years to boost Catalonia's life sciences and healthcare ecosystem performance and help shape the future of the industry. We work together with the innovative and research communities from the biopharma, medtech and healthtech industries to improve the wellbeing of people around the world and foster the global competitiveness of local innovative industry.

This is an exciting time for Barcelona and Catalonia, with many promising evidences of recovery after years of crisis and uncertainty. The hard work put in by many stakeholders has given real momentum to Catalonia's life sciences and healthcare industries, and now we are thrilled anticipating a positive "perfect storm" of factors that will help transform Catalonia's BioRegion into a major innovation world player. We are seeing a positive evolution of this innovative ecosystem, scaling-up from its start-up stage to a fully deployed industry, showcasing an exponential growth and the potential for huge impact.

But, what is in the essence of an innovative ecosystem? What makes it thrive? Which are the key driving forces are critical to its evolution? We could outline some key factors: a sound system of research institutions, with a marked specialization in the life sciences; the deployment of a set of policies fostering excellence rolled out over the past 3 decades; a leveraging public investment in science, aligned with excellence policies and smart specialization strategies; local entrepreneurial and risk-taking cultures; a growing local and international investment industry; a pool of talent with expertise in all aspects of biopharma industry development; and finally, hospitals with the capacity to conduct clinical research to the highest standards.

Now, with the perspective that comes from having this evolution in mind, Biocat is drafting an ambitious Vision 2025, with Catalonia, and its capital Barcelona, ranking among the top 3 biomedical hubs in Europe. Our vision is a top destination for the sector to invest, thanks to its top universities, hospitals and research infrastructures, excellent science, breakthrough innovations, investment capabilities and great entrepreneurial and professional talent.

To achieve this Vision 2025, Biocat is putting in place actions to consolidate Catalonia's tremendous assets, boosting its amazing capacities to keep it on top in the global Life Sciences industry. Our strategy as a key innovation driver will be to significantly and effectively contribute to achieving a set of goals for 2025:

- Make the most of Catalonia's innovation capabilities, embracing exponential changes in technology to tackle some of the biggest healthcare challenges of our time, with a mission-driven approach.
- Align Catalonia's innovative ecosystem with the social impact core values embedded in the UN's 2030 Agenda and the EU's research and innovation policies.
- Boost the connection between our knowledge and innovation model, built on research excellence and entrepreneurial spirit, and the mid-sized and large pharma and life sciences companies based in Catalonia.
- Attract and retain global talent at all levels: scientific, entrepreneurial, investment, and management.
- Triple the current investment in life sciences and healthcare innovative start-ups and scale-ups, reaching over 500 M€ by 2025.
- Make effective the BioRegion of Catalonia's global contribution with 10 new and significant therapies developed in Catalonia by 2025.

The strategies to achieve these objectives might involve putting in place bold policies to ensure sustained and growing investment in cutting-edge science and a set of encouraging regulation reforms such as deployment of supportive tax stimuli to incentivize private investment in research and innovation.

From an internal perspective, further engagement of local mid-size and big pharma companies in innovation activities with local entrepreneurs and start-ups would lead to more start-ups becoming scale-ups companies, generating growth in investment, jobs and ultimately, solutions for patients and for the society. We can only do this effectively if we manage the life sciences ecosystem as an integrated community of science, health, economic development and social impact, with all public and private stakeholders working together.

Health innovation is a global activity, with increasing contributions and competition from all parts of the world, and particularly from the east and west coasts of the United States, the Asia-Pacific region and Europe. Catalonia should reveal itself as the outstanding hub that must be on the radar for investors and innovators from all over the globe.

The orientation to mission has to be central to our strategy: improving human health through innovation is a message that all the different interests and ideologies can share, and it is one that will help build the alliances of public and private stakeholders needed to drive change.

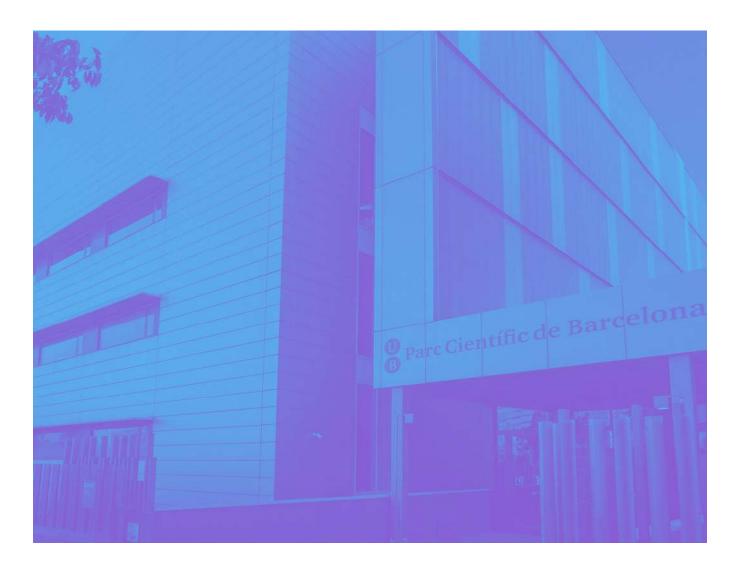
One central idea must permeate all levels of our dialogue with academia, entrepreneurs, investors, the administration, companies large and small, and society as a whole: a competitive Life Sciences and Healthcare ecosystem like the BioRegion provides good science and good business, occupies a position of global leadership, accelerates therapies that improve society's health, helps create jobs and fuels economic growth.

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Executive summary

SCALING-UP THE BIOREGION OF CATALONIA: KEY FINDINGS AND RECOMMENDATIONS



Scaling-up the BioRegion of Catalonia: key findings and recommendations

"Catalonia is one of the three most dynamic hubs in healthcare and life sciences worldwide", according to Joseph Damond¹, an experienced biotech industry executive with a sound international insight. Around 1,060 companies operate in the BioRegion of Catalonia (including biotech, pharma, medtech, healthtech, CROs, service and goods providers and distributors, as well as investing organizations). In addition to these are 89 research institutions (research centers, universities, university hospitals, large research infrastructures, technology centers and science and technology parks with life sciences and health activities), complemented with a network of healthcare agents providing diagnosis and treatments to patients.

The life sciences and healthcare sector in Catalonia generates €31,087 M per year and represents 7.2% of its Gross Domestic Product (GDP). In total, more than 223,000 people are employed by the sector, representing around 7% of the working population in Catalonia (2016).

Catalonia ranks top among Spain's autonomous communities in terms of internal expenditure on biotech R&D activities, reaching €454.7 M in 2015 (29.5% of Spain's total and higher than its GDP share, 20%). The increasing attractiveness of investing in BioRegion start-ups has resulted in a threefold increase in the period 2015-2017. compared to the previous period 2013-2015. This sound investment ecosystem is growing stronger with both local and international investors. In the 2015-2017 period, up to 214 investment operations took place, 24 of these involving international capital. These 24 operations accounted for €198.1 M, which is equivalent to almost 60% of all capital raised. Regarding pipeline progress, focusing for example on the therapeutics clinical pipeline, there are currently (2018) 18 drug therapies being developed by Catalan companies, 11 more than in 2013. In addition, three molecules are already in Phase III. The new therapies advancing to the market are also growing substantially in the medtech, diagnostics and healthtech areas.

The notable, even outstanding, increases in resources and outcomes are accompanied by a growing interest in Catalonia as "the next place to be". In fact, both the technology and the business hubs of global multinational firms have been setting up facilities at a good page.

Early in 2018, the Financial Times group recognized Catalonia as one of the best European regions for investment in 2018 and 2019. This

is an exciting time for Barcelona and Catalonia, with many promising signs of recovery after years of crisis and uncertainty. The hard work of many stakeholders has given real momentum to Catalonia's life sciences sector, and we are now anticipating a positive "perfect storm" of factors that will help transform the BioRegion of Catalonia into a major world player in innovation.

We are witnessing a rapid evolution of our innovation ecosystem, which is scaling-up from its start-up stage to a fully-deployed industry, displaying exponential growth and high impact potential. The current report explores the driving forces that have helped Catalonia to create such a thriving life sciences and healthcare ecosystem and it provides an in-depth analysis of its performance during the period 2015-2017.

CATALONIA, ONE OF EUROPE'S MAIN INNOVATION HUBS

In terms of GDP and population, we can compare Catalonia to European Union countries such as Sweden, Belgium, Denmark, Austria and Ireland. With a population similar to that of Austria and slightly higher than Denmark's, and a GDP similar to that of Finland and Denmark, this can be considered a natural group for this European region to belong to.

Barcelona is said to be one of the most connected ecosystems in the world². The convergence of strategies from the Government of Catalonia, Barcelona City Council, Mobile World Capital Barcelona Foundation and certain universities, research and technology centers and companies, is already helping to create a smart environment. It has become the new "place to be" in Europe: in fact, in the first semester of 2018, 17 multinationals announced new set ups in the city or in the surrounding area.

RESEARCH EXCELLENCE

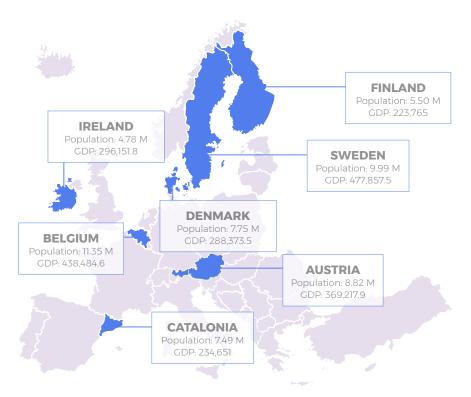
For 30 years, Catalonia's successive governments have been investing in higher education and scientific excellence, with specific programs designed to attract top-level researchers in all disciplines³, and funding topnotch universities and research institutions⁴. In fact, the real drivers of this success are

Catalonia's universities, research centers and large R&D infrastructures, along with a set of policies focused on excellence that provide the institutions with the flexibility and autonomy they need to perform their activities.

As a result, the number of publications in the biomedical arena has nearly quadrupled in Catalonia over the past 20 years, and one out of six (16.5%) biomedical publications signed by researchers in the BioRegion are among the most cited documents in the world, tripling the percentage of publications of excellence expected as a result of its volume of production.

Some of the BioRegion's indicators of research success even outperform those of

MAP 1. Map of Europe highlighting the group of countries used in this report for comparison with Catalonia



Sources: Eurostat and Idescat (January 2018). Population in million people. GDP in M€.

FIGURE 1. Some major companies setting up new innovation centers in Catalonia in 2018



other European companies. The total number of ERC grants received in Catalonia since 2007 is equal to that of Belgium and Sweden and higher to that of Austria. The BioRegion's research productivity indicators are also comparable to the indicators of these countries.

Catalonia's research organizations and firms are also leaders in attracting H2020 funds. Despite representing only 1.2% of the European Research Area population, Catalonia has already attracted 4.6% of H2020 FET Flagship funds⁵. Regarding the "SME Instrument", 176 small and medium-sized Catalan firms have secured €72.7 M for 189 innovation projects, more than any other country in this group of European economies used for comparison.

TABLE 1. EU contribution in €M to different countries.

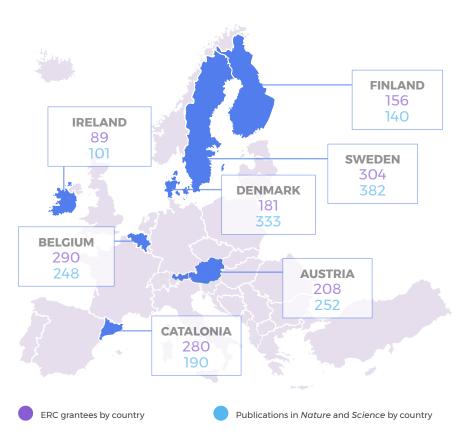
Country	H2020 funds attracted
Belgium	1,555.5
Sweden	1,135.5
Austria	925.8
Catalonia	830.0
Denmark	821.7
Finland	723.7
Ireland	566.1

Source: CDTI and Cordis 2018.6

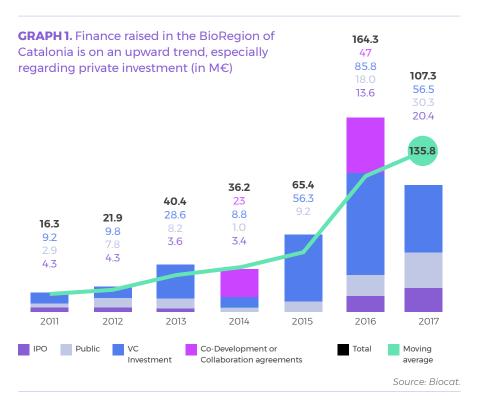
A GROWING INTERNATIONAL INVESTMENT ECOSYSTEM

Since 2008, at the beginning of the crisis, investment in Catalonia's life sciences and healthcare companies has multiplied by 12. Specifically, in the 2015-2017 period, BioRegion start-ups attracted investments of almost €340 M, more than threefold the amount reached in the previous two-year period (2013-2015)7.

MAP 2. ERC grantees and publications in Nature and Science by country

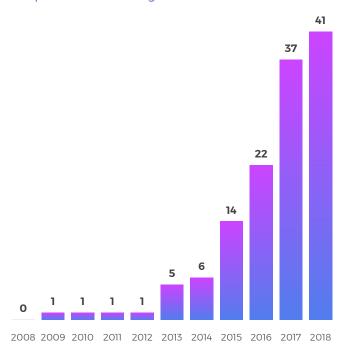


Sources: AGAUR (2007-March 2018); Web of Science (2013-2017)



The investment ecosystem is solid and it is becoming stronger. In addition to local, specialized investors like Ysios Capital, Caixa Capital Risk, HealthEquity, Inveready and Alta Life Sciences operating in Catalonia, the BioRegion is seeing a spectacular growth in international investors participating in life sciences and healthcare companies. In the space of 10 years, their presence has increased from 0 to more than 40. In the past four years alone, investors have increased from 6 (2014) to 41 (June 2018) (Graph 2). International investors participating in companies in the BioRegion come from 16 different countries. Almost 50% of these are from the US.

GRAPH 2. International investors participating in companies in the BioRegion of Catalonia



Source: Biocat (June 2018).

BioRegion firms can boast some success stories in terms of raising funds, in both the €11-50 M and the €1-10 M range. In the 2015-2017 period alone, more than 214 investment operations took place. Despite only 11% of these operations corresponding to international capital, 60% (€198.1 M) of the total investment was obtained. This international funding was mainly focused in the biotech (€118.4 M), techmed (€64.1 M) and healthtech (€15.6 M) industries.

MOVING CUTTING-EDGE SCIENCE TOWARDS PATIENTS

There are currently (2018) there are 18 drug therapies by Catalan companies in the pipeline, up from only seven in 2013. This shows that BioRegion is progressing steadily from a cutting-edge science system to the business landscape, advancing therapies to clinical development. The next obvious step is for these therapies to enter into late clinical development and to reach the market over the

FIGURE 2. Success stories in the BioRegion of Catalonia in terms of funds raised

	1-10M€	11-50M€
2015	ClinicPoint	Minoryx Therapeutics
	Galgo Medical	Oryzon Genomics
	Genmedica Therapeutics	
	Greenaltech	
	iSalud	
	Medtep	
	Psious	
	Top Doctors	
	Transplant Biomedicals	
2016	Albajuna Therapeutics	AB-Biotics
	Bioprognos	Aelix Therapeutics
	Cebiotex	Oryzon Genomics
	Cuantum Medical Cosmetics	STAT-Dx
	IDP Pharma	
	Inbiomotion	
	Iproteos	
	Leukos Biotech	
	Pangaea Oncology	
	Peptomyc	
	Promofarma	
	Thrombotargets Europe	
2017	Bionure	Anaconda Biomed
	Bwom Technologies	Oryzon Genomics
	Glycardial Diagnostics	
	Devicare	
	iMicroQ	
	Inkemia IUCT Group	
	Linkcare	
	QMENTA	
	Peptomyc	
	SOM Biotech	
	Transmural Biotech	
	Top Doctors	
	Transplant Biomedicals	
2018	Ahead Therapeutics	Abac Therapeutics
	Bionure	
	Elma Care	
	Mediquo	
	ProteoDesign	

Source: Biocat (Updated to May 2018)

ORPHAN & RARE DERMATOLOGY PHASE I DISEASES PHASE II **VACCINES &** CARDIOVASCULAR INFECTIOUS DISEASES SP14019-F01 AND BLOOD • HTI Aelix Spherium Biomed Therapeutics MIN-102 Minoryx Therapeutics RUTI Archivel PHASE /III Ox-01 FreeOx Biotech Farma TT-173 ABTL0812 ORY-1001 Thrombotargets Europe Ability Oryzon Genomics Pharma **DIABETES &** • AX-024 Mucomel ONCOLOGY INFLAMMATION Spherium Biomed AVX012 Biopharma Avizorex • ORY-2001 • SP12006 Pharma Oryzon Spherium Biomed JAN12006-01 Spherium Biomed BN201 Bionure SOM0226 SP15016 Spherium Biomed SOM Biotech OPHTALMOLOGY MUSCOSKELETAL, PAIN. **NEPHROLOGY** CENTRAL NERVOUS SYSTEM

FIGURE 3. Pipeline of biotechnology companies of the BioRegion of Catalonia (therapeutics)

Source: Biocat's Directory and clinicaltrials.gov (updated to June 2018)

coming years. If we focus on medical devices, diagnostics and other health technologies, the market is also progressing at the same level, but it is slightly more difficult to quantify as to what extent.

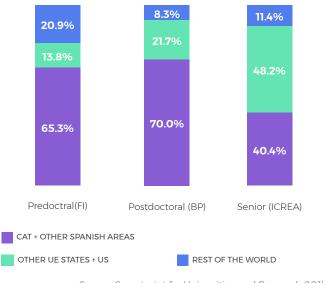
ATTRACTIVENESS TO TALENT

International competition and an increased focus on research and innovation as the key to economic and technological leadership have made talent a primary asset for countries and industries.

Catalonia attracts professionals from around the world to a research, development and innovation system recognized as a worldwide benchmark of excellence in research in areas such as biomedicine. photonics, energy, economy and nanotechnology.

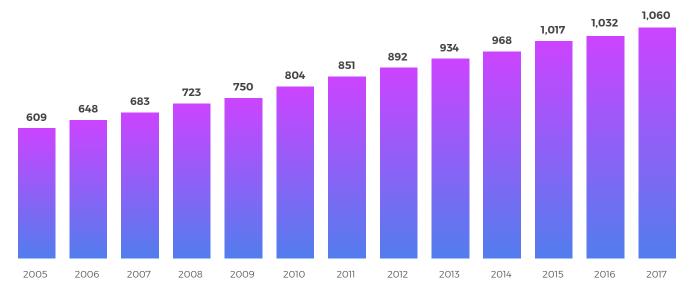
Since 2001, ICREA (the Catalan Institution for Research and Advanced Studies) has been hiring top-notch scientists and academics to compete with other research systems on a similar footing, which has contributed to a large extent to boosting the excellence and competitiveness of Catalonia's research system. The program is 100% funded by the Catalan Government. There are currently 254 ICREA researchers from 26 different countries, 29% of them work-

GRAPH 3. Origin of researchers working in the BioRegion of Catalonia



Source: Secretariat for Universities and Research 2017.

GRAPH 4. Yearly evolution in companies in the BioRegion of Catalonia (2005-2017)



Source: Biocat and Crunchbase.

ing in life sciences. In 2017, ICREA researchers attracted €90 M in competitive funds, 40% in life sciences. Since the beginning of the program, ICREA researchers have created 24 spin-offs (5 of them in 2017) which have raised €90 M. Most ICREA spin-offs (20) work in life sciences.

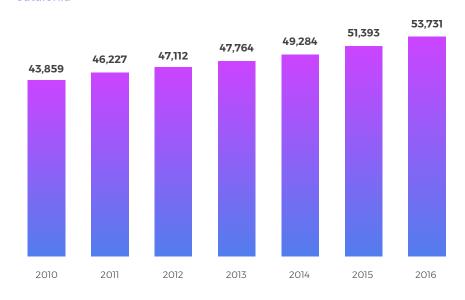
A LAND OF ENTREPRENEURS

According to the recent Global Entrepreneur Monitor report⁸, entrepreneurial activity increased over 8% in Catalonia in 2017, above the European average (7.8%). The company creation rate is about one new company per week. The main source of this activity within the BioRegion are spin-offs from top research institutions (one out of five new companies created since 2005 have their origin in those top research institutions).

There are 1,060 companies operating in the life sciences and healthcare industries in Catalonia. The 2016 turnover of the BioRegion companies was 8% of Catalonia's GDP (€17,802 M), with a 2.4% average annual growth between 2000 and 2016.

According to data provided by the industry's employers' organizations, Catalonia is the leading Spanish autonomous community in pharma companies (51.2%)9.

GRAPH 5. Yearly evolution of employees in companies in the BioRegion of Catalonia



Sources: Biocat and SABI.

According to data from the Asebio 2017 Report, Catalonia accounts for more than 40% of the total investment raised by companies in the biotechnology sector in Spain (58.9 million euros out of a total of 145.8) including private capital injections, injection of funding from listed corporations, ENISA loans and other regional corporations. It should be noted, however, that Asebio

only collects data on some of the companies that use biotechnology, not the total number of companies that operate in the BioRegion and who also work in the field of medical and healthtech technologies. For this reason, the total investment figures stated by Asebio are significantly lower than those included in this Biocat report. In addition, 11 of the 20 companies chosen

by Asebio to feature in their successful case studies report are from the BioRegion.

Another piece of data that helps us to visualize the real weight of the BioRegion in health innovation in Spain is the Catalan presence in national competitive grant calls.

For example, BioRegion companies have received 11 of the 15 Head-start Funding grants awarded by EIT Health Spain in 2018, obtaining up to 50,000 euros to accelerate their time-to-market and increase their chances of attracting private investors. With regard to the research results transfer program Caixalmpulse, 54 of the 78 projects selected since the beginning of the program are from the BioRegion. Another state call recognized in the sector is that of the Botín Foundation, which also reflects the weight of Catalonia: 41% of research groups funded by the life sciences program and 33% of projects.

Catalonia also relies on a wide network of CMOs, CROs, hospitals for trials, consultants, regulatory advisors, market access specialists, technology, etc. Any company can execute operations at the top level just by using local providers and professionals.

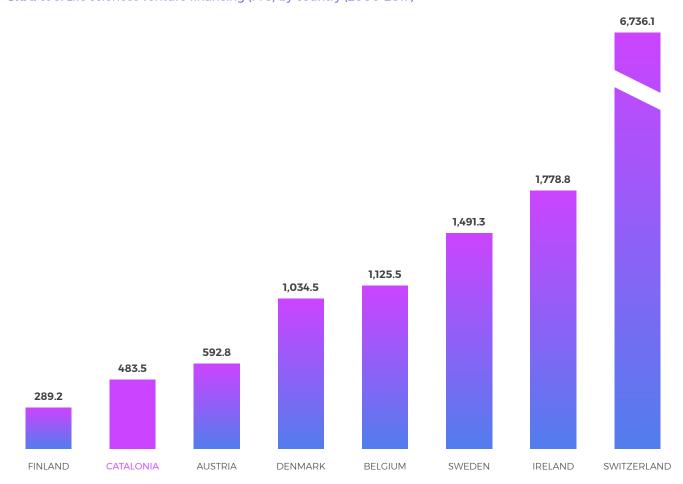
This is in fact one of the main assets and challenges of a thriving ecosystem: availability of investable teams. Although the current proportion of first-timers is higher, and seasoned teams are still scarce, the capabilities are evolving rapidly because there is a large base of professionals that are able to adapt to the start-up rules, and also because it is very easy to import talent from abroad and establish it in Barcelona.

BUILDING THE FUTURE BY LEVERAGING THE BIOREGION OF CATALONIA'S POTENTIAL

Catalonia's potential and its scientific quality, which are similar or even higher than comparable European countries, offer untapped opportunities for investment. This is a huge gap to be filled during the coming years.

If we project a 20-25% CAGR (Compound Annual Growth Rate) over the average investment rate in past years, we can predict reaching €500+ M in private investment in life sciences by 2025. Catalonia can multiply in seven years the total investment, investors and its position as a life sciences hub with outstanding figures in Europe.

GRAPH 6. Life sciences venture financing (M€) by country (2000-2017)



Sources: Crunchbase and Biocat.

Given the evolution of the sector, in terms of social impact, Biocat expects at least 10 advanced products and technologies to reach patients by 2025.

TABLE 2. Catalonia can multiply in seven years the total investment, investors and its position as a life sciences hub with outstanding figures in Europe

	CURRENT	2025
Yearly investment in innovative emergent life sciences companies	€130M/year	€500M/year
International investors investing in BioRegion startups	41	+100
Products in clinical development (therapies)	18	50
Catalonia: most innovative life sciences hub in Europe	#5	#3
		Source: Biocat.

RECOMMENDATIONS

The following section reviews the BioRegion's assets and shortcomings both by main development areas and by key underlying enablers, in order to gather a few recommendations addressed to the different stakeholders

CAPABILITIES, SHORTCOMINGS AND RECOMMENDATIONS, BY DEVELOPMENT AREA

Regarding the BioRegion's knowledge system, professional networks and healthcare providers' assets and immediate needs, the excellent scientists and solid research ecosystem require clear stimuli to foster tech transfer, along with a systematic approach in order to translate papers into solutions for society. The proof of concept testing area, based on specialized research capabilities and local expertise, is attracting increasing interest from investors. However, we lack market perspective, a connected and comprehensive drug discovery platform and public and private funds to be able to prepare a preclinical regulatory package for an area that is currently based on a solid network of experts and providers and knowledge from local pharmas but which needs early-stage financing. With regard to clinical development, the BioRegion has professional expertise, a network of top-level hospitals and specialized CROs, but there is still too much bureaucracy and absence of integrated business development of clinical trial capabilities. Finally, Catalonia has an integrated health system (CatSalut) that would favor market access, but which lacks innovation alignment from within the system.

Consequently, our recommendations regarding the different development areas are:

- Improve tech transfer incentives for researchers
- Foster a closer relationship between scientists, pharma and investors to better define proof of concept initiatives
- Strengthen local drug discovery platforms
- Provide specific public funding in this stage; for example, by matching them with private investment funds
- Further involve the CatSalut health system in streamlining clinical trial capabilities
- Improve the innovative capabilities of the Catalan health system
- Implement innovative public procurement programs

CAPABILITIES, SHORTCOMINGS AND RECOMMENDATIONS, BY KEY UNDERLYING ENABLERS

Targeting the key enablers, the BioRegion of Catalonia has an excellent network of academic TTOs who foster knowledge transfer despite being understaffed, underfinanced and who are not coordinated or working together at country level. We also have a network of professionals and providers from the local pharma industry but do not have enough C-level management teams with years of experience in founding and scaling-up start-ups and serial entrepreneurs. We do have local mid pharmas and some big pharma headquarters but the three levels are not well connected (start-ups, local mid pharmas, big international pharmas), nor do we have midtier innovative companies. On the fiscal side we have clumsy fiscal incentives and lack the necessary culture whereby tax incentives are considered effective mechanisms for promoting R&D+i. An entrepreneurial culture, business angels, local VCs and new entrant international VCs are not enough if we do not have an organized and

comprehensive public view of the relevance of private investment in promoting innovation in health.

Consequently, our recommendations for the ecosystem's different key stakeholders are:

- Better funding for TTOs, mainly by channeling PoC funding through them
- · Promote coordinating structures beyond the TTO level
- · Attract, retain, train and mentor C-level talent
- Encourage local pharmas to capture innovation from local companies
- Encourage big pharmas to scout for innovation in Catalonia
- Promote partnerships between established pharma companies and innovative start-ups
- Establish an R&D tax credit system
- Develop enterprise investment schemes for business angels and investors
- Attract capital through tax stimuli
- Commit public funding through smart public-private instruments

RECOMMENDATIONS FOR PUBLIC STAKEHOLDERS

From a public action perspective, a healthy ecosystem should rely on natural selection of the best initiatives and should not be directed top down. However, there are several ideas that should permeate public actions in order to contribute to the success of the ecosystem. We outline some of them here:

- Promote and defend basic science: all major innovations can be traced to specific scientists working in a free, creative scientific environment in which they can develop their ideas and embrace risk. The market should not direct basic research, scientists should first of all be free to pursue their curiosity.
- Leverage existing facilities: Catalonia has built specific facilities and platforms that can be scaled-up to become global innovation centers. Examples include the Banc de Sang i de Teixits and associated advanced cell therapy and production platforms.
- Take advantage of the high quality and centralization of the Catalan health system by promoting an open data sharing scheme that, while keeping personal patient data anonymized, can pool current health and future omics data into an open access data lake that can be analyzed by scientists and companies all over the world. This invaluable resource of data-driven research should evolve into a powerful tool to improve citizens' health, and the Government should foster an alliance between society, industry, scientists and the health care system.
- Support for entrepreneur training at all levels, incentivizing varied careers and migration of academic scientists into industry and back to academia to increase influx of talented scientists and entrepreneurs in the public and private sectors.
- Promote smart-investment initiatives, combining public funding and stimuli in simple ways such as (1) funds to finance smart proof of concept tests; (2) funds to match existing private investment funds, and (3) tax stimuli for business angels, entrepreneurs and investors

Notes

- ¹ Executive Vice President,for International Affairs,at the Biotechnology Innovation Organization (BIO).
- Startup Ecosystem Report, https://startupgenome.com/ barcelona-report/
- ³ ICREA Program, https://www.icrea.cat/
- ⁴ CERCA centers, http://cerca.cat/en/
- ⁵ FET Flagships are visionary, science-driven, large-scale research initiatives addressing Scientific and Technological (S&T) grand challenges. They are expected to run for approximately 10 years have a total budget of around 1 billion euros and bring together a large number of research organisations, including academia, large industry and SMEs. http://ec.europa.eu/programmes/horizon2020/en/h2020-section/fet-flagships.
- https://webgate.ec.europa.eu/dashboard/sense/app/93297a69-09fd-4ef5-889f-b83c4e21d33e/sheet/PbZJnb/state/analysis
- 7 The reason for this two-year period division is due to the Biocat report methodology. These are the periods covered by each edition.
- 8 https://www.gemconsortium.org/
- ⁹ Farmaindustria (Spanish Association of Pharma Companies)

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Innovation performance and potential of the BioRegion of Catalonia



Innovation performance and potential of the BioRegion of Catalonia

DRIVING FORCES

"Catalonia is one of the three most dynamic hubs in healthcare and life sciences worldwide", says Joseph Damond¹o, an experienced biotech industry executive, highlighting the importance of Catalonia as an attractive international hub for entrepreneurs and investors. What are the driving forces that have helped Catalonia build a thriving life sciences ecosystem? As Karin Ezbiansky Pavese, vice president of Innovation & Sustainability at the New York Academy of Sciences says, "many people think that investing money in scientific research guarantees economic growth, but investment in research is not enough to stay competitive. You must have the infrastructure in place to support these research investments and maximize their impact." To the tangible assets, we can add intangible aspects derived from the ecosystem's networks and culture that go beyond the most obvious elements.

To analyze the current situation of the BioRegion and the future we want to achieve, we will consider the following aspects as the main driving forces:

- Country model
- Scientific excellence and innovative potential
- Adaptability to catch up with opportunities
- Investment capabilities
- Pipeline progress
- Attractiveness to talent

COUNTRY MODEL

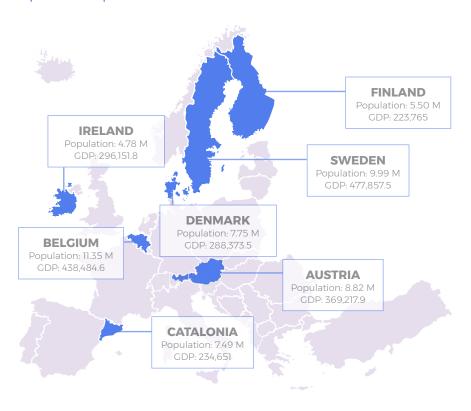
Recent analysis by international institutions such as the OECD, IMF and certain think tanks, argue the notion that some countries are models for others to follow¹¹. In terms of population and GDP, Catalonia could be placed in a group –as suggested by the

authors of the present report for comparative purposes- composed of European Union countries such as Sweden, Belgium, Denmark, Finland, Austria and Ireland. Two characteristics shared by all of these countries, including Catalonia, are their small populations and a GDP per capita above the EU average.

Most of the countries in this group share additional positive characteristics. All of them rank among the 30 richest countries in the world¹², a list dominated by some of the smallest countries. Almost all of them are among the top 10 "most inclusive advanced economies", according to a new metric¹³ recently introduced by the World Economic Forum that identifies 15 areas of structural economic policy and institutional strength that can have a wider impact on a country's competitiveness.

The countries in our comparison group also rank among the top 10 European countries in the Global Human Development Index, which combines Gross National Income (the total domestic and foreign output)¹⁴ and education and health metrics. These economies are also classified either as strong innovators (Ireland, Belgium and

MAP 3. Map of Europe highlighting the group of countries used in this report for comparison with Catalonia



Sources: Eurostat and Idescat (January 2018).

TABLE 3. Most inclusive advanced economies

Country	Rank
Norway	1
Iceland	2
Luxembourg	3
Switzerland	4
Denmark	5
Sweden	6
Netherlands	7
Ireland	8
Australia	9
Austria	10

Source: World Economic Forum Report 2018.

Austria) or innovator leaders (Sweden, Denmark and Finland) in the 2018 edition of the European Innovation Scoreboard¹⁵. In the regional counterpart of this report (RIS 2017)¹⁶. Catalonia appears as moderate innovator but is the top-ranking region in the Moderate Innovators group, with a performance of 88.5% of the EU average. According to a 2014 report from the Credit Suisse Research Institute¹⁷, small countries make up over half of the world's top 30 countries. This report includes Catalonia in its HDI league table, and ranks it among the top 10 in the EU. Almost all members of the group depicted in Map 1 are found in this top 10 list. Including Catalonia in this group in terms of comparison may seem quite bold, but with a population similar to Austria's and slightly higher than Denmark's, and a GDP similar to Finland's and Denmark's, it can be considered a natural group for this European region to belong to.

SCIENTIFIC EXCELLENCE AND INNOVATIVE POTENTIAL

For 30 years, Catalonia's successive governments have been investing in higher education and scientific excellence, with specific programs designed to attract top-level researchers in all disciplines¹⁸, and funding top-notch universities and research institutions¹⁹. Catalonia is currently one of the leading research hubs in Europe, after impressively managing to catch up with their performance in research, technology and innovation.

If we take a closer look at Catalonia's performance in research and technology, it becomes evident that some of our indicators of success even outperform those of other successful European economies used for comparison. Catalonia leads this group in terms of the prestigious European Research Council's grants per population, being one of the largest ERC recipients per million inhabitants in the EU, second only to the Netherlands. The total number of ERC

TABLE 4. EU contribution in M€ to different countries

Country	H2020 funds attracted
Belgium	1,555.5
Sweden	1,135.5
Austria	925.8
Catalonia	830.0
Denmark	821.7
Finland	723.7
Ireland	566.1

Source: CDTI and Cordis 2018.20

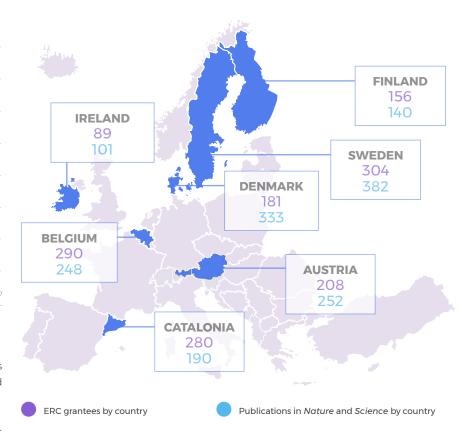
grants received in Catalonia since 2007 is equal to that of Belgium and Sweden and higher than that of Austria.

Among these outputs, if we consider research productivity as an acceptable proxy of the scientific potential of a country, we can see that our indicators are also comparable to the European economies with which we measure ourselves up. The number of publications in the biomedical arena has almost quadrupled in Catalonia in 20 years, and one out of six (16.5%) biomedical publications signed by researchers in the BioRegion are among the most cited documents in the world, tripling the percentage of publications of excellence expected as a result of its volume of production.

Catalonia's research organizations and firms are also leaders in attracting H2020 funds. Updated Cordis data place Catalonia right in the middle of this group of countries, above Denmark, Finland and Ireland in absolute figures (Table 4).

In fact, the sciences policies that model Catalonia's R&D system are designed to boost competitive funds and attract excellent talent. With the inputs-outputs-outcomes-impact logic model, and by providing top-notch institutions with excellent

MAP 4. ERC grantees and publications in Nature and Science by country



Sources: AGAUR (2007-March 2018); Web of Science (2013-2017)

human resources, more funding can be obtained through competitive calls. These ingredients are necessary for generating outstanding outputs and outcomes, which is reflected in the following figures: despite representing only 1.2% of the population of the European Research Area, Catalonia has already attracted 4.6% of H2020 FET Flagship funds²¹. Several of Catalonia's academic and research institutions are at the core of the two FET Flagship projects launched to date by the EC ("Graphene" and the "Human Brain Project"). If successful in the 2018 call, two more FET Flagships. "Personalised Health Care" and "Quantum Technologies", will be developed under the next framework program, Horizon Europe, which also has strong participation from Catalonia

The European funding provides the mechanism to face the next challenges. Catalonia is already in a good position, as prov-

en by SME Instrument, one of the main research and technology tools for driving impact, part of the European Innovation Council's H2020 program. Catalonia is the most successful European region in attracting resources for small and medium-sized businesses innovation projects. Specifically, 176 Catalan SMEs have obtained €72.7 M for the launch of 189 innovation projects, more than any other country in the European economies group used for comparison purposes in this report (Map 5).

Regarding the Spanish context, a piece of data that helps us to visualize the real weight of the BioRegion in health innovation in Spain is the Catalan presence in national competitive grant calls. For example, BioRegion companies have received 11 of the 15 Headstart Funding grants awarded by EIT Health Spain in 2018, obtaining up to 50,000 euros to accelerate their time-

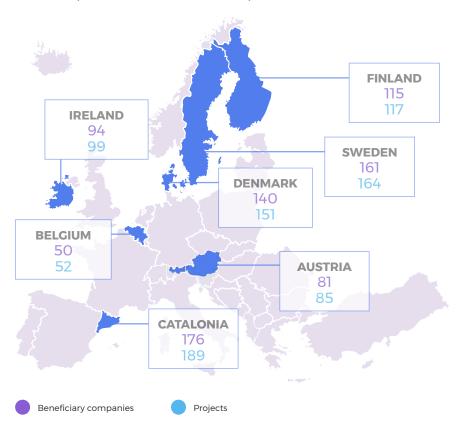
to-market and increase their chances of attracting private investors. With regard to the research results transfer program Caixalmpulse, 54 of the 78 projects selected since the beginning of the program are from the BioRegion. Another state call recognized in the sector is that of the Botín Foundation, which also reflects the weight of Catalonia: 41% of research groups funded by the life sciences program and 33% of projects.

Several institutions are promoting innovation by encouraging the formation of start-ups. We can also see that, having the same scientific level, some research centers and universities are already advancing at a faster pace in terms of professional investment raised for their spin-off companies. Universities create more spin-offs than any other category of entities, but those created by health research institutes tend to be more attractive to investors.

ADAPTABILITY TO CATCH UP WITH OPPORTUNITIES

An innovative ecosystem is a relational network in which talent and information flow through a sustained collaborative system. Innovative life sciences ecosystems need, therefore, to break down barriers between

MAP 5. European Innovation Council SME Instrument figures for the group of Small European Economies used for comparison with Catalonia



Catalonia leads the indicator in terms of number of beneficiaries and number of projects.

Source: EIC SME Instrument data hub.

TABLE 5. Top research organizations based on funds raised by their spin-offs

Research entities	Finance raised by spin-off companies (M€)
Vall d'Hebron (VHIR, VHIO)	54.5
Universitat de Barcelona (UB)*	54.4
Institut Químic de Sarrià (IQS)	34.8
Universitat Autònoma de Barcelona (UAB)	29.2
Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)	21.3
Institut de Recerca de la Sida (IrsiCaixa)	15.3
Hospital Clínic de Barcelona	14.6
Institut de Recerca Biomèdica de Barcelona (IRB Barcelona)	10.8
Institut de Biologia Molecular de Barcelona (IBMB)	9.4
Institut de Recerca Contra la Leucèmia Josep Carreras (IJC)	3.8
Universitat Pompeu Fabra (UPF)	3.8
Universitat Politècnica de Catalunya (UPC)	3.7
Universitat Rovira i Virgili (URV)	3
Hospital de Sant Joan de Déu (HSJD)	2.6
Universitat de Girona (UdG)	2.5

*Except Oryzon Genomics - Every spin-off can be accounted for more than one research entity

Source: Biocat.

FIGURE 4. The NEXTHEALTH Community, coordinated by Biocat, includes five projects led by the University of Barcelona, Hospital Sant Joan de Déu, Eurecat, Institut Universitari de Ciència i Tecnologia and Institut Guttmann





Accelerator to develop advanced therapies in Catalonia

Platform to develop new therapeutic strategies for rare diseases

HL 4.0

Liquid Hospital 4.0



Personalized care for chronic patients in a digital healthcare framework



New technologies for innovation in rehabilitation and cognitive stimulation

organizations and individuals, allowing for collaboration across different disciplines and sectors. Taking advantage of disruptive technologies, changing geopolitical scenarios (tax reform in the United States, Brexit in the United Kingdom, the European Union redefining economic and monetary issues) and demographic and economic changes create opportunities and increase the need for diversified talent with suitable skills. Innovative life sciences ecosystems must meet these uncertainty-driven opportunities and challenges by following an adaptive strategy and embracing new rules. Catalonia has the elements necessary to catch up with these opportunities.

NEXTHEALTH, a RIS3CAT Community (practical application of Catalonia's Smart Specialization Strategy) coordinated by Biocat, brings together 22 companies from different sectors and 35 stakeholders from the research, development and innovation system to boost multidisciplinary solutions for the coming challenges in health. This kind of initiative is intended to promote new collaborative models and business opportunities. Other communities selected for funding in the 2018 Government call include "Utilities 4:0", "Industries of the future" and "3D printing", all of which have an expected impact on the health sector.

These will take place in an environment that is said to be one of the most connected ecosystems in the world²², a key determinant of ecosystem performance. The European EIT Health project is an example of the connectivity of Catalonia's life sciences ecosystem. The consortium, with nodes in Barcelona (Spain), Paris (France), London (United Kingdom), Rotterdam (Benelux), Stockholm (Sweden/Denmark) and Heidelberg (Germany), comprises more than 50 core partners and 90 associated partners from 14 countries in the European Union.

The technological transformation of Catalonia includes converting Catalonia and Barcelona into a European digital innovation hub within the 5G field. The convergence of strategies from the Government of Catalonia, Barcelona City Council, Mobile World Capital Barcelona Foundation, and certain companies, universities, research and technology centers is already helping to create a smart environment that will be available to the general public and leading economic sectors, such as life sciences. Several global companies such as Facebook, Microsoft, Siemens, Nestle and many others are establishing their innovation centers here. Among the driving forces indicated in the publication "Expansión" is the dynamism of the entrepreneurial ecosystem²³.

INVESTMENT CAPABILITIES

The investment ecosystem is solid and it is becoming stronger. In the period 2016-2017, Catalonia attracted €270 M in investment in biotech companies, with an average of €135 M per year.

TABLE 6. Barcelona is increasingly attracting the technological centers of large firms

The table includes new tech centers that have existing operations, or are starting new operations, between 2016 and 2018.

Company	Facility	Location	Team
Roche	Diabetes Care Digital Hub	Sant Cugat del Vallès 530	
Amazon	Seller Support Hub + Machine Learning Center of Excellence	Barcelona	500
Facebook	Competence Call Center	Barcelona	500
Adesso	1st office in Spain	Sant Cugat del Vallès	300
Zurich	Big Data World Center	Barcelona	200
Allianz	Technology Center and new ICT Hub	Barcelona	150
ThoughtWorks	Software development	Barcelona	125
Nestlé	Global Digital Hub	Esplugues	100
Zeptolab	Videogames	Barcelona	100
N26 (Mobile Bank)	Digital Bank Tech Hub	Barcelona	100
Asics	Innovation Center	Barcelona	70
IGG	European operations headquarters	Barcelona	60
Microsoft	Design Center and Quantum Lab	Barcelona	60
Siemens	New Digital Innovation Center	Cornellà	50
Deloitte	Cibersecurity Center	Barcelona	50
Nestlé Purina	Hub digital Purina Studios	Esplugues	40
Visa Global Payments, Samsung, Arval, CaixaBank	Payment Digitalization Methods	Barcelona	15
Moodle	European Operations Headquarters	Barcelona	10
Satellogic	European Headquarters	Barcelona	10
GFT	Cloud Data	Sant Cugat del Vallès	10
International Advanced Manufacturing 3D Hub	3D Printing Tech Center	Barcelona	
King (Candy Crush)	Southern European Headquarters	Barcelona	
Lidl	Center of Excellence	Barcelona	
N26 (Mobile Bank)	2nd European office	Barcelona	
Oracle	New Development Center Oracle NetSuite	Barcelona	
Scoot	1st office outside US	Barcelona	
Urgo Medical	Southern European Hub	Barcelona	
Nestlé	Global IT	Esplugues	
Dynatrace	R&D Lab	Barcelona	
Cisco	IoT and Smart Cities solutions	Barcelona	

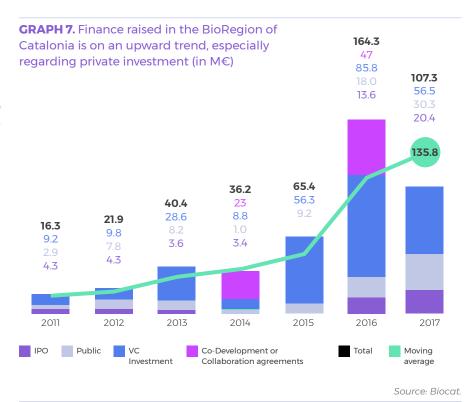
Font: Biocat.

Venture capital firms are the main investors in product development companies. Besides growth in private venture capital (VC) investment, we should point out that IPO funding (mostly Mercado Alternativo Bursatil) is also becoming a main source of private financing for companies, with other sources of funding being public debt and institutional investors, as well as industrial partners: 55% of pharmaceutical companies have stakes in biotechnology companies²⁴.

The progression to the public markets shows a sector that is maturing as companies move through the funding cycle. According to a 2018 European Investment Bank Working Paper²⁵ on the access to finance and innovative activity of EU firms, the increased access to a diversified pool of funding options is critical for innovation.

The ecosystem has reached a critical tipping point whereby good projects can have reasonable access to professional funds. The investment capabilities are solid and are growing stronger.

In addition to local, specialized investors like Ysios Capital, Caixa Capital Risk, Heal-thEquity, Inveready and Alta Life Sciences



operating in Catalonia (Table 7), we are seeing a spectacular growth of international investors participating in life sciences and healthcare companies. Over the past 10

years their presence has increased from 0 to more than 40, specifically in the past 4 years, increasing from 6 (2014) to 41 (June 2018) (Graph 8).

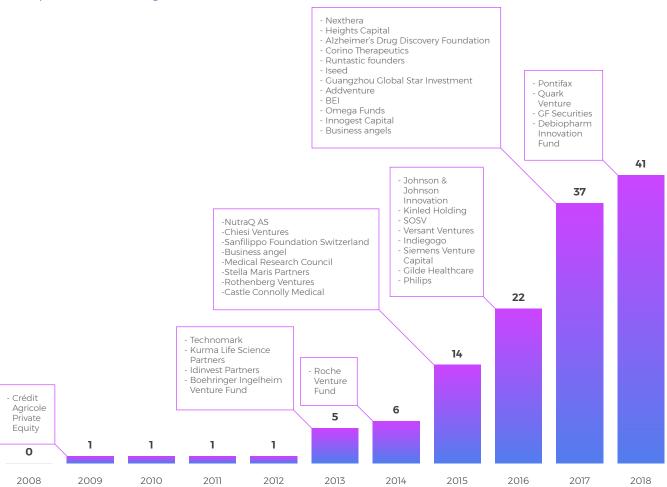
TABLE 7. The total local private funds dedicated to life sciences available in the BioRegion of Catalonia amounts to €527 M

Origin	VC	Fund	M€	Туре	Year
CAT	Inkemia	Fondo Capital Conocimiento	4	Seed	2011
CAT	Inveready	Inveready Innvierte Biotech II	17	Start-up	2013
CAT	Healthequity	Healthequity	11	Start-up	2013
CAT	Caixa Capital Risc	Caixa Innvierte BioMed II	46.5	Start-up	2014
CAT	Ysios Capital	Ysios BioFund II Innvierte	126	Start-up	2014
CAT	Caixa Capital Risc	Caixa Innvierte Start	21.5	Seed	2016
ES	Columbus VP**	Columbus Life Science	50*	Seed	2016
CAT	Alta Life Sciences	Alta Life Sciences Spain I	125*	Start-up	2017
CAT	Inkemia	InKemia Fond-ICO Global	10	Seed	2017
ES	Uninvest**	Uninvest Tech Transfer III	31*	Early	2018
CAT	Asabys Partners	Sabadell Asabys Health Innovation Fund	60*	Early	2018
CAT	Inveready	Inveready Innvierte Biotech III	25*	Start-up	2018
			Total: 527		

*Expected **Spain

Source: Biocat.



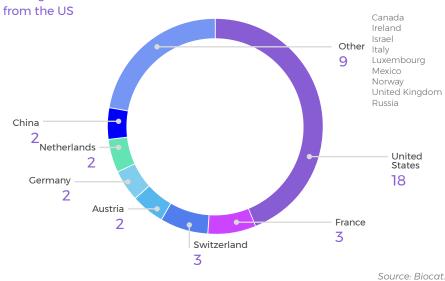


Source: Biocat (June 2018).

These, together with larger investment rounds, have been the main trends observed in the last few years. Investment in BioRegion firms has resulted in some success stories in terms of funds raised, both in the €11-25 M and the €1-10 M range. In the top range, from the Oryzon and Minoryx investment agreements in 2015 to the latest one, Abac Therapeutics, in 2018, a total of 10 investment deals have been closed during this three-year period. And in the bottom range, 45 investment deals involving 40 companies have been closed. We are also starting to see the relevant exits one expects to see in an expanding environment, such as the acquisition of STAT-DX by Qiagen and the sale of Advance Medical.

Venture capital raised by the BioRegion's biotech companies in 2017 (€57 M) may be

GRAPH 9. International investors participating in companies in the BioRegion of Catalonia come from 16 different countries. Almost 50% are



far from the figures of other European countries, including some of the countries in our "comparison group", such as Ireland (Map 6 and Graph 10). However, Catalonia is starting to appear on the global map of places for investing in biomedical innovation. And our figures show the high potential for growth and the attractive investment opportunities that are there for the taking.

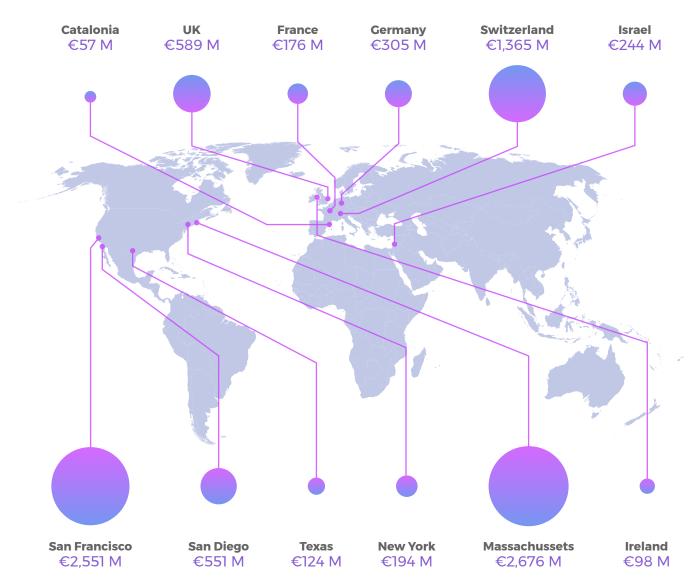
PIPELINE PROGRESS

The financial aspects are only one side of the life sciences innovation endeavor. As we've already seen, two major drivers are transforming the life sciences sector: embracing new technologies and a patient-centric culture. We will now focus on the emotional and transcendental driver for having a meaningful impact on patients' lives.

The question immediately rises: how is Catalonia performing in terms of advancing significant treatments for patients? We can see that we are steadily progressing in line with our potential and will soon see a number of health innovations invented and developed here that will impact on patients' lives and on society as a whole.

There are currently (2018) 18 drug therapies by Catalan companies in the pipeline, up from only seven in 2013. This shows that we are progressing steadily from a cutting-edge science system to the business landscape, advancing therapies to clinical development. The next obvious step is for these therapies to enter into late clinical development and to reach the market over the coming years. These 18 therapies are distributed among diverse therapeutic indications such as oncology, central nervous system, orphan diseases, vaccines, etc.

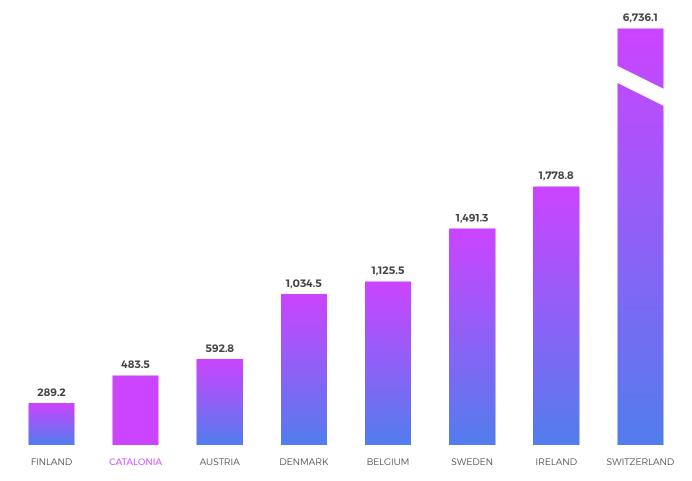
MAP 6. Venture capital raised by different clusters in biotechnology



Data for Catalonia has been included for comparison

Source: Pipeline progress: The UK's Global Bioscience Cluster in 2017 [Data from Informa; Strategic Transactions, Scrip].

GRAPH 10. Life sciences venture financing (M€) by country (2000-2017)



Sources: Crunchbase and Biocat

If we shift the focus from new therapies (mostly drugs) to medical devices, diagnostics and other health technologies, we see that this market is progressing at the same rate, but it is slightly more difficult to quantify as to what extent.

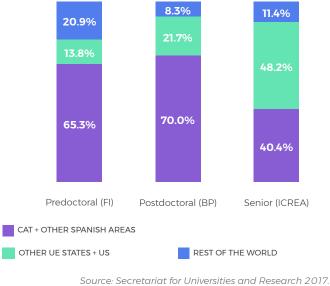
ATTRACTIVENESS TO TALENT

International competition and an increased focus on research and innovation as the key to economic and technological leadership have made talent a primary asset for countries and industries. Therefore, much attention is being paid to training and attracting and retaining critical talent around the world. "We are on the threshold of a 'human era' - one in which pooling and supplying money is secondary to amassing the brainpower to create positive change", said Christal Morehouse, Senior Program Officer at the Open Society Initiative for Europe (OSIFE) in 2014 26 .

R&D talent attraction and retention

Catalonia attracts professionals from around the world to a research, development and innovation system recognized as a worldwide benchmark of excellence in research in areas such as biomedicine, photonics, energy, economy and nanotechnology. The population dedicated to R&D&i activities increased

GRAPH 11. Origin of researchers working in the BioRegion of Catalonia



by 60% between 2002 and 2015. Policies facilitating this success have focused on creating open, flexible, excellence-driven institutions and programs for the attraction and retention of highly talented and internationally outstanding scientists.

Entrepreneurial spirit

Catalonia is a land of entrepreneurs. According to a recent GEM²⁷ study, entrepreneurial activity rose in Catalonia in 2017 by just over 8%, above the European average (7.8%). We are an entrepreneurial global hub in mobile and e-commerce start-ups and industrial technologies, as seen in Figure 4. There are 24 accelerators in Catalonia that have hosted life sciences and healthcare projects, and 10 of these are specialized in this area. On top of that, the rate of company creation is around one company per week.

The size of the region and its competitive advantage as a knowledge hub are aligned with a shared effort to build a better country for all. This translates into personal and professional values more similar to those of the Small European Economies group used for comparison in this report, and a determination to do things the right way.

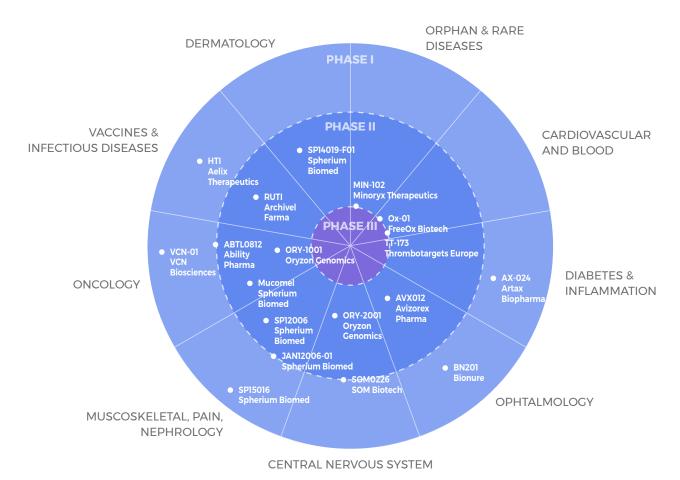
Professional talent

Due to the long tradition of medium-sized Catalan pharma companies (Grifols, Almirall, Esteve, Ferrer, Uriach, etc.), all the talent needed for preclinical, clinical and technological operations can be found within the BioRegion, along with continued reliable access to the global talent pool. The nature of life sciences jobs is changing, and the capacity to adapt will again prove crucial. Specializations in specific niches and a greater focus on certain skills such as big data, artificial intelligence, machine learning, robotics and nanotechnology with a strong biopharmaceutical orientation mark the present and the future of the sector. Catalonia, with a total of 1,076 bachelor's and master's degrees, 46% of which relate to STEMS and life sciences, provides a specialized pool of talent ready to enter this scenario.

Network of specialized providers and clinical trial sites

There is a wide network of CMOS, CROS, and hospitals where trials can be conducted, consultants, regulatory advisers, market access specialists, technology providers, etc. Any company can execute operations at the top level using only local providers and professionals.

FIGURE 5. Pipeline of biotechnology companies of the BioRegion of Catalonia (therapeutics)



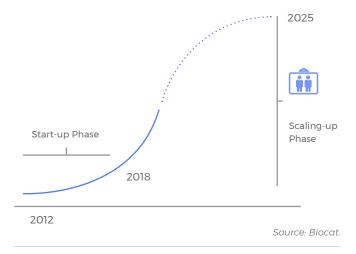
Source: Biocat's Directory and clinicaltrials.gov (updated to June 2018)

This solid ecosystem of technology providers and specialized companies ensures the execution of all innovation and development activities in an efficient and cost-effective manner. Moreover, one can find local, world-class hospitals for conducting top-level clinical research, such as Hospital Clínic, Vall d'Hebron and Sant Joan de Déu (children's hospital).

Investable teams

One key element of a thriving ecosystem is the availability of investable teams: small teams of three to five people, typically Chief Executive Officers or Chief Medical Officers, who have pharmaceutical development experience in an investor-supported start-up biotech company. Although the current proportion of first-timers is higher, and seasoned teams are still scarce, the capabilities are evolving rapidly because (1) there is a large base of professionals able to adapt to the start-up rules, and (2) it is very easy to import talent from abroad and establish it in Barcelona. The dynamism to create these investable teams is also a driving force in Catalonia.

GRAPH 12. The high-skilled and competitive life sciences economy of the BioRegion shows the potential to grow and succeed as a scaling-up ecosystem



BUILDING THE FUTURE BY LEVERAGING CATALONIA'S POTENTIAL

The opportunity gap is easy to identify. We highlighted earlier a set of indicators that help us compare Catalonia to a group of small European economies like Sweden, Denmark, Ireland, Austria and Belgium. However, as we have already mentioned, the innovation level of Catalonia in general, and the current investment in life sciences companies in particular, are still lower.

But this fact in itself presents an opportunity for investors. From our perspective, Catalonia's potential and its scientific quality, which is similar or even higher than the comparable European countries, offer untapped opportunities for investment. This is a huge gap to be filled during the coming years.

According to the World Economic Forum 2015-16 Global Competitiveness Report²⁸, an environment conducive to innovative activity requires the presence of high-quality scientific research institutions that can generate the basic knowledge needed to build the new technologies. Excellent science is indeed the most difficult part of the growth equation: it takes decades to build a strong scientific base that can develop innovative advancements. We already have this base. The next steps -investment and growth- are easier to deploy under the right conditions. We are at the base of an exponential growth curve.

If we project a 20-25% CAGR (Compound Annual Growth Rate) over the average investment rate in past years, we can predict reaching €500+ M in private investment in life sciences by 2025. Our vision is that Catalonia can multiply in seven years the total investment, investors and its position as a life sciences hub with outstanding figures in Europe.

There are a multitude of factors that are likely to influence scale-up success, including market conditions, management, strategic choices, regulation, and finance. According to David Gann (Vice President, Imperial College) and Mark Dodgson (Director, Technology and Innovation Management Centre, University of Queensland Business School), "Clusters count". And so does the process of encouraging start-ups and creating spin-outs, the presence of universities and research institutions as contributors to the growth of science-based

TABLE 8. Catalonia can multiply in seven years the total investment, investors and its position as a life sciences hub with outstanding figures in Europe

	Current	2025
Yearly investment in innovative emergent life sciences companies	€130M/ year	€500M/year
International investors investing in BioRegion start-ups	41	+100
Products in clinical development (therapies)	18	50
Catalonia most innovative hub in life sciences in Europe	#5	#3

Given the evolution of the sector, Biocat expects, in terms of social impact, at least 10 advanced products and technologies to reach patients by 2025.

Source: Biocat.

companies in fields such as the life sciences, new materials and machine learning; access to skilled labor and specialized knowledge; powerful networking and support structures... those are aspects we are reviewing in this report.

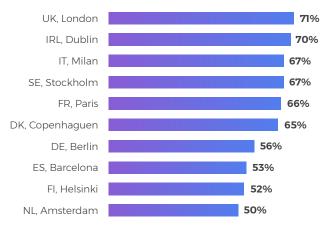
The 2017 European Scale-Up Report provides some interesting tips for our case. First of all, campuses, labs and research organizations play a role in patentable hard tech in specific areas such as medtech, biotech life sciences, encryption, materials science, robotics, nanotechnology, semiconductors, and the like²⁹. According to this report, healthtech is the second-largest industry in terms of capital raised in Europe and also in terms of deals per industry, just behind fintech. The top four scale-up cities in 2017 are the same as those in 2016. However, in fifth place, scaling up one position, is Barcelona, the eighth city in terms of the amount raised in European venture capital. Moreover, what is remarkable is the percentage of scale-ups (concentration) in a single city per country. Proximity counts when it comes to ecosystems. Barcelona is eight in Europe, with 53% of scale-ups concentrated in the city.

RECOMMENDATIONS

This section reviews the BioRegion's assets and shortcomings by main development areas and key underlying enablers, to provide a number of recommendations for the various stakeholders.

Regarding the BioRegion's knowledge system, professional networks and healthcare providers' assets and immediate needs, the excellent scientists and solid research ecosystem require clear stimuli to foster tech transfer, along with a systematic approach in order to translate papers into solutions for society. The proof of concept testing area, based on specialized research capabilities and local expertise, is attracting increasing interest from investors. However, we lack market perspective, a connected and comprehensive drug discovery platform and public and private funds to be able to prepare

GRAPH 13. The importance of tech hubs within countries (the percentage shows the concentration of scale-ups in a single city per country)



Source: Sirris 2017 European Scale-ups Report.

a preclinical regulatory package for an area that is currently based on a solid network of experts and providers and knowledge from local pharmas but which needs early-stage financing. With regard to clinical development, the BioRegion has professional expertise, a network of top-level hospitals and specialized CROs, but there is still too much bureaucracy and absence of integrated business development of clinical trial capabilities. Finally, Catalonia has an integrated health system (CatSalut) that would favor market access, but which lacks innovation alignment from within the system.

Consequently, our recommendations regarding the different development areas are:

- Improve tech transfer incentives for researchers
- Foster a closer relationship between scientists, pharma and investors to better define proof of concept initiatives
- · Strengthen local drug discovery platforms
- Provide specific public funding in this stage; for example, by matching them with private investment funds
- Further involve the CatSalut health system in streamlining clinical trial capabilities
- Improve the innovative capabilities of the Catalan health system
- Implement innovative public procurement programs

From another perspective, targeting the key enablers, we have an excellent network of academic TTOs who foster knowledge transfer despite being understaffed, underfinanced and who are not coordinated or working together at country level. We also have a network of professionals and providers from the local pharma industry but do not have enough C-level management teams with years of experience in founding and scaling-up start-ups and serial entrepreneurs. We do have local mid pharmas and some big pharma headquarters but the three levels are not well connected (start-ups, local mid pharmas, big international pharmas), nor do we have mid-tier innovative companies. On the fiscal side we have clumsy fiscal incentives and lack the necessary culture whereby tax incentives are considered effective mechanisms for promoting R&D&i. An entrepreneurial culture, business angels, local VCs and new entrant international VCs are not enough if we do not have an organized and comprehensive public view of the relevance of private investment in promoting innovation in health

Consequently, our recommendations for the ecosystem's different key stakeholders are:

- Better funding for TTOs, mainly by channeling PoC funding through them
- Promote coordinating structures beyond the TTO level
- · Attract, retain, train and mentor C-level talent

CAPABILITIES, SHORTCOMINGS AND RECOMMENDATIONS, BY DEVELOPMENT AREA

Area	What we have	What we don't have (pains)	What we should do
Basic research	Excellent scientists and a solid research ecosystem	 Clear stimuli for tech transfer Systematic approach to translate papers into solutions for society 	Improve tech transfer in- centives for researchers
Proof of concept testing ("killer" experiments) Preclinical and regulatory	Specialized research capabilities and local expertise Investors interest in intervening at this early stage A solid network of experts and providers Knowledge from local pharmas	 Market perspective Serious commitment with starting clinical development by academia A connected and comprehensive drug discovery platform Public and private early-stage financing to prepare a preclinical regulatory package 	 Scientists, pharma and investors need to work together to better define PoC experiments Strengthen local drug discovery platforms Provide specific public funding in this stage, for example, by matching private investment funds
Clinical development	 Professional expertise A network of top-level hospitals Specialized CROs 	Integrated business development of Catalan clinical trial capabilities Room for improvement with clinical research ethics committees and local hospitals. Still too much bureaucracy	Further involve the CatSalut health system in streamlining clinical trial capabilities
Market access	An integrated health system (CatSalut)	 Innovation alignment from within the system Low level of innovation incorporation The health system leading innovation by defining own needs 	 Improve innovative capabilities of the Catalan health system Implement innovative public procurement programs

Source: Biocat.

CAPABILITIES, SHORTCOMINGS AND RECOMMENDATIONS, BY KEY UNDERLYING ENABLERS

Area	What we have	What we don't have (pains)	What we should do
Knowledge transfer	An excellent network of academic TTOs	 TTOs understaffed and not correctly financed TTOs not coordinated and not working together at country level 	 Finance TTOs, mostly by channeling PoC funding through them Promote coordinating structures beyond the TTO level
Management and professional talent	A network of professionals and providers from local pharma industry	 Dozens of C-level management teams with years of experience in founding and scaling-up start-ups Serial entrepreneurs 	Attract, retain, train, and mentor C-level talent
Cluster strategy	Local mid pharmas and some big pharma headquarters	Connection between the three levels (start-ups, local mid-pharmas, large international pharmas) Mid-tier innovative companies	 Encourage local pharmas to capture innovation from local companies Encourage big pharmas to scout for innovation in Catalonia Promote partnerships between established pharma companies and innovative start-ups
Fiscal climate	Clumsy fiscal incentives for R&D&i	The culture of considering tax incentives as effective mechanisms to promote R&D&i	 Establish an R&D tax credit system Develop enterprise investment schemes for business angels and investors
Finance	Entrepreneurial culture, business angels, local VCs and newly entrant international VCs	Organized and comprehensive public view of the relevance of private investment in promo- ting innovation in health	 Attract capital through tax stimuli Commit public funding through smart public-private instruments

Source: Biocat.

- Encourage local pharmas to capture innovation from local companies
- Encourage big pharmas to scout for innovation in Catalonia
- Promote partnerships between established pharma companies and innovative start-ups
- · Establish an R&D tax credit system
- Develop enterprise investment schemes for business angels and investors
- Attract capital through tax stimuli
- Commit public funding through smart public-private instruments

RECOMMENDATIONS FOR PUBLIC STAKEHOLDERS

Last, but not least, a healthy ecosystem should rely on natural selection of the best initiatives and should not be directed top down. However, there are several ideas that should permeate public actions in order to contribute to the success of the ecosystem. We outline some of them here:

- Promote and defend basic science: all major innovations can be traced to specific scientists working in a free, creative scientific environment in which they can develop their ideas and embrace risk.
 The market should not direct basic research, scientists should first of all be free to pursue their curiosity.
- Leverage existing facilities: Catalonia has built specific facilities and platforms that can be scaled-up to become global innovation centers. Examples include the Banc de Sang i de Teixits and associated advanced cell therapy and production platforms.
- Take advantage of the high quality and centralization of the Catalan health system by promoting an open data sharing scheme that, while keeping personal patient data anonymized, can pool current health and future omics data into an open access data lake that can be analyzed by scientists and companies all over the world. This invaluable resource of data-driven research should evolve into a powerful tool to improve citizens' health, and the Government should foster an alliance between society, industry, scientists and the health care system.
- Support for entrepreneur training at all levels, incentivizing varied careers and migration of academic scientists into industry and back to academia to increase influx of talented scientists and entrepreneurs in the public and private sectors.
- Promote smart-investment initiatives, combining public funding and stimuli in simple ways such as (1) funds to finance smart proof of concept tests; (2) funds to match existing private investment funds, and (3) tax stimuli for business angels, entrepreneurs and investors

Notes

- ¹⁰ Joseph Damond, Executive Vice President for International Affairs at the Biotechnology Innovation Organization, highlighted the relevance of the BioRegion at the BIO 2017 Convention.
- ¹¹ https://publications.credit-suisse.com/tasks/render/file/?fileID=1CC21D53-CD3A-CB77-C15AD96D67EE1210
- ¹² According to an analysis by Global Finance Magazine based on data from the International Monetary Fund 2016 (https://www.gfmag.com/global-data/economic-data/worlds-richest-and-poorest-countries)
- ¹³ Inclusive Development Index 2018, World Economic Forum (http://reports.weforum.org/the-inclusive-development-index-2018/shareable-infographics/?code=wr124)
- ¹⁴ The GNI is the basis of calculation of the largest part of contributions to the EU budget.
- https://ec.europa.eu/docsroom/documents/30281/ attachments/1/translations/en/renditions/native
- ¹⁶ https://ec.europa.eu/growth/industry/innovation/facts-figures/scoreboards en.
- https://publications.credit-suisse.com/tasks/render/file/?fileID=1CC21D53-CD3A-CB77-C15AD96D67EE1210
- ¹⁸ ICREA Program, https://www.icrea.cat/
- 19 CERCA centers, http://cerca.cat/en/
- https://webgate.ec.europa.eu/dashboard/sense/app/93297a69-09fd-4ef5-889f-b83c4e21d33e/sheet/PbZJnb/state/analysis
- ²¹ FET Flagships are visionary, science-driven, large-scale research initiatives addressing Scientific and Technological (S&T) grand challenges. They are expected to run for approximately 10 years, have a total budget of around 1 billion euros and bring together a large number of research organisations, including academia, large industry and SMEs. http://ec.europa.eu/programmes/horizon2020/en/h2020-section/fet-flagships.
- ²² Startup Ecosystem Report, https://startupgenome.com/barcelona-report/
- $^{\rm 23}~{\rm http://www.biocat.cat/sites/default/files/ilovepdf_merged.pdf}$
- Study on investment in the biomedical industry in Catalonia: Achievements and future challenges https://media. timtul.com/media/web_cataloniabioht/CataloniaBioHT_EY_ StudyInvestment_2018_en_web_20180612061242.pdf
- 25 http://www.eib.org/attachments/efs/economics_working_ paper 2018 02 en.pdf
- http://www.policy-network.net/pno_detail. aspx?ID=4710&title=Europe+needs+a+talent+offensive
- ²⁷ https://www.gemconsortium.org/
- http://www3.weforum.org/docs/gcr/2015-2016/Global_ Competitiveness_Report_2015-2016.pdf
- ²⁹ https://www.scale-ups.eu/the-scale-up-landscape/2017/sirriseuropean-scaleups-report-q1-2017

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

The BioRegion of Catalonia: ecosystem stakeholders

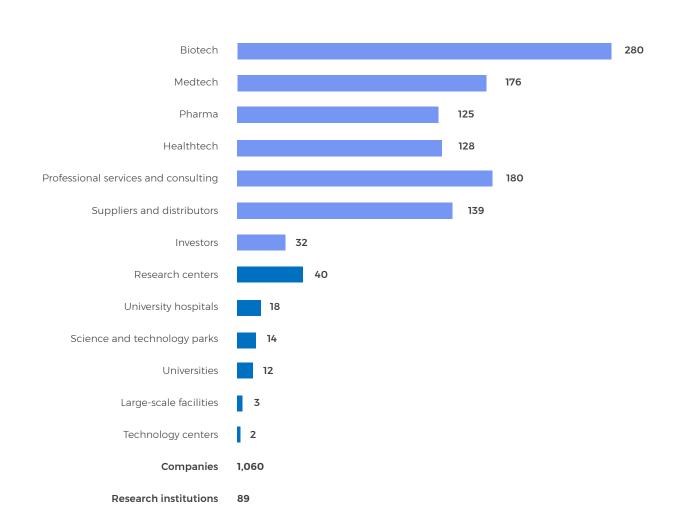


The BioRegion of Catalonia: ecosystem stakeholders

The BioRegion of Catalonia has 1,060 companies (including biotechnology, pharmaceutical, medical technology, healthtech and professional services companies, plus suppliers, distributors and investors) and 89 research organizations (including research centers, universities, university hospitals, large-scale facilities, technology centers and science and technology parks working in the life sciences), as well as a network of healthcare activities facilitating diagnostic and medical treatments for patients.

The healthcare and life sciences sector in Catalonia generates a total joint turnover of \in 31,087 billion each year, or 7.2% of the Catalan GDP. As a whole, the sector employs 223,000 people or 7% of the total working population of Catalonia (2016).

GRAPH 14. Ecosystem of the BioRegion of Catalonia (2017)

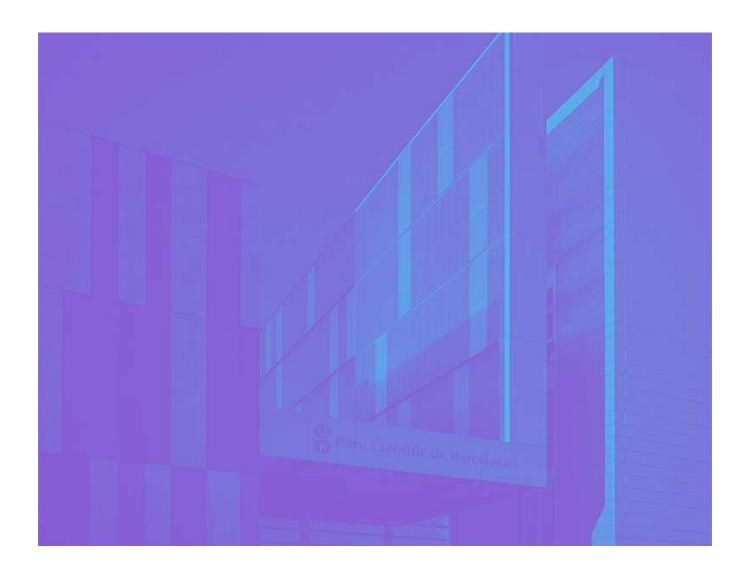


Source: Biocat Directory.

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Business sector



Business sector

The BioRegion of Catalonia has a total of 1,060 companies, up 44.4% from the 2015 Biocat Report (734 businesses). In analyzing the data, it is important to differentiate between organic growth, from the creation of new companies, and Biocat's work to locate stakeholders. So, the organic growth of the business sector led to the creation of 144 new companies between 2015 and 2017.³⁰

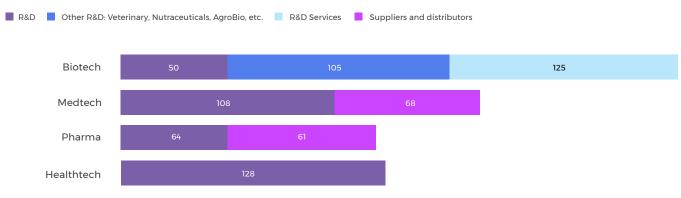
The breakdown by sector (Graph 15) shows that, of the 1,060 companies in the BioRegion, the largest group is the 280 businesses in the biotechnology sector, 50 of which focus on new therapeutics and diagnostic tools, 125 on R&D services and 105 on applications in other fields (like veterinary, industrial biotechnology, food, agriculture and the environment). Plus, the BioRegion has 176 medical technology companies (108 as their main activity and 68 specialized suppliers and distributors), 125 companies in the pharmaceutical sector (64 pharmaceutical corporations and 61 specialized suppliers and distributors), and, new in this report, 128 companies offering healthtech products or services.

Regarding other companies associated with the healthcare and life sciences sector in Catalonia, the largest group is made up of the 180 professional services and consulting companies, followed by the 139 suppliers and distributors and, finally, the 32 investment organizations.

In Spain as a whole, there are three sectorial associations that publish data periodically: the Spanish Bioindustry Association (Asebio), the employers' association for biotechnology companies; the National Trade Association of the Spanish-based Pharmaceutical Industry (Farmaindustria), the employers' association for pharmaceutical companies; and the Federación Española de Empresas de Tecnología Sanitaria (Fenin), the employers' association for medical technology companies.

Asebio counts a total of 2,981 biotechnology companies in Spain (as of 2015), 654 which carry out activities associated with biotechnology as their main focus.³¹ According to data from Asebio, Catalonia makes up 27.6% of all Spanish companies whose main activity is biotechnology, followed by Madrid (16.1%), Andalusia (12.3%) and the Valencian Community (9.9%). However, it must be noted that Asebio uses a survey conducted by the Spanish Statistical Office (INE), whose random methodology could generate a much lower number of biotechnology companies than those





truly operating in Catalonia (according to the Biocat Directory, Catalan companies would make up approximately 40% of the Spanish total).

In the pharmaceutical sector, Farmalndustria has 166 members, 85 of which are located in Catalonia (51.2% of the total), 72 in Madrid and 9 in other autonomous communities. Additionally, Fenin puts 240 companies in the healthcare technology arena, 41.9% of which are located in Madrid and 38% in Catalonia.³³ Nevertheless, it must be noted that Farmalndustria and Fenin only count their members when giving indicators, while the Biocat Directory aims to compile a list of all companies established in the BioRegion.

In Catalonia, the CataloniaBio (biotechnology) and Health Tech Cluster (medical technology) employers' associations merged in 2017. The resulting association, called CataloniaBio & HealthTech, represents more than 170 companies.

Source: Biocat.

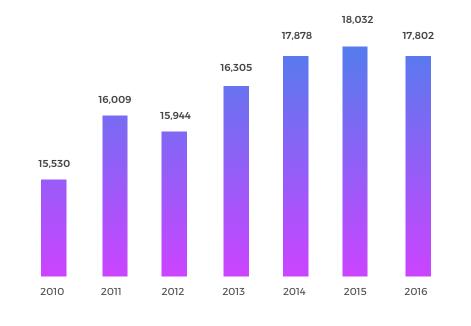
TURNOVER AND EMPLOYMENT. MACROECONOMIC INDICATORS

As a whole, companies in the BioRegion of Catalonia posted turnover of €17,802 billion in 2016. For the 2010-2016 period, in nominal terms, turnover rose 2.4% per year, going from €15.53 billion (2010) to €17,802 billion (2016).

If we look at the sector as a whole, taking into account both turnover of companies in the industrial subsector and the value of production of healthcare services (€13,285 billion in 2014, according to data from Idescat), the total business volume of the BioRegion is €31,087 billion.

The turnover of companies in the BioRegion of Catalonia in 2016 made up 8% of the Catalan GDP. If we subtract the estimated intermediate consumption (Table 9), the gross value added (GVA) generated by companies in the BioRegion makes up 3.4% of the GDP. And, if we add in healthcare services to look at the sector as a whole (according to the aforementioned data from Idescat), it accounts for up to 7.2% of the GDP. The figures confirm, therefore, a trend towards growth and the BioRegion's increasingly significant

GRAPH 16. Evolution of companies' turnover (in M€) in the BioRegion of Catalonia (2010-2016)



Source: Biocat and SABI.

TABLE 9. Macroeconomic data and ratios on the BioRegion of Catalonia (2016)

SECTOR	Turnover (M€)	Intermediate consumption (M€)	Gross value added (GVA) (M€)	% of Catalan GDP
Industrial subsector	17,802	10,252	7,550	3.4
Biotechnology	3,706	2,224	1,482	0.7
Pharmaceutical	8,355	5,013	3,342	1.5
Medical technology	2,897	1,593	1,304	0.6
Healthtech	62	31	31	0
Other	2,782	1,391	1,391	0.6
Healthcare Services	13,285	4,775	8,510	3.8
TOTAL	31,087	15,027	16,060	7.2
Memo item: Catalan GDP (M€)	223,629			

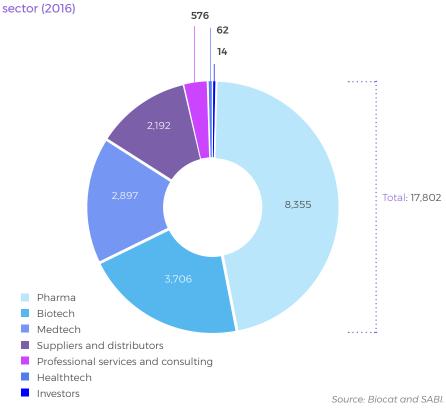
Source: Biocat and Idescat. Note: The data on healthcare services from Idescat is for 2014.

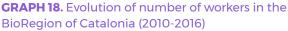
contribution to the Catalan economy as a whole.

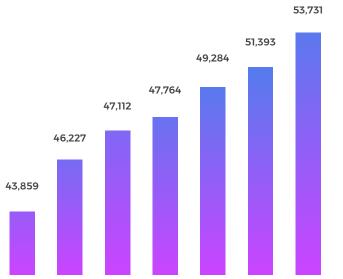
The breakdown of operational income by sector (Graph 17) shows that 46.9% comes from pharmaceutical corporations (€8,355 billion), followed by 20.8% from biotechnology companies (€3,706 billion) and 16.3% from medical technology firms (€2,897 billion). However, the new healthtech sector still shows only modest revenue: €62 million, or 0.3% of the total. Finally, 15.6% of all turnover corresponds to other companies (€2,782 billion) with ties to healthcare and life sciences companies in Catalonia, such as consultancy firms and suppliers and distributors of technological materials and services.

In terms of employment, the healthcare and life sciences sector in Catalonia employs 223,731 people, of which 53,731 work for biotechnology, pharmaceutical, medical technology, healthtech and professional services companies or sector suppliers, distributors and investment bodies, and 170,000 work in the healthcare network.

GRAPH 17. Turnover (in M€) of companies in the BioRegion of Catalonia, by sector (2016)







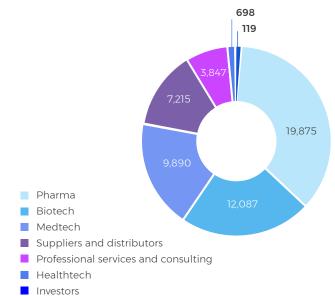
2013

2010

2011

2012

GRAPH 19. Number of workers at companies in the BioRegion of Catalonia, by sector (2016)



Source: Biocat and SABI.

2016

2015

Source: Biocat and SABI.

TABLE 10. Productivity indicators for the BioRegion of Catalonia, by sector (2016)

2014

Sector	Production per employed individual	Gross value added per employed individual
Industrial subsector	331,317.1	140,515.7
Biotechnology	306,610.4	122,644.2
Pharmaceutical	420,377.4	168,150.9
Medical technology	292,922.1	131,815.0
Healthtech	88,825.2	44,412.6
Other	248,815.0	124,407.5
Healthcare services	78,147.1	50,058.8
TOTAL	138,948.1	71,782.9
Catalan economy	120,279.9	57,148.0

Source: Biocat and Idescat. Note: The data on healthcare services and production per employee for the Catalan economy are for 2014. As Graph 18 shows, the number of workers at companies in the industrial subsector has increased in recent years, with average year-on-year growth of 3.7%, from 43,859 in 2010 to 53,731 today. With these figures, the healthcare and life sciences sector makes up 7% of the working population of Catalonia.

Analysis of the productivity indicators for industry in the BioRegion (Table 10) shows that the sector is clearly above the average for the Catalan economy. So, in terms of gross value added per employee, the figure for the industrial subsector as a whole is more than twice of the Catalan economy. The pharmaceutical sector has the highest labor productivity, followed by the medtech and biotech sectors.

Healthcare services has more modest productivity results, in line with the fact that it is a labor-intensive sector.

The breakdown by sector (Graph 19) shows that 42,550 workers (79.2% of all those employed in companies in the BioRegion) are at companies directly associated with healthcare and life sciences in Catalonia, above all pharmaceutical corporations

(19,875 workers, 36.9% of the total), biotechnology companies (12,087, 22.5%) and medical technology firms (9,890, 18.4%).

BUSINESS CREATION

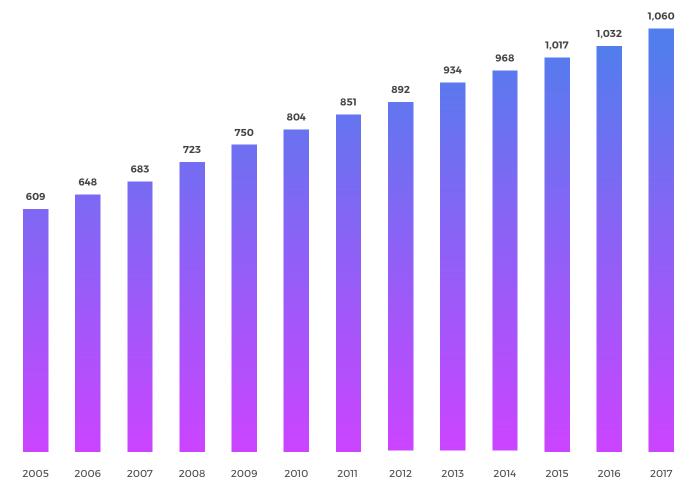
The evolution of the number of companies in the BioRegion of Catalonia, which went from 609 in 2005 to 1,060 in 2017 (Graph 20), shows a clear upward trend with average year-on-year growth of 4.7%. To see the real growth in the sector, the graph only shows active companies. It is worth noting, additionally, that newly created active companies are normally only detected after approximately two years, which means the real figure for companies created in 2016 and 2017 won't be complete until the next report.

Over the past 12 years, 605 new business projects have been launched in the BioRegion, 62 of which have since closed down (10.2%), with an average lifespan of 5.3 years. The main reasons companies close down are well defined: lack of solid scientific results, trouble getting funding and, finally, difficulties in business management. Compared to the high mortality rate among technology

start-ups, which is at roughly 70%-95% (Start up Genome Report Extra on Premature Scaling, 2011), the rate of 10.9% for start-ups in the BioRegion is a positive indicator.

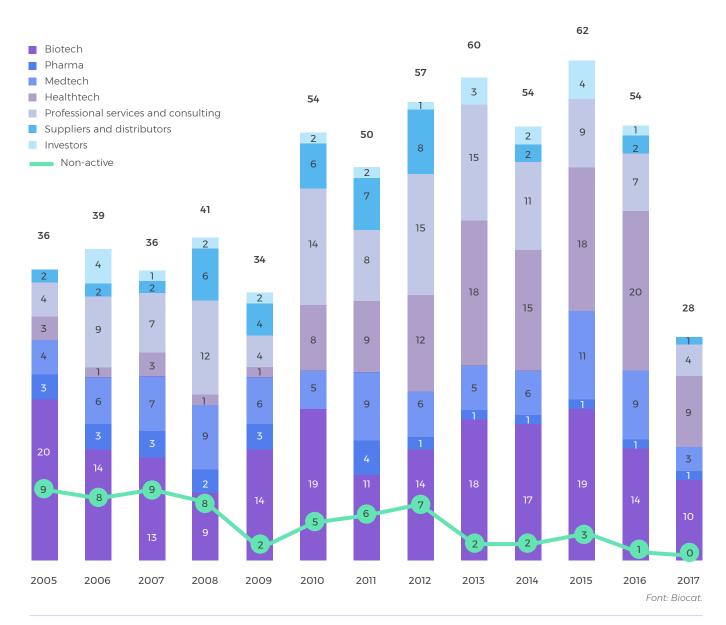
By sector (Graph 21), the companies created between 2005 and 2017 are mainly biotechnology firms (192, 31.7% of the total), followed by professional services companies (119, 19.7%), healthtech firms (118, 19.5%) and medical technology businesses (86, 14.2%). Companies working directly in the healthcare and life sciences field make up 69.4% of all new businesses. As mentioned before, the organic growth of the business sector between 2015 and 2017 led to the creation of 144 new companies (Graph 21), most of which are healthtech firms (47), biotechnology companies (43) and medical technology businesses (23), although there are new companies in all sectors. They are mostly microenterprises and 17.5% are spin-offs of universities, research centers or hospitals. The pace of growth in the BioRegion in recent years is also noteworthy, reflecting the entrepreneurial spirit of the ecosystem with the business creation rate of nearly one new company per week.

GRAPH 20. Evolution of number of companies in the BioRegion of Catalonia, by year (2005-2017)



Source: Biocat.

GRAPH 21. Companies created (active and inactive) in the BioRegion of Catalonia, by sector (2005-2017)



Analyzed by year, 2015 showed the highest number of new companies created so far (62 businesses). 55.7% of the companies were created between 2011 and 2016. Since 2011, 365 new companies have been created in the sector. As noted above, however, detecting new companies that are actually working in the sector takes roughly two years to offer a real snapshot of the creation of new business projects for 2016-2017.

The latest report from the Global Entrepreneurship Monitor (GEM) puts Catalonia and the Barcelona region as a leader in Europe in new and consolidated entrepreneurs.³⁴ A good example is the roughly 100 organizations that have coexisted in the PierOl building, led by Barcelona Tech City, since 2016. In the field of the healthcare and life sciences, the space is home to investors (Alta Life Sciences, PDG Invest, Capital Cell and mVenturesBcn), accelerators

(Numa Growth -mVentures Bcn and Conector -Bankia) and expects to welcome many more projects from this sector.

The start-up boom has brought new stakeholders that enrich the ecosystem (incubators or venture builders, business angels, crowdfunding platforms, venture capital organizations, etc.) and aim to grow early-stage projects. There has also been growth in the number of acceleration programs and accelerators, meaning programs with a specific length, based on cohorts, that include mentoring and training and normally culminate with a demo day or investors day.

Of the 24 accelerators active in Catalonia that healthcare and life sciences projects or start-ups have participated in (Table 11), 10 specialize in this area and the rest are focused on technology or various sectors. The 10 specialized accelerators (with their correspond-

ing promoters) are: Caixalmpulse ("la Caixa" Banking Foundation); CRAASH Barcelona (Biocat); d·HEALTH Barcelona (Biocat); Grants 4 App Accelerator (Bayer); Health-U (Sanofi); Inkemia, Kenko Health Accelerator (TecnoCampus); Moebio (Biocat); NeoStart (Chiesi); Tech4Health (Caixa Capital Risc, DKV, Esteve, Hospital Sant Joan de Déu, Nae, Ship2B); What if! Barcelona (Innovation Forum).

FUNDING AND INVESTMENT

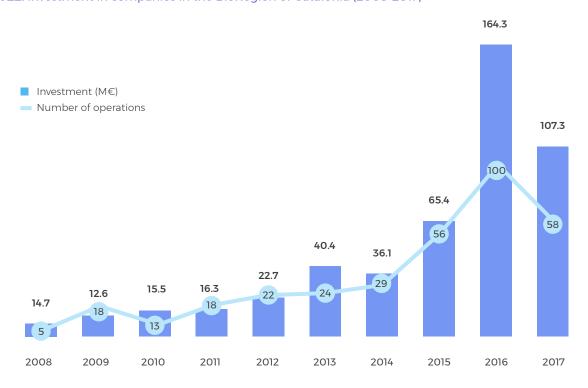
Start-ups in the BioRegion attracted a total of €337 million in investment between 2015 and 2017, with a continued upward trend (Graph 22). So, in 2016 the funds raised showed 151.2% growth over 2015, which was up 81.2% from 2014. The 100 operations valued at €164.3 million in 2016 were a highly significant milestone, although

TABLE 11. Accelerators in Catalonia that healthcare and life sciences projects or start-ups have participated in

Program/Accelerator	Promoters	Sector
Antai Venture Builder	Antai	Digital
Bstartup	Banc de Sabadell	Digital
Caixalmpulse	La Caixa	Life sciences
CRAASH Barcelona	Biocat	Life sciences
Conector	Bankia	Digital
d·HEALTH Barcelona	Biocat	Life sciences
Empenta	Generalitat de Catalunya, Ajuntament de St. Cugat	Any sector
Founder Institute	Founder Institute	Any sector
Grants 4 App Accelerator	Bayer	Healthtech
Health-U	Sanofi	Life sciences
InKemia	Grup InKemia	Life sciences
IQS Next Tech	IQS Tech Factory	Any sector
Itnig	Itnig	Digital
Kautic40	Orbital 40	Digital
Kenko Health accelerator	TecnoCampus	Life sciences
NeoStart	Chiesi	Life sciences
OgilvyUpcelerator	Ogilvy	Any sector
Seedrocket	Seedrocket-Angels	Digital
Startup Next	Techstars	Any sector
Startupbootcamp	Startupbootcamp	Any sector
The Collider	Mobile World Capital Barcelona	Digital
Tech4Health	Hospital Sant Joan de Déu, Esteve, Caixa Capital Risc, Nae, Ship2B, DKV	Digital health
Innovation Forum - Barcelona Branch	Innovation Forum	Life sciences
Wayra	Telefónica	Any sector

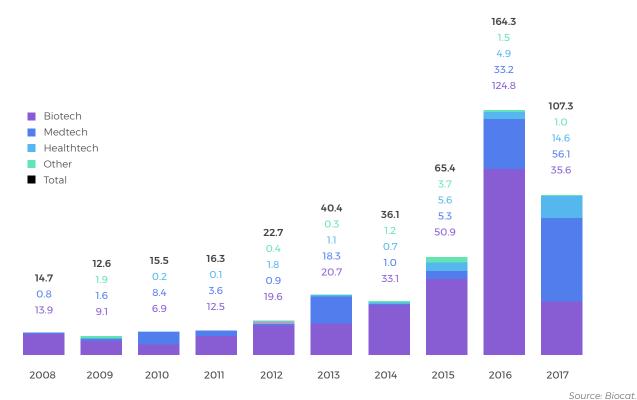
Source: Biocat.

GRAPH 22. Investment in companies in the BioRegion of Catalonia (2008-2017)



Source: Biocat. Note: Data compiled from information available as of December 2017.

GRAPH 23. Investment in companies in the BioRegion of Catalonia (in M€), by sector (2008-2017)



it must be taken into account that two large operations made up €76 million of this total.

Moreover, 2016 was a highly noteworthy year for both direct investment (€150.7 million) and raising funds through the Spanish Alternative Stock Exchange (MAB), €13.6 million. Between 2008 and 2016, investment in companies in the BioRegion of Catalonia increased twelve-fold despite the economic crisis.

Investment attracted in 2017 (with data as of 30 December) shows a continuation of this upward trend and once again it is in triple digits, with €107.3 million in 58 operations. It is worth noting that 2017 saw roughly half the number of operations as the previous year, but the average amount raised per operation was up, at nearly €3 million. Meaning there were fewer operations but they were bigger in volume.

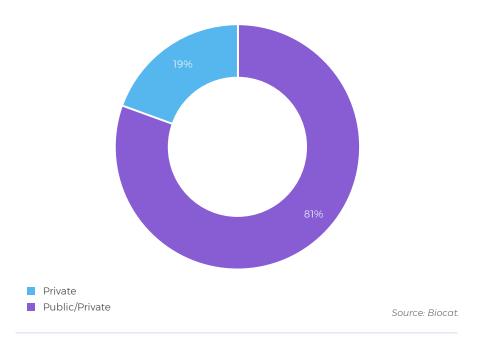
From a sectorial standpoint, the majority of investments over the past two years (2015-2017) went to biotechnology companies (\in 211.3 million) and medical technology firms (\in 94.5 million) (Graph 23). Investment in the healthtech sector ranked third (\in 25 million), with a clear upward trend, despite the fact that investment in the sector is always on a smaller scale. This trend has been predominant in recent years, with biotech investment making up 62.1% of all investment over this period (2015-2017).

Private investors contributed 81% of investment, while the remaining 19% came from operations with public investors alone or in collaboration with private stakeholders (Graph 24).

From a sectorial standpoint, if we analyze the different types of investment by main sector, it is clear that most investment comes from private investors in biotechnology companies (€187.4 million, 88.7% of the total), medical technology firms (€61.2 million, 64.8%) and healthtech businesses (€20 million, 80%). The rest of the investment came from public organizations on their own or in conjunction with private entities.

Over the 2015-2017 period, 46 rounds of funding valued over €1 million were closed by 37 companies. Broken down by year, Table 12 shows the companies in the BioRe-

GRAPH 24. Breakdown of investment in the BioRegion of Catalonia by type of funding (2015-2017) ³⁵



GRAPH 25. Type of investment in the BioRegion of Catalonia by sector (2015-2017) ³⁶

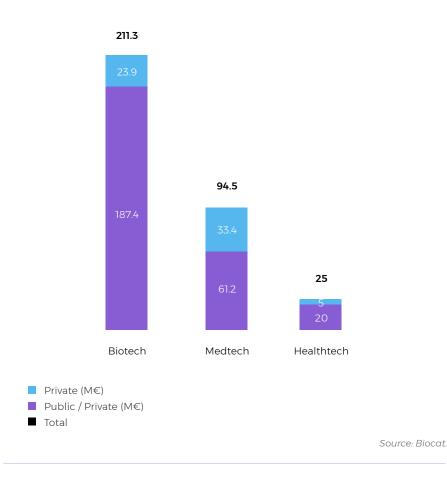


TABLE 12. Companies in the BioRegion of Catalonia that have attracted more than €1 million, by year (2015-2017)

	1-10M€	11-50M€
2015	ClinicPoint (1) Galgo Medical (1) Genmedica Therapeutics (2.5) Greenaltech (2) iSalud (1) Medtep (1.8) Psious (1) Top Doctors (1.1) Transplant Biomedicals (1.5)	Minoryx Therapeutics (22.4) Oryzon Genomics (16.5)
2016	Albajuna Therapeutics (3.75) Bioprognos (1) Cebiotex (1.8) Cuantum Medical Cosmetics (1.8) IDP Pharma (1.9) Inbiomotion (2.2) Iproteos (2) Leukos Biotech (3.8) Pangaea Oncology (3.8) Peptomyc (1.8) Promofarma (2.6) Thrombotargets Europe (1.8)	AB-Biotics (11.7) Aelix Therapeutics (11.5) Oryzon Genomics (15.8) STAT Diagnostica (29.1) Undisclosed (47)
2017	Bionure (1.2) Bwom Technologies (1) Glycardial Diagnostics (2.4) Devicare (5) iMicroQ (1.5)	Anaconda Biomed (15) Oryzon Genomics (18.4)

Source: Biocat.

Note: Companies are classified by the total private investment attracted over the course of the year (either in one or several rounds of funding).

Inkemia IUCT Group (2.2)

Transplant Biomedicals (8.5)

Linkcare (5)

QMENTA (2.7)

Peptomyc (4.4)

SOM Biotech (2)

Transmural Biotech (2.7)

Top Doctors (3)

TABLE 13. Main rounds of funding in the BioRegion of Catalonia with international investors (2015-2017)

Year	Company	Sector	Investment (M€)	Investors
2016	STAT-Dx	Medtech	29.1	Gilde Healthcare Partners, Ysios Capital Partners, Kurma Partners, Caixa Capital Risc, Boehringer Ingelheim Venture Fund, Axis, Idinvest Partners, Siemens Venture Capital, Philips
2015	Minoryx Therapeutics	Biotech	19.4	Ysios Capital, Kurma Partners, Roche Venture Fund, Idinvest Partners, Chiesi Ventures, Caixa Capital Risc, Healthequity
2017	Oryzon Genomics	Biotech	18.2	Nexthera, Heights Capital and other International Investors
2015	Oryzon Genomics	Biotech	16.5	J. Fernandez, CEO of Active Motif and other private investors
2017	Anaconda Biomed	Medtech	15	Ysios Capital, Omega Funds, Innogest Capital, Banc Sabadell
2016	Aelix Therapeutics	Biotech	11.5	Ysios Capital, Caixa Capital Risc, Johnson & Johnson Innovation
2017	Linkcare	Healthtech	5	Guangzhou Global Star Investment
2017	Top Doctors	Healthtech	3	Addventure

Source: Biocat.

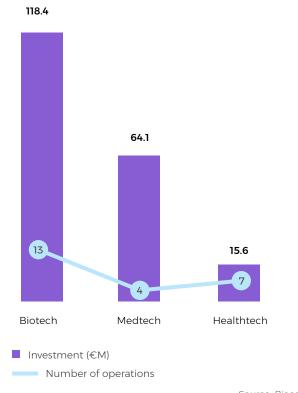
Note: The table does not include a confidential operation of nearly €50 million.

gion of Catalonia that have attracted more than €1 million a year in one or several rounds of funding. According to CBS Insights, Spain is ranked fourth in Europe by number of investment operations and millions of euros attracted, and Catalonia is the most active region in Spain, with double the investment volume of Madrid. Specifically, the healthcare sector saw the highest average volume per operation.

According to data from the 2017 Asebio Report, Catalonia makes up over 40% of all investment attracted by companies in the biotechnology sector in Spain (€58.9 million of a total of €145.8 million), including private capital increases, increases by publicly traded companies and loans from ENISA and other regional societies. It must be noted, however, that Asebio only compiles data from some companies that use biotechnology and not all of the companies that actually operate in the BioRegion and also work in the medical technology and healthtech arena. So, the total investment figures attributed by the employers' association are significantly lower than those found in this Biocat Report. Nevertheless, of the 20 companies selected by Asebio for its success stories report, 11 are from the BioRegion.

Regarding companies that attracted over €10 million between 2015 and 2017, in addition to a confidential operation valued at €47 million, other noteworthy examples include: Oryzon Genomics (€50.7 million), STAT Diagnostica (€29.1 million), Minoryx Therapeutics (€21.7 million), Anaconda Biomed (€15 million), AB-Biotics (€10.8 million), Aelix Therapeutics (€11.5 million) and Transplant Biomedicals (€10 million).

GRAPH 26. Investments with international participation, by sector (2015-2017)



Source: Biocat.

TABLE 14. Main investors in the BioRegion of Catalonia and number of operations each participated in (2015-2017)

Catalan investors	Number of operations 2017	Number of operations 2016	Number of operations 2015
ICF	1	2	6
Inkemia IUCT	2	3	0
Capital Cell	4	4	2
Crowdcube	2	1	2
Caixa Capital Risc	3	7	8
The crowd angel	1	0	0
Ysios Capital	1	3	1
Healthequity	1	1	2
Inveready	0	3	3
CG Health Ventures	0	1	1
Alta Life Sciences	1	0	0

Source: Biocat.

International investors have been drawn to companies in the BioRegion, participating in nearly all the main rounds of funding between 2015 and 2017 (Table 13). Specifically, there were 8 important rounds (from \in 3 million to \in 29 million), with international investors putting in a joint total of \in 117.7 million. Of these 8 rounds, 3 were made up exclusively of international investors.

Additionally, in July 2017 Roche terminated its deal with Oryzon Genomics for clinical development of ORY-1001. As a result, Oryzon recovered its rights to the drug.

If we take into account the 214 investment operations between 2015 and 2017, 24 (11%) included foreign participants, but these operations made up €198.1 million, or 58% of all funding obtained (Graph 26). Foreign investors preferred biotechnology companies (€118.4 million), medical technology firms (€64.1 million) and healthtech businesses (€15.6 million). It is worth noting that Catalan investors are increasingly international and, therefore, can participate more in international markets, as well as attracting foreign investment to the BioRegion.

In this regard, and in terms of foreign direct investment,³⁷ between 2015 and 2017 the BioRegion attracted more than 20 investment projects, the most noteworthy of which were (in chronological order):

- · Fresenius (€19 million), Roche (€24 million) and Bbraun (€77 million) invested in their facilities in Catalonia (2015).
- Farmacfactoring España invested €33 million in new offices in Barcelona and to boost growth in the sector of the sale of loans without recourse (2016).

- Orpea Ibérica invested €45 million to continue expansion in the dependent care sector (2016).
- Merck invested €6 million in the plant it opened in Mollet, the only one in Europe producing only meglumine (2017).
- Boehringer Ingelheim invested €100 million in the new production plant it is building in Sant Cugat (2017).

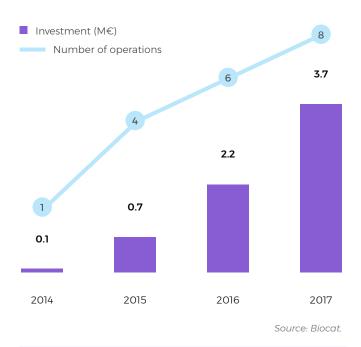
The BioRegion of Catalonia is home to 32 investment bodies. These include everything from private investors and business angels to venture capital firms (Ysios and the sectorial investment vehicles of Caixa Capital Risc), as well as family offices (like those run by the Gallardo family) and crowdfunding platforms (Capital Cell, Crowdcube). Other essential financial instruments for SMEs include the MAB (Spanish Alternative Stock Exchange) and participating loans from organizations like ICF, ENISA and the CDTI.

The eight venture capital organizations that specialize in the sector are: Caixa Capital Risc, Ysios Capital, Healthequity, Inveready, Goodgrower, CG Health Ventures, IUCT Emprèn and Alta Life Sciences.

Table 14 shows the most noteworthy Catalan investors, with the number of rounds each one participated in each year between 2015 and 2017. Catalan investors participated in 66 operations. By number of operations, the top three investment bodies are Caixa Capital Risc (18 operations), Capital Cell (10) and the Catalan Institute of Finance (ICF) (9).

Some of the investment and venture capital bodies in the BioRegion with the most noteworthy activity over the period analyzed in this report were (in chronological order):

GRAPH 27. Investment raised through crowdfunding and crowdequity by companies in the BioRegion of Catalonia (2014-2017)



- La Caixa launched a venture capital fund endowed with €20 million to promote the creation and growth of start-ups in the science arena. So, they now manage €180 million in investment and have consolidated their place as the benchmark multi-specialization investor in Spain for early-stage companies. They have 8 investment vehicles, 3 of which are in the life sciences, and a portfolio of 175 companies (March 2016).
- Ysios Capital closed its second investment fund, Ysios BioFund II Innvierte, with €126 million (October 2016).
- Ysios Capital and Caixa Capital Risc participated in the largest round of funding in the medical technology sector in Spain and one of the most important in all of Europe in 2017, led by Edmond de Rothschild Investment Partners (EdRIP). Madrid-based Medlumics raised €34.4 million to take to market a catheter to treat atrial fibrillation for cardiac arrhythmia (March 2017).
- Nauta Capital raised an additional €95 million for its fourth fund, although it hasn't made public any investments in companies in the life sciences (April 2017).
- InKemia IUCT created a €10 million fund for health start-ups (May 2017).

Over the past two years, more investment funds have appeared focusing on companies in the healthcare and life sciences sector, some of which are specialized like, for example, Genesis Ventures, CG Health Ventures, Bagi Xarxa d'Àngels Inversors de Girona and

PDG Invest, the IESE investment vehicle for start-ups. Moreover, in early 2017 the creation of Alta Life Sciences was announced, another venture capital fund specializing in the life sciences.

With regard to mergers and acquisitions (M&A), the following are of note (in chronological order):

- Almirall acquired ThermiGen for €73 million and entered the medical aesthetics market (February 2016).
- Reig Jofre acquired the diagnostics division of Oryzon Genomics (May 2016).
- Doctoralia merged with DocPlanner (June 2016), becoming the largest healthcare marketplace in the world.
- Mosaic Biomedicals merged with Canadian firm Northern Biologics (December 2016).
- Grifols acquired the diagnostics division of US company Hologic for €1.75 billion (December 2016). They also acquired 49% of US company Access Biologicals for €48 million (January 2017). Finally, they opened up new lines of research by acquiring 44% of GigaGen, which specializes in developing biotherapeutic drugs, for €35 million (July 2017).
- Mind the Byte acquired Intelligent Pharma (December 2017), making it the leading business in the bioinformatics sector in Catalonia.

With regard to presence on the Spanish stock market, the BioRegion of Catalonia has 4 of the 10 publicly traded companies in the sector: Grifols, Almirall, Oryzon and Reig Jofre. Between 2015 and 2017, no new companies went public. Regarding the MAB, 3 of the 7 companies in the sector traded on the alternate exchange are Catalan: AB-Biotics, InKemia IUCT Group and, since December 2016, Pangaea Oncology (a leader in liquid biopsies).

In terms of alternates sources of funding for small, innovative companies, the investment raised through crowdfunding (mainly crowdequity) since we are aware of the first operations (2014) has reached ${\in}6.7$ million. These financial resources went to 19 investments in 16 companies, above all biotechnology firms (\${\in}4.7\$ million) and healthtech companies (\${\in}1.5\$ million), with an increase in investment in the latter. There is a clear upward trend in number and volume of investments (8 investments with \${\in}3.7\$ million in 2017), although only one was over \${\in}1\$ million (Bionure) and only two over \${\in}0.5\$ million. Noteworthy among the companies working in this area is Capital Cell, which in 2017 became the first crowdequity platform in Spain to offer a return on investment (ZeClinics).

Furthermore, there are numerous philanthropic research initiatives in Catalonia, some of the most relevant in the healthcare and life sciences sector being those run by Fundació La Marató de TV3, "la Caixa" Banking Foundation and Cellex Foundation. According to data from 2011, general philanthropy in Catalonia raised €349 million (29% of the Spanish total) and, specifically, €48 million went to R&D activities. Since then,

no new large foundations have been created, although there has been slight growth because individual donations to foundations like, for example, Pasqual Maragall Foundation are increasing in size. Furthermore, the "la Caixa" Banking Foundation expects to triple its investment in research between 2016 and 2019, to €90 million, making this organization the fourth largest philanthropic entity in the world and the second in Europe in supporting medical research, surpassed only by the Bill and Melinda Gates Foundation (USA), Howard Hughes Medical Institute (USA) and Wellcome Trust (United Kingdom).

INTERNATIONALIZATION

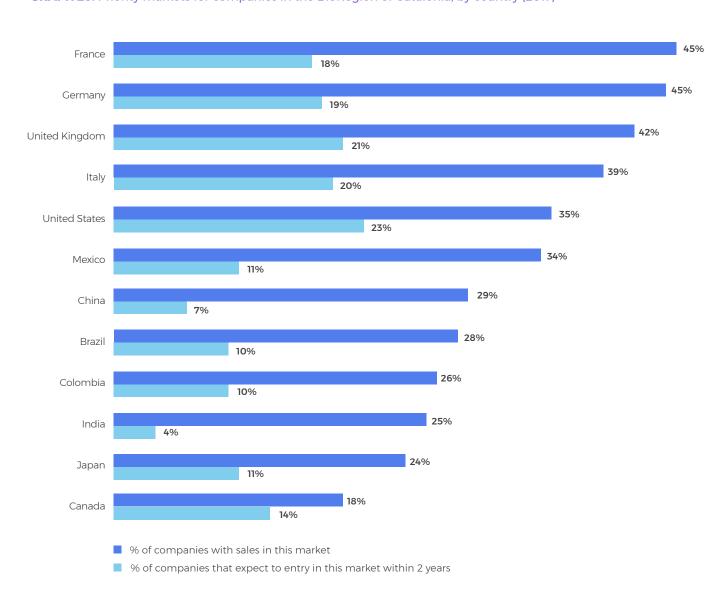
The information analyzed in this section is taken from an electronic survey sent out in July 2017 to 669 product and services companies

(including those in the technology development phase), with a response rate of 27% (181 companies).

The results of the survey show international roll-out is quite solid in companies in the BioRegion, although their main market continues to be Spain. Of the companies that have a product or service, 83% sell on international markets or have international clients.

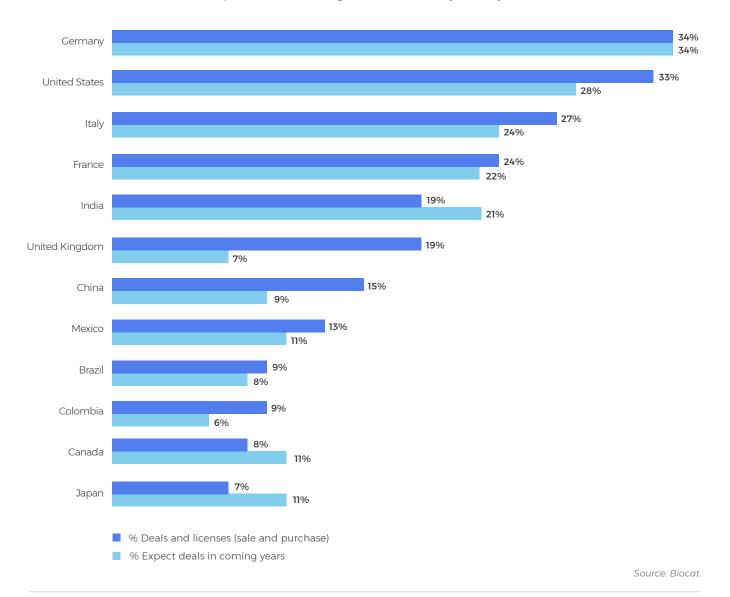
In general, the bigger the company, the greater the percentage of internationalization. So, only 49% of the product microenterprises that responded to the survey report international sales, as they are often still in the technology development phase. In this regard, only 2 of the 12 biotechnology companies specializing in therapeutics and diagnostics that responded to the survey have sales abroad.

GRAPH 28. Priority markets for companies in the BioRegion of Catalonia, by country (2017)



Source: Biocat.

GRAPH 29. Collaborations of companies in the BioRegion of Catalonia, by country (2017)



We must remember that there is a wide variety of business models in the sector. Specifically, pharmaceutical corporations and medical device companies tend to handle technology development processes, industrial production, commercialization and exports. However, biotechnology companies focus more often on the early stages, with business models geared towards offering services that can be distributed commercially in other countries or licensing products to larger businesses.

In terms of operating revenue, in 2016, sales abroad made up 50.3% of turnover for companies selling products and 42% for those with services.

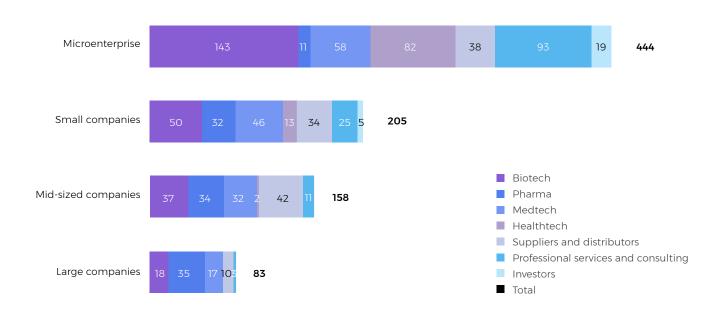
France, Germany, the United Kingdom and Italy are the top priorities and see the highest concentration of sales abroad for companies in the BioRegion (Graph 28). Outside of Europe, the United States, Mexico and China occupy the top spots in the ranking. Moreover, the ge-

ographic spread (presence in nearly 80 countries on all continents) is a significant figure regarding the international expansion of Catalan companies. In many cases, activity prior to export (investment or technological cooperation) allows companies to activate markets that would otherwise go unnoticed for purely macroeconomic reasons.

According to data from the survey, 15% of companies have a production plant or R&D center outside of Spain and 22% have commercial subsidiaries and other countries. Additionally, nearly 62% of companies surveyed have distribution agreements to further their commercial reach. This figure highlights the sector's capacity for internationalization, which is the most common distribution model.

With regard to expectations to open new markets over the coming two years, the USA leads the ranking (Graph 29), followed by the four large European markets (the United Kingdom, Germany, France and Italy), Canada, Japan and Mexico. It is also worth noting

GRAPH 30. Number of companies in the BioRegion of Catalonia, by size (turnover and workers) and sector (2017)



Source: Biocat and SABI.

Note: To analyze by size, only companies with information available on their turnover and number of workers are counted (90% of companies in the BioRegion of Catalonia)

Catalan companies' interest in countries like Chile and Portugal, despite not having been explicitly listed on the electronic survey.

In terms of standing international agreements, companies in the BioRegion with products are clearly inclined to out-licensing, as can be seen in the majority of growing ecosystems, as there is a lack of funding to continue with clinical development. On the other hand, services companies are mainly interested in scientific and technological development agreements, as in many cases this is a way to open up new markets with preferential fiscal conditions. In both cases, it seems only a minority is looking to purchase licenses.

The collaboration countries continue to be the same as in the previous report, although with some noteworthy changes (Graph 29). So, the USA is in a higher position than in market data, but has lost leadership to Germany, which has a great tradition of technology transfer and is more accessible than the innovation hubs in Boston, the Bay Area, Durham and San Diego. Plus, the United Kingdom dropped from third to fifth position amidst the process underway there to leave the EU. Asian countries are at the bottom, despite having important innovation milestones in recent years and a lot of interest in acquiring licenses and collaborating on technology. This may be due to cultural differences or a lack of technological internationalization strategies.

In terms of expectations for collaboration agreements over the coming years, Germany and the United States are also the top pri-

ority (Graph 29). Likewise, it must be noted that expectations for the United Kingdom, Canada and Japan surpass the current percentage of agreements, while the opposite is true for India and China.

Additionally, in terms of commercializing technology, collaboration continues to be the most common plan among companies, while interaction with other R&D stakeholders (universities, research centers or hospitals) is in the minority, according to the responses to this survey.

With regard to internationalization strategy, companies' main activity aims to improve the penetration of their products or open up new markets (39%), followed by establishing development collaborations (22%) and out-licensing (21%). As we've seen previously, in-licensing by companies in the BioRegion continues to be a minority trend, mainly in Catalan mid-pharma companies that are looking for molecules for pivotal trials (clinical studies that provide scientific evidence for approval of the drug by regulatory agencies) and to commercialize in Europe.

The main challenges in terms of internationalization are the lack of financial resources (38%), knowledge of the markets (29%) and an internationalization strategy (14%). Companies also noted other issues on the survey, like for example complex regulatory frameworks, established competitors and difficulties locating partners, which are in line with the lack of knowledge on the markets.

SIZE. LOCATION

In global terms, 91% of companies in the BioRegion are SMEs (Graph 30). Specifically, the great bulk of them are microenterprises,³⁹ making up 49.8% of all companies, followed by small companies⁴⁰ at 23%. Most small or micro-companies are in the core specialization sectors (biotech, medtech, healthtech, small pharmaceutical laboratories). As it is an innovation- and research-intensive sector, the main characteristic of these projects is that nearly all of their human resources are devoted to R&D&i.

Medium-sized companies make up 17.7% of the sector and only 9.3% are considered large companies (with more than 250 employees). Of these large companies, more than 40% are pharmaceutical corporations.

Additionally, there are no investment organizations among the medium or large companies and there are no healthtech businesses that fall into the latter category. On the other hand, medical technology companies have the most balanced spread across all the categories.

In terms of new projects, of the 569 companies created over the past 12 years, only 4.4% are currently medium or large corporations, which shows that most entrepreneurial projects in the healthcare and life sciences sector are, in addition to a very young business sector, a group of companies that grow very slowly in number of workers and operating revenue.

In terms of location, companies are concentrated in the province of Barcelona, which is home to 93.8% of the total. Furthermore, more than half of the companies are based in the city of Barcelona: 51.9%. It is worth noting the high percentage of investment bodies (83.3%) and professional services and consulting companies (80.6%) in the Catalan capital. Medical technology companies and suppliers and distributors, however, are more commonly located outside of the city of Barcelona (61.9% and 68.3%, respectively).

COMPANY SPECIALIZATION

There are 1,060 companies in the healthcare and life sciences sector in Catalonia: 280 biotechnology companies, 176 medical technology firms, 125 pharmaceutical corporations, 128 health-tech companies, 180 professional services and consulting firms, 139 non-specialized suppliers and distributors and 32 investment bodies

BIOTECHNOLOGY THERAPEUTICS AND DIAGNOSTICS COMPANIES

Of the 280 biotechnology companies in the BioRegion, 50 (17.9%) focus on therapeutics and diagnostics, specializing in 12 fields (Graph 31). The four main areas are: small molecules, peptides, antibodies and vaccines. This subsector is intensive in capital and risk, but also highly scalable and profitable. This is why it has a higher rate of company disappearance, as they depend on the positive re-

sults of research and/or financial and structural support for clinical development of molecules.

With regard to the therapeutic areas of biotechnology therapeutics and diagnostics companies (Graph 32), we see a very noteworthy presence in the field of neoplasms, cancer and oncology (38%). As a whole, the three main areas are in line with the research being done internationally: neoplasms, cancer and oncology; diseases of the nervous system, infectious and parasitic diseases; and, finally, dermatology.

BIOTECHNOLOGY R&D SERVICES COMPANIES

The BioRegion of Catalonia has 125 biotechnology companies that offer R&D services, 43.9% of all biotechnology firms. Of the 13 areas of specialization in these services companies (Graph 33), the main ones are: Contract Research Organizations, which covers all clinical CROs that provide clinical services to pharmaceutical companies and companies working under contract on basic and translational research; analytical services; and, finally, diagnostic services.

Compared to the previous report, it is worth noting the increase in bioinformatics companies, which in just two years have gone from making up 4% of the total (2015) to 11% (2017). This increase coincides with Catalonia's consolidation as a bioinformatics node with the Centre Nacional d'Anàlisi Genòmica (CNAG-CRG), Barcelona Supercomputing Center (BSC) and Bioinformatics Barcelona Association (BIB), as well as attracting many renowned scientists in this field. Moreover, as mentioned in the section on mergers and acquisitions, in late 2017 Mind the Byte acquired Intelligent Pharma, making it one of the largest companies in Europe using artificial intelligence for drug discovery.

OTHER BIOTECHNOLOGY COMPANIES

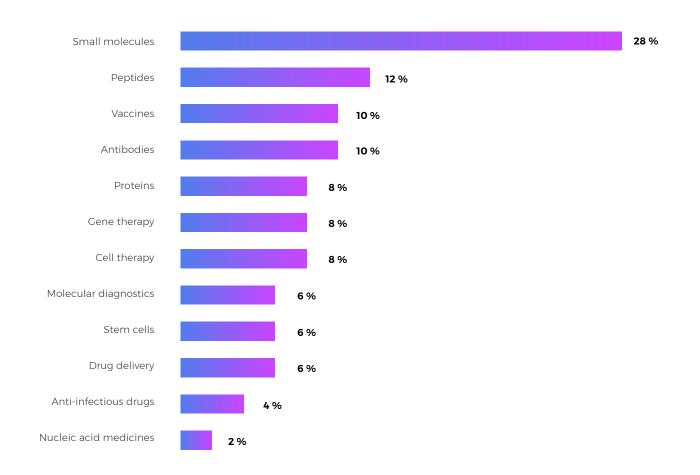
There are 105 companies in the BioRegion (37.5% of all biotechnology companies) that fall into the subsector of other biotechnology companies, working in seven different fields (Graph 34), mainly veterinary science. It is also worth noting the fields of nutraceuticals (a term coined by combining 'nutrition' and 'pharmaceuticals', which accounted for less than 10% in 2015 and now makes up 19%), food, cosmetics and agrobiotechnology. Furthermore, there are 2 specialized suppliers and distributors.

PHARMACEUTICAL COMPANIES

The BioRegion is home to 125 pharmaceutical companies, of which 64 are pharmaceutical laboratories and the other 61, companies that supply, distribute or market their own or licensed drugs. Of the 11 fields of specialization (Graph 35), the 64 pharmaceutical companies in the BioRegion stand out in generics, anti-infectious drugs and small molecules and biosimilars. These areas are associated with classical chemistry-based pharmacological production.

From the standpoint of therapeutic areas, the snapshot of the pharmaceutical companies in the BioRegion (Graph 36) differs from that of the biotechnology therapeutics and diagnostics companies. So, the distribution among the different areas is more balanced,

GRAPH 31. Specialization of biotechnology therapeutics and diagnostics companies in the BioRegion of Catalonia, by field (2017)



led by infectious and parasitic diseases (36%) and dermatological conditions (33%).

ulatory changes in Europe have slowed the creation of new companies in the early stages.

MEDICAL TECHNOLOGY COMPANIES

The medical technology subsector is made up of 176 companies (68 suppliers and distributors) focusing on 17 areas of specialization (Graph 37). The main ones are: electro-mechanical medical devices, single-use disposable devices, dental devices and reusable instruments.

Compared to the previous report, the leading areas are the same but in a different order, though the small percentage of companies working in diagnostic devices and innovative and emerging fields (biomaterials and regenerative medicine) remains the same. These subsectors are highly innovative and found mainly at public bodies (universities, research centers and hospitals). Moreover, recent reg-

HEALTHTECH COMPANIES

For the first time, this Biocat Report is looking at the 128 companies in the healthtech subsector separately, based on 13 areas of specialization (Graph 38). So, the most representative activities are mobile apps for health and fitness, electronic medical records (EMR) and telehealth.

The healthtech subsector is emerging and has a wide range of applications (many geared directly towards use by patients and others to improving healthcare providers). It is the result of the convergence of two highly dynamic sectors: healthcare and life sciences and information and communication technology (ICT). It is, therefore, a highly volatile sector, where new companies appear and dis-

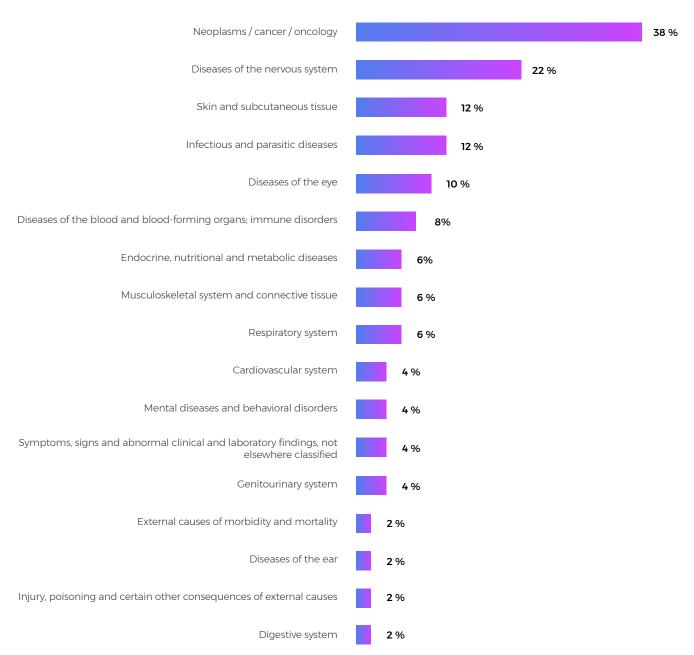
appear faster because their survival depends on how useful their products actually are and whether they find a place in healthcare systems.

shows that the Catalan health analytics and big data scene is still sparse.

According to a study conducted by the European Commission,⁴¹ Catalonia is one of the leading European regions in terms of density of companies and organizations working in big data, an important area in the healthtech sector. Nevertheless, Graph 38

The presence of healthcare at the Mobile World Congress (MWC) and 4 Years From Now (4YFN) is an interesting catalyst for this subsector, as it allows for contact among the various stakeholders and speeds up the pace of innovation. Moreover, the government is providing instruments to bring these innovations into the public sector.

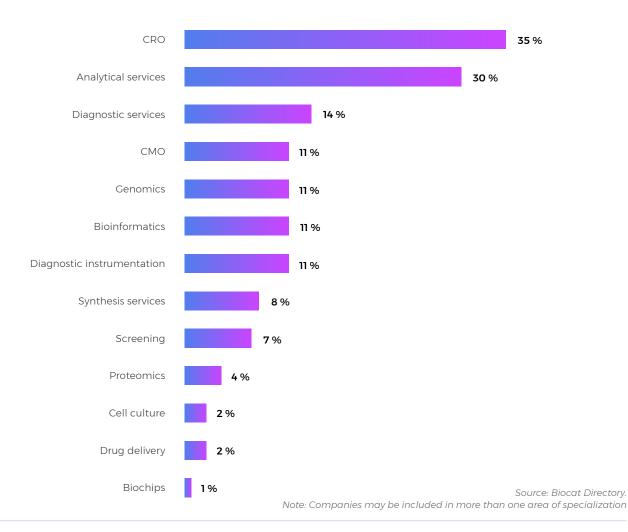
GRAPH 32. Therapeutic areas of biotechnology therapeutics and diagnostics companies in the BioRegion of Catalonia (2017)



Source: Biocat Directory.

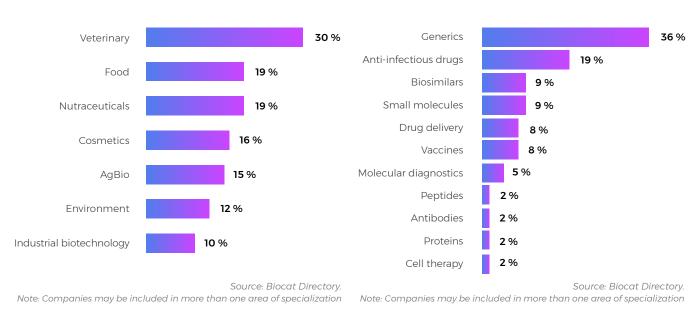
Note: Companies may be included in more than one area of specialization

GRAPH 33. Specialization of biotechnology R&D companies in the BioRegion of Catalonia, by field (2017)

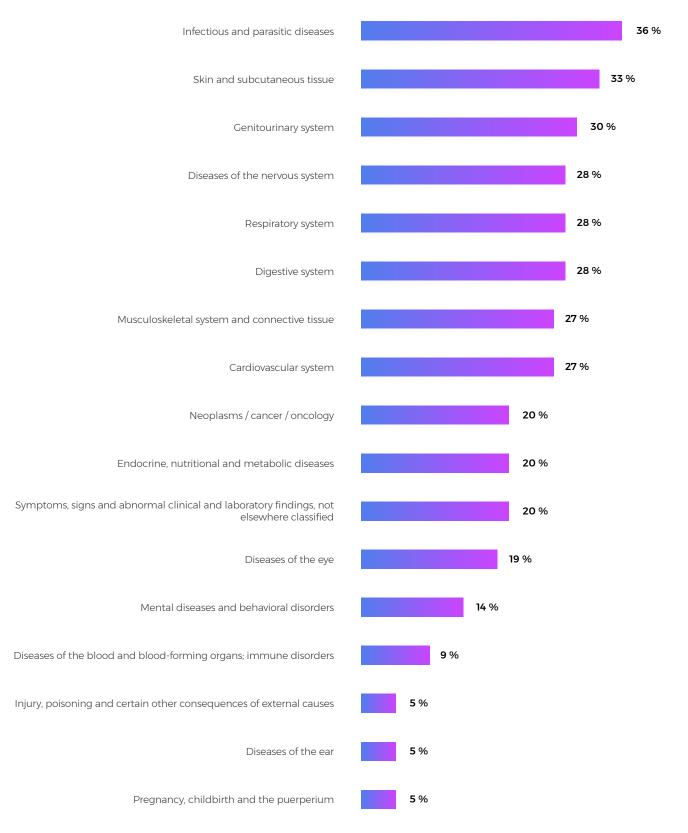


GRAPH 34. Specialization of other biotechnology companies in the BioRegion of Catalonia, by field (2017)

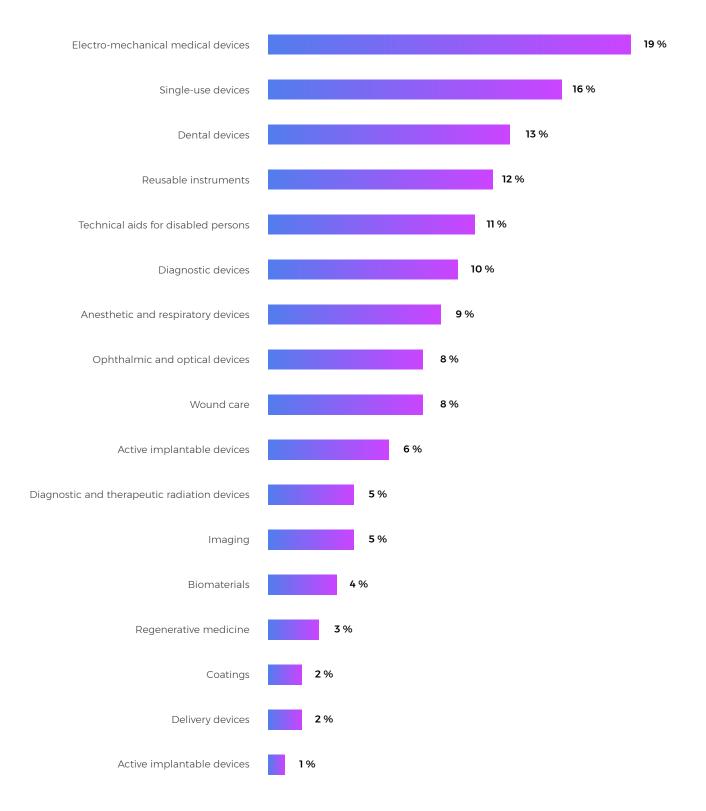
GRAPH 35. Specialization of pharmaceutical companies in the BioRegion of Catalonia, by field (2017)



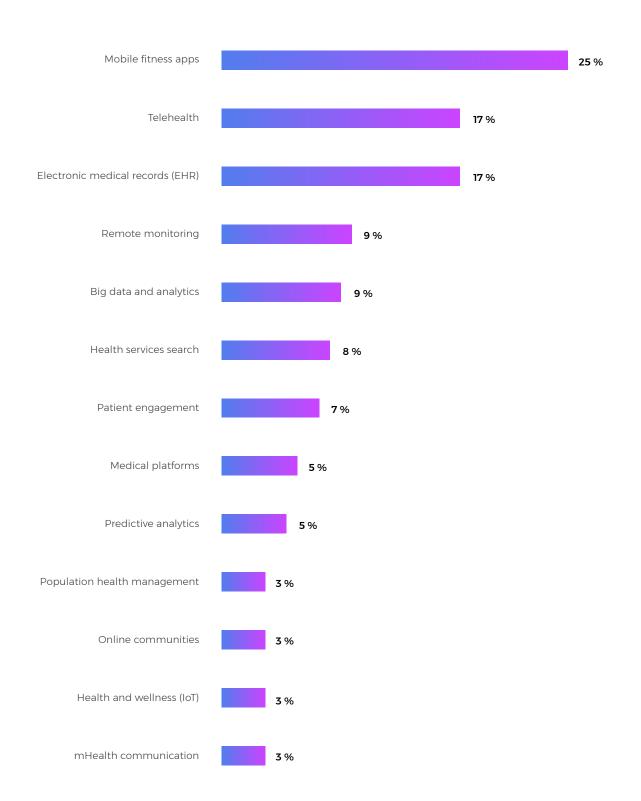
GRAPH 36. Therapeutic areas of pharmaceutical companies in the BioRegion of Catalonia (2017)



GRAPH 37. Specialization of medical technology companies in the BioRegion of Catalonia, by field (2017)



GRAPH 38. Specialization of healthtech companies in the BioRegion of Catalonia, by field (2017)



Notes

- ³⁰ See Methodology section.
- ³¹ ASEBIO. 2016 ASEBIO Report. [http://www.asebio.com/es/informe anual.cfm].
- ³² Farmalndustria. 2016 Annual report. [http://www.farmaindustria. es/web/documento/memoria-anual-2016/].
- ³³ FENIN. Memoria anual de sostenibilidad 2016. [http://tinyurl.com/yaxlygp6].
- ³⁴ Global Entrepreneurship Monitor (GEM): Catalonia Executive Report 2016 [http://tinyurl.com/yau9k3ta].
- ³⁵ Note: This graph only includes capital funding for emerging or innovative Catalan companies, so funding for traditional pharmaceutical corporations is not included. The Public/Private category includes investment by public bodies that are exclusively public and those in conjunction with the private category, which encompasses venture capital firms, licensing deals, private debt, industrial partners, MAB, business angels/family offices, crowdfunding, entrepreneurs and FFF (family, fools, friends).
- ³⁶ Note: This graph only includes capital funding for emerging or innovative Catalan companies, so funding for traditional pharmaceutical corporations is not included. The Public/Private category includes investment by public bodies that are exclusively public and those in conjunction with the private category, which encompasses venture capital firms, licensing deals, private debt, industrial partners, MAB, business angels/family offices, crowdfunding, entrepreneurs and FFF (family, fools, friends).
- ³⁷ ACCIÓ based on FDI Markets.
- ³⁸ Bigorrra, Joan; Bosch, Fèlix. Philanthropy in biosanitary research and innovation in Catalonia. Esteve Foundation [http://www.raco.cat/index.php/QuadernsFDAE/issue/view/22054/showToc].
- ³⁹ Microenterprise: company with fewer than 10 employees and operational income under €2 million per year.
- 40 Small company: company with fewer than 50 employees and turnover under \in 10 million.
- ⁴¹ European Commission. DataLandscape [http://datalandscape.eu].

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Research system and bodies in the BioRegion of Catalonia



Research system and bodies in the BioRegion of Catalonia

CATALAN RESEARCH SYSTEM

Since the 2015 Biocat Report was published, the Catalan health-care and life sciences research system hasn't seen any large-scale changes, although some research and technology centers have banded together in order to gain in critical mass and be able to better compete internationally. In this regard, most indicators continue to show the internal efficiency and external competitiveness of Catalonia's research model.

Before looking at the various research stakeholders (centers, universities, groups, hospitals, etc.), we will focus on defining and analyzing the five transversal elements in the Catalan scientific system: researchers and ICREA researchers, ERC grants, production of scientific papers, number of resulting companies, and latest news from the period covered in this report.

NEWS IN THE RESEARCH SYSTEM

The 2015-2017 period brought about some noteworthy news in the health research arena, as well as new and consolidating public initiatives to promote the scientific transfer of knowledge generated in Catalonia.

In April 2017, Barcelona was announced as the new home to the European Molecular Biology Laboratory (EMBL), specializing in the biology of organs and tissues, congenital defects and diseases of the immune system. Its headquarters will be located at the Barcelona Biomedical Research Park (PRBB) to facilitate work with researchers at the Center for Genomic Regulation (CRG). The total investment through 2021 will be €24 million, contributed by the EMBL (€16 million), the Spanish government (€6 million) and the Government of Catalonia (€2 million).

In September 2017, the news came of a new center being created: the Center for the Integration of Medicine and Innovative Technologies in Catalonia (CIMTI). Its goal is to promote innovation in the social and healthcare system through projects with a significant

impact on improving patients' wellbeing. CIMTI was promoted by the LEITAT technology center, with support from the Government of Catalonia Ministry of Health and the Agency for Health Quality and Assessment of Catalonia (AQuAS).

Additionally, the city of Barcelona submitted its candidacy to host the European Medicines Agency (EMA) when it leaves London due to Brexit. The candidacy had public and private support and came fifth out of the 16 candidacies in number of votes, surpassed by Bratislava and the three finalists: Milan, Copenhagen and the winner, Amsterdam.

Previously, the Government of Catalonia had invested in health-care research through direct structural subsidies for institutes and centers in this area of knowledge. Now, the Catalan Ministry of Health's Strategic Plan for Health Research and Innovation (PERIS 2016-2020)⁴² is a powerful, innovative planning instrument that has already closed the first calls open through the end of 2016, with €19.9 million invested, 40 multi-center projects granted and 19 organizations receiving funds.⁴³

This plan is a huge opportunity for the research entities in the healthcare sciences in Catalonia.⁴⁴ The new system of awarding subsidies on a competitive basis seeks to promote professional talent and employability, strengthen institutions, promote knowledge of excellence, support scientific and technical facilities and, finally, foster innovation and health.

Another noteworthy development is the Public Data Analysis for Health Research and Innovation Program (PADRIS), a project by AQuAS.⁴⁵ This program gives the scientific community access to relevant healthcare data in order to promote research, innovation and assessment in healthcare by reusing and cross-referencing healthcare data generated by the Integrated Public Health System of Catalonia (SISCAT).

Looking now at public initiatives to transfer scientific knowledge, the Government of Catalonia Industrial PhD program⁴⁶ has promoted the research projects of companies and institutions with PhD candidates doing research training, in collaboration with a university or research center, which is then used for a PhD dissertation.

Between 2012 and 2016, the Industrial PhD program approved 345 projects, 70 of which were in the life sciences (20.3%). So far, the Program has leveraged €48 million (two thirds from the private sector) with involvement from 235 companies, 11 universities, 18 CERCA centers and 2 large-scale facilities.

In 2016, the Government of Catalonia kicked off the Knowledge Industry Program in order to promote the development of new science-based companies derived from the research.

Additionally, the Gínjol⁴⁷ patent fund is a program promoted by the CERCA Institution in agreement with some of its centers to strengthen knowledge-transfer projects by protecting intellectual and industrial property. Funding can be requested to cover services required to protect, valorize and market the results of research generated through the project submitted. So far, there have been

two editions (2016, 2017), which funded 18 projects with a total of \leq 180,000 (15 in the healthcare and life sciences sector).

In February 2018, Biocat launched the CRAASH Barcelona acceleration program: a 12-week course to help research teams from Cata-Ionia and other European countries successfully launch innovations to market in the fields of medical devices, diagnostics and e-health and digital health. The program selects and trains eight research teams, so they can market their technology within 3 to 5 years. The projects are guided by expert mentors from CIMIT (Boston), the most experienced accelerator in the world. In 15 years, CIMIT has successfully accelerated more than 600 healthtech projects, has doubled the product-to-market rate and has halved the time it takes to reach the next phase. The teams participating in CRAASH Barcelona will validate their project in some of the best health ecosystems in the USA and Europe, and will present them to investors and other members of the Boston ecosystem. CRAASH Barcelona is organized by Biocat in collaboration with CIMIT and is part of the EIT Health bootcamps program.

INTERNAL R&D SPENDING AND STAFF

In 2015, internal spending on R&D activities in Catalonia totaled $\tt \leqslant 3.1068$ billion, 1.52% of the Catalan Gross National Product (GDP) and 23.6% of all investment in Spain. 48

Catalonia continues to be above the Spanish average in internal R&D expenditure as a percentage of the GDP (Table 15),⁴⁹ but this indicator has only fallen since 2009 and, in any case, is far from the level seen in the world's top economies. Since the beginning of the recession, convergence with the European Union (EU) has been staunched in the middle term. On a national level, the 2017 Cotec Report⁵⁰ warns that Spanish R&D investment has dropped 10% since the beginning of the recession, while it is up 25% in the EU as a whole.

In absolute terms, internal R&D expenditure in Catalonia fell 5.7% between 2009 and 2015. In terms of the percentage of the GDP, Catalonia has seen this figure drop 10.6%. By sector, the private arena (companies and private nonprofit organizations – NPO) have seen the greatest decrease (7.3%), which has consolidated the specific loss of importance of this arena, going from 68.4% (2000) to 57.5% (2015). This phenomenon contrasts with the main economies in the world, where private initiative is clearly the majority in terms of promoting R&D investment.

Additionally, Catalan investment in R&D for higher education and public administration has contracted 5.3% and 1.5%, respectively. In this area, it must be noted that the Government of Catalonia has attempted to maintain R&D investment levels while public spending in Spain as a whole dropped 13.9% between 2009 and 2015.

R&D activities are essential to the healthcare and life sciences business sector, but most specifically for biotechnology and pharmaceutical companies. This business sector is considered highly innovative, research-intensive, highly productive, a source of qualified jobs and highly dynamic in foreign trade. Between 2015 and 2017,

TABLE 15. R&D expenditure as a percentage of the GDP (international, 2000-2015)

Country	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Germany	2.4	2.4	2.4	2.5	2.4	2.4	2.5	2.5	2.6	2.7	2.7	2.8	2.9	2.8	2.9	2.9
Catalonia	1.1	1	1.2	1.3	1.3	1.4	1.4	1.5	1.6	1.7	1.7	1.6	1.5	1.5	1.5	1.5
South Korea	2.2	2.3	2.3	2.4	2.5	2.6	2.8	3	3.1	3.3	3.5	3.7	4	4.2	4.3	4.2
Spain	0.9	0.9	1	1	1	1.1	1.2	1.2	1.3	1.4	1.4	1.3	1.3	1.3	1.2	1.2
USA	2.6	2.6	2.6	2.6	2.5	2.5	2.6	2.6	2.8	2.8	2.7	2.8	2.7	2.7	2.8	2.8
France	2.1	2.1	2.2	2.1	2.1	2	2.1	2	2.1	2.2	2.2	2.2	2.2	2.2	2.2	2.2
Italy	1	1	1.1	1.1	1.1	1.1	1.1	1.1	1.2	1.2	1.2	1.2	1.3	1.3	1.4	1.3
Japan	2.9	3	3	3	3	3.2	3.3	3.3	3.3	3.2	3.1	3.2	3.2	3.3	3.4	3.3
OECD	2.1	2.2	2.1	2.1	2.1	2.1	2.2	2.2	2.3	2.3	2.3	2.3	2.3	2.4	2.4	2.4
United Kingdom	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.6	1.7	1.7	1.7
EU	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.9	1.9	1.9	2	2
China	0.9	0.9	1.1	1.1	1.2	1.3	1.4	1.4	1.4	1.7	1.7	1.8	1.9	2	2	2.1

Source: OECD and the Spanish R&D+l Observatory (ICONO) of the Spanish Foundation for Science and Technology (FECYT).

business indicators for R&D spending on staff tended to return to pre-recession levels.

The 2015 INE survey on the use of biotechnology⁵¹ puts Catalonia as the leading Spanish community in internal spending on R&D activities in biotechnology, with \leqslant 454.7 million in 2015. This is 29.5% of all Spanish spending in biotechnology and 14.6% of the overall internal expenditure in Catalonia.

Specifically, Catalan companies account for €188 million, 32.5% of the Spanish total (in 2014, total spending was €149.4 million). Current investment equals approximately 5% of the joint turnover in the biotechnology sector.

According to Farmalndustria, Catalan pharmaceutical companies make up 40.6% of internal national spending in R&D (€238.8 million) and 24.4% of external spending (€101.7 million). Nevertheless, the investment of Catalan pharmaceutical companies in R&D activities is just slightly more than 4% of their joint turnover, while the European Federation of Pharmaceutical Industries and Associations (EFPIA) calculates the European industry invests more than 17%.52

With regard to human resources devoted to R&D activities in full-time equivalent (FTE), the number of researchers in all sectors was up from 14,812 (2000) to 26,403 (2015) and, over the same period, total staff (including technicians and support staff) rose from 25,107

TABLE 16. Researchers compared to employed population (international, 2000-2015)

Country	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Germany	6.5	6.6	6.7	6.9	6.9	6.9	7.1	7.2	7.4	7.8	8	8.2	8.4	8.4	8.3	9
Catalonia	5.4	5.2	5.4	6.1	6.7	6.8	7	7	7.4	8.2	8.3	7.9	8.4	8.6	8.4	8.6
South Korea	5.1	6.3	6.4	6.8	6.9	7.9	8.6	9.5	10	10.4	11.1	11.9	12.8	12.8	13.5	13.7
Spain	4.6	4.6	4.7	5.1	5.3	5.6	5.6	5.8	6.1	6.7	6.9	6.8	6.9	6.9	6.8	6.6
USA	7.1	7.3	7.6	8	7.8	7.7	7.7	7.6	8.1	8.8	8.5	8.8	8.7	8.9	9.1	9.1
France	6.7	6.8	7.1	7.4	7.7	7.7	7.9	8.2	8.4	8.7	9.1	9.2	9.5	9.7	9.9	10.1
Italy	2.9	2.8	3	2.9	3	3.4	3.5	3.7	3.8	4.1	4.2	4.3	4.5	4.8	4.9	4.9
Japan	9.9	10	9.6	10.1	10.1	10.4	10.4	10.3	9.9	10	10	10	9.9	10.1	10.4	10
OECD	6.1	6.3	6.4	6.8	6.8	7	7.1	7	7.2	7.6	7.6	7.8	7.9	8.1	8.2	8.3
United Kingdom	6.2	6.6	7.1	7.7	8	8.6	8.7	8.6	8.5	8.8	8.8	8.6	8.6	8.9	9	9.3
EU	5.2	5.4	5.6	5.8	6	6.2	6.3	6.4	6.6	6.8	7.1	7.2	7.5	7.7	7.8	8
China	1	1	1.1	1.2	1.3	1.5	1.6	1.9	2.1	1.5	1.6	1.7	1.8	1.9	2	2.1

Source: OECD and the Spanish R&D+I Observatory (ICONO) of the Spanish Foundation for Science and Technology (FECYT).

Note: Number of researchers per 1,000 people employed.

TABLE 17. Staff devoted to R&D activities compared to employed population (international, 2000-2015)

Country	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Germany	12.1	12.1	12.1	12.1	12	12.1	12.3	12.6	12.8	13.1	13.4	13.8	14.1	13.9	14.2	14.9
Catalonia	9.1	9.2	9.8	11.1	11.8	11.5	11.7	12	13	14.4	14.3	13.9	14.7	15	14.5	14.6
South Korea	6.5	7.7	7.8	8.4	8.6	9.4	10.3	11.5	12.5	13.2	14.1	14.9	16	16	16.8	17
Spain	7.2	7.3	7.6	8.3	8.5	8.8	9.2	9.5	10.1	11.1	11.3	11.3	11.4	11.4	11.1	10.9
USA																
France	12.8	12.8	13	13.1	13.4	13.3	13.7	13.9	14.1	14.5	14.8	14.9	15.1	15.3	15.5	15.6
Italy	6.5	6.6	6.9	6.7	6.7	7.2	7.7	8.2	8.7	9.1	9.1	9.2	9.7	10.2	10.3	10.1
Japan	13.7	13.3	12.9	13.3	13.4	13.7	13.8	13.7	13.3	13.4	13.4	13.3	13.1	13.2	13.6	13.2
OECD																
United Kingdom	10.5	10.8	11.1	11.2	11.2	11.3	11.5	11.7	11.6	11.9	12	12.1	12	12.6	12.9	13.3
EU	9.4	9.5	9.6	9.7	9.8	10	10.2	10.4	10.7	10.9	11.3	11.6	11.9	12.1	12.3	12.5
China	1.3	1.3	1.4	1.5	1.6	1.8	2	2.3	2.6	3	3.4	3.8	4.2	4.6	4.8	4.9

Source: OECD and the Spanish R&D+I Observatory (ICONO) of the Spanish Foundation for Science and Technology (FECYT).

Note: Number of people devoted to R&D activities per 1,000 people employed.

Data for the United States of America (USA) and the OECD is not available.

to 44,826. So, growth of these two indicators was nearly 80%, despite the effects of the recession. Staff and researchers in Catalonia make up, respectively, 22.3% and 21.6% of all those in Spain.

With regard to the working population (Table 16 and 17), the indicators for human resources in the Catalan system are above the EU average and not far from those of other leading international economies.

In terms of employees at companies in the sector, the INE⁵³ estimates there are 2,008 FTE employees devoted to R&D activities (27.9% of the national total; 1,707 in 2014) at Catalan biotechnology firms, of which 1,199 are researchers (28%; 995 in 2014). At Catalan pharmaceutical companies, there were an estimated 2,500 FTE employees devoted to R&D in 2015, 1,300 of which would be researchers.

Regarding the state of innovation in Catalonia, the 2017 Regional Innovation Scoreboard⁵⁴ study looks at the innovative development of 220 European regions. According to the regional classification, in 2017 there were 53 leading regions in innovation; 60 were strongly innovative; 85, moderately innovative; and 22, modestly innovative. Catalonia appears as moderate innovator but is the top-ranking region in the Moderate Innovators group, with a performance of 88.5% of the EU average.

PARTICIPATION IN EUROPEAN RESEARCH AND INNOVATION INITIATIVES

Over the past 20 years, Catalonia has increased its capacity to attract European funds nearly 30-fold, while the resources the EU earmarks for this have only grown 7-fold. The Catalan research system has gone from attracting €131.8 million under the 5th Framework program (1998-2002) to attracting €992.4 million in the 7th Framework program (2007-2013).⁵⁵

TABLE 18. H2020 Program: Funds by type of organization (Catalonia, 2014-2017)

Type of organization	Resources (M€)	% Catalonia
Companies	185	28
CERCA centers	159.2	24
Universities	141.4	21
Other R&D bodies	57.4	9
Technology centers	32.5	5
Other	31.1	5
Public administrations	26.9	4
Large-scale facilities	26.9	4
Science and technology parks	3	0

Source: AGAUR (data through October 2017).

Horizon 2020 (H2020) is the European Commission's current program to fund research, innovation and competitiveness for the 2014-2020 period, with a total budget of €77 billion. Over the first years of H2020 (2014-2017), Catalonia attracted €664 million. These funds have gone to 503 organizations participating in over 1,600 projects. The volume of funds attracted by Catalan organizations (companies, universities, research centers, etc.) makes up 28.8% of all the funds granted to Spain and 2.7% of the European total (EU-28). These figures are nearly double what would be expected based on population.⁵⁶

The classification by type of body (Table 18) shows that 73% of all resources granted in Catalonia under the H2020 program between 2014 and 2017 went to research centers, companies and universities

The funds attracted through particularly important calls are especially noteworthy, like the Future and Emerging Technology (FET) call, at 4.6%, and the Marie Skłodowska-Curie actions (MSCA), taking 4.3% of all funds. With regard to programs to tackle social challenges, projects in healthcare, demographic change and wellbeing took 3.3% of all funds.

Grants from the European Research Council (ERC) deserve to be looked at separately, with Catalonia making up 3.2% of the European Research Area (ERA) and 52.64% of the grants awarded.

Smart specialization is a prerequisite for any investment in research and innovation co-funded by the European Commission. The member states and regions have to detect their areas with potential and concentrate the European funds on economic activities that truly have the ability to transform their territory. The research and innovation strategy for the smart specialization of Catalonia (RIS3CAT) lays out the priorities for public R&D&i policy. The first RIS3CAT calls approved 131 projects involving more than 250 bodies, with €114.89 million in investment. Research and technology centers, with nearly €50 million in investment, benefited from more than 43% of the total investment and obtained 53% of the grants from the ERDF operational program.

In the calls analyzed in this report (those closed as of June 2017), healthcare (with ${\in}56.54$ million) has consolidated its leadership in investment in the sector by area, and biotechnology (with ${\in}53.59$ million), in investment in facilitating technology.

In the first call for RIS3CAT communities, 5 communities were accredited (one coordinated by Biocat) with projects valued at a total of €45.6 million. Healthcare makes up 40% of all investment.

PATENTS IN HEALTHCARE AND LIFE SCIENCES

The indicators on generating and exploiting patents have been one of the recurring weaknesses of the science and technology system in Catalonia and the rest of Spain.

This report analyzes the Catalan patents in the healthcare and life sciences sector filed between 2010 and 2016 with the European Patent Office (EPO) and the World Intellectual Property Organization (WIPO), through the Patent Corporation Treaty (PCT). Any patent with at least one applicant with an address in Catalonia is included. Unfortunately, the same detail of information is not available for patents granted.⁵⁸

Records have been found of 2,489 Catalan patents in the healthcare and life sciences sector filed with the EPO, 41.1% of the Spanish total. Moreover, there's a clear upward trend (up 20.4%) from 2015 to 2016 (Table 19), which should continue to be looked at in future editions of this report. Additionally, 1,531 PCT patents were found filed with the WIPO by Catalan applicants, 23.8% of the Spanish total.

These figures show that organizations in the BioRegion filed 335.23 and 206.2 patents per million inhabitants with the EPO and WIPO, respectively, well above the Spanish average (130.31 and 138.72) (Table 20). These figures, however, are still far from the leading countries: Switzerland, Luxembourg, Netherlands, Denmark and Germany. The ranking is led by Switzerland, with 3,293.94 and 1,885.66 patents in healthcare and life sciences per million inhabitants filed with the EPO and WIPO, respectively, almost 10 times the Catalan indicators.

Regarding the sectors of the Catalan applicants, the breakdown of patents filed with the WIPO shows the predominance of filings from the business arena (60.5%) and, to a lesser degree, research bodies (32.4%). Moreover, just 5.2% of patents filed resulted from a collaboration between the two sectors and the remaining 1.8% were filed by individuals. Additionally, the number of patents generated through collaboration with other organizations from the same sector is much higher among patents from research bodies (54.4%) than among those with two or more companies on the application (only 3.9%).

The Catalan companies with a significant number of patent applications in the healthcare and life sciences sector filed with the EPO are pharmaceutical corporations: Esteve, Almirall, Grifols, Ferrer and Medichem. However, we must recognize the efforts to patent made by research bodies like, for example, Catalan Institution for Research and Advanced Studies (ICREA), Autonomous University of Barcelona (UAB), University of Barcelona (UB), Vall d'Hebron Research Institute (VHIR) and Hospital Clinic Barcelona.

A WIPO⁵⁹ report identified the 100 top innovation clusters in the

TABLE 19. Healthcare and life sciences patents filed with the EPO and WIPO (Catalonia, 2010-2016)

Patents office	2010	2011	2012	2013	2014	2015	2016	total
EPO patents	339	346	368	353	358	329	396	2,489
WIPO patents	227	220	230	231	202	203	218	1,531

Source: Compiled internally from EPO and WIPO patent databases.

TABLE 20. Healthcare and life sciences patents filed with the EPO and WIPO (international, 2010-2016)

	EPO			WIPO		
Country	Patents	Population	Pat/Pob	Patents	Population	Pat/Pob
Switzerland	31,396	9.8	3,203.9	18,478	9.8	1,885.7
Luxembourg	1,684	0.6	2,961.1	1,002	0.6	1,761.9
Netherlands	23,022	16.9	1,359.7	17,699	16.9	1,045.3
Denmark	7,637	5.7	1,344.1	5,195	5.7	914.3
Germany	99,320	81.7	1,215.9	53,172	81.7	650.9
Sweden	10,403	9.7	1,072.9	7,597	9.7	783.5
Finland	5,715	5.5	1,042.8	5,171	5.5	943.5
Israel	7,361	8.4	878.7	7,977	8.4	952.3
Austria	7,179	8.6	831.9	3,915	8.6	453.7
Japan	102,185	126.8	806.0	122,676	126.8	967.6
Ireland	3,356	4.6	723.0	2,376	4.6	511.9
Belgium	8,066	11.2	719.4	5,891	11.2	525.4
United States	210,869	321.7	655.5	212,819	321.7	661.5
France	40,620	66.5	610.8	28,289	66.5	425.4
South Korea	24,307	50.6	480.2	33,450	50.6	660.9
Norway	2,092	5.2	403.0	1,959	5.2	377.4
United Kingdom	24,178	65.1	371.3	23,979	65.1	368.3
Slovenia	697	2.1	337.9	441	2.1	213.8
Catalonia	2,489	7.4	335.2	1,531	7.4	206.2
Canada	10,988	35.9	306.5	11,981	35.9	334.2
Italy	14,984	60.7	246.7	9,029	60.7	148.7
Australia	5,285	24.1	219.6	6,796	24.1	282.4
Spain	6,050	46.4	130.3	6,440	46.4	138.7
World	665,560	7,349.0	90.6	596,646	7,349.0	81.2
Latvia	146	2.0	73.8	114	2.0	57.6
Czechia	699	10.5	66.3	745	10.5	70.7
Portugal	508	10.4	49.0	618	10.4	59.7
Greece	401	10.9	36.9	394	10.9	36.3
Poland	1,343	38.5	34.9	1,142	38.5	29.7
Slovakia	110	5.4	20.3	173	5.4	31.9
South Africa	566	55.0	10.3	1,046	55.0	19.0
China	10,808	1,374.6	7.9	44,093	1,374.6	32.1
Russian Federation	1,119	146.3	7.7	3,153	146.3	21.6
Romania	112	19.9	5.6	178	19.9	9.0
Brazil	862	207.8	4.2	1,986	207.8	9.6
India	3,994	1,311.0	3.1	9,034	1,311.0	6.9

Source: Compiled internally from EPO and WIPO patent databases. Note: Population in million inhabitants.

world. Barcelona, at 52nd (2,003 patents between 2011 and 2015), is the highest ranked cluster in Spain. In terms of specialization, according to this report, Barcelona stands out above all in the pharmaceutical arena (9.4%), where it is ranked sixth among the top 15 clusters in the world.

Information on patents licensed would be extremely interesting, however there is hardly any data on the research sector, where the

indicators are quite low. The Agency for Health Quality and Assessment of Catalonia (AQuAS)⁶⁰ highlights a growing trend of patents out-licensed/transferred by the 11 healthcare research institutes in Catalonia from 2012, reaching a total of 40 patents in 2015. Additionally, Conferencia de Rectores de las Universidades Españolas (CRUE)⁶¹ puts income from licensing at €697,000 (2015) for the seven Catalan public universities.

RESEARCHERS AT THE CATALAN INSTITUTION FOR RESEARCH AND ADVANCED STUDIES (ICREA)

Since 2001, ICREA has made a firm commitment to attracting scientific talent, which has boosted the excellence and competitiveness of the Catalan research system. It is a foundation created by the Government of Catalonia to hire researchers from around the world and make it easier for Catalan researchers to return from abroad. However, the resources attracted and results obtained by ICREA researchers are attributed to their host institution (above all, universities and research centers).

In 2017, Catalonia had 254 ICREA researchers of 26 different nationalities, who attracted €90 million in competitive funds, half through European programs.⁶² 29% of ICREA researchers work in the life sciences and 40% of the competitive funds went to this area of research.

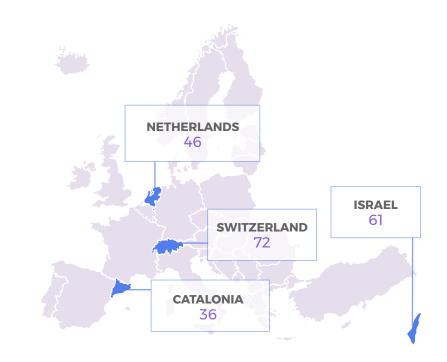
As a whole, the ICREA researchers have published 2,002 scientific papers (93% in journals in the first quartile), which were cited 2.3 times more than the average in each discipline. The excellence of their publications is 9.2 times higher than the expected value given the volume of publications in Catalonia (RHCP 9.237), according to a study Biocat commissioned to the Research Group on Bibliometrics (BAC).

One in three ICREA researchers have been awarded an ERC grant, and each ICREA researcher maintains an average of 7.2 full-time jobs. Moreover, since 2001, ICREA researchers have created a total of 21 spin-offs (5 in 2017) that have attracted a total of €90 million. Of these 24 companies, 20 are in the life sciences arena.

GRANTS FROM THE EUROPEAN RESEARCH COUNCIL (ERC)

Under the framework of the H2020 program, the ERC awards grants for ground-breaking high-risk projects to advance scientific research beyond the frontiers of knowledge. The proposals undergo a rigorous evaluation process, based exclusively on their scientific excellence.

MAP 7. ERC grants per million inhabitants



Source: AGAUR (December 2017).

From 2007 to December 2017, Catalonia received 269 ERC grants, 52.6% of all those awarded in Spain and 3.2% of the global total in the European Research Area (ERA),63 So, the Catalan research system has attracted funding for projects of excellence valued at approximately €419 million.

By organization, the breakdown of ERC grants is as follows: CERCA centers, 50.2%; universities, 37.2%; Spanish National Research Council centers (CSIC), 7.3%; other research centers, 2.7%; large-scale facilities, 2.3%; and science and technology parks, 0.4%.

Of the 269 ERC grants awarded to scientists working in Catalonia, 126 were in engineering and the physical sciences (47%), 77 in the life sciences (30%) and 65 in humanities and the social sciences (23%).

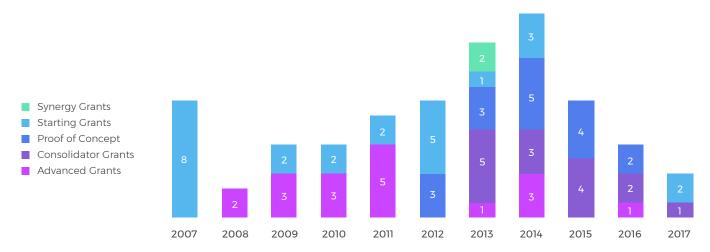
By number of grants per million inhabitants, Catalonia is ranked fourth in the ERA and second among EU member states, surpassed only by Switzerland, Israel and the Netherlands.

By type of ERC grant, the category in which

research in the BioRegion has been most successful is the Starting Grants, geared towards postdoc researchers that will set up their own research teams within two to seven years. Since 2007, researchers in the life sciences established in the BioRegion have been awarded 25 grants of this type. The next category is the Advanced Grants. for senior researchers with more than 10 years of experience: research in the BioRegion was awarded 18 of these grants. With regard to the Proof of Concept category, which supports projects that have already received ERC funding previously, 17 were awarded here. Additionally, Catalan research groups benefited from 15 Consolidator Grants, the category that aims to consolidate groups led by head researchers with 7 to 12 years of experience. Finally, the BioRegion has been awarded 2 Synergy Grants, for projects led by 2-4 researchers.

By beneficiaries, the Center for Genomic Regulation (CRG) has the most grants in all ERC categories (21). It is followed by the Institute for Research in Biomedicine (IRB), with 8 grants; Institute for Bioengineering of Catalonia (IBEC), with 7; Vall d'Hebron In-

GRAPH 39. ERC grants awarded to researchers in the BioRegion of Catalonia, by type and year



Source: AGAUR (December 2017).

stitute of Oncology (VHIO), with 6; and the Autonomous University of Barcelona (UAB), with 5. IDIBELL and Pompeu Fabra University have each been granted 4.

SCIENTIFIC PRODUCTION

According to the study Biocat commissioned to the Research Group on Bibliometrics (BAC)⁶⁴ in 2017, over the past 20 years, the number of publications in the biomedical arena in the BioRegion of Catalonia has nearly quadrupled: from 2,145 publications in 1996 to 8,177 documents in 2016. Between 2012 and 2016, research bodies in the BioRegion produced a total of 38,169 scientific publications in healthcare and life sciences (biomedicine) with at least one author residing in Catalonia. This is 41.5% of all scientific production generated in Catalonia over this period.

One in six scientific publications in the BioRegion (16.5%) is among the top 1% most cited documents in the world in its specialization, triple the percentage expected based on production volume. Catalan biomedical publications between 2012 and 2016 generated 566,254 citations, with a normalized impact of 15.7% above the global average.

Catalan scientific production in biomedicine over the 2012-2016 period made up 1.2% of the global total, 3.5% of that of Europe (EU-28), and 34.1% of the Spanish

total. Between 2012 and 2016, the United States, China, the United Kingdom, Germany, Japan, Italy, Canada, France, Australia and Spain (including Catalan production) were the top 10 countries on the global ranking by volume of biomedical publications. With 38,169 documents published in this arena, Catalonia would be ranked 23rd in the world in absolute production.

Eliminating the distorting effect of country size by measuring the contribution each country makes to knowledge in biomedicine compared to its contribution

to science as a whole, meaning the relative contribution to biomedical knowledge, Catalonia would be ranked fifth in the world with 23%, surpassed only by the Netherlands (42%), Denmark (39%), the United States (30%) and Sweden (25%). This means that Catalonia contributes 23% more to global biomedical knowledge than it does to science in general.

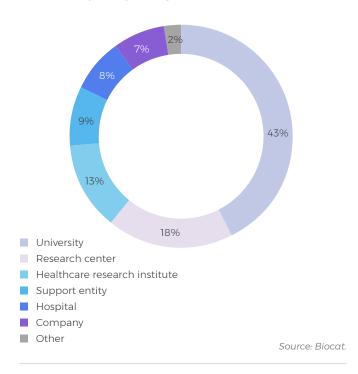
Catalonia was the Spanish region with the most scientific production in general and in the biomedical arena between 2012 and 2016. More than half (52.4%) of all Catalan

TABLE 21. Highly cited researchers in the healthcare and life sciences (Catalonia, 2016)

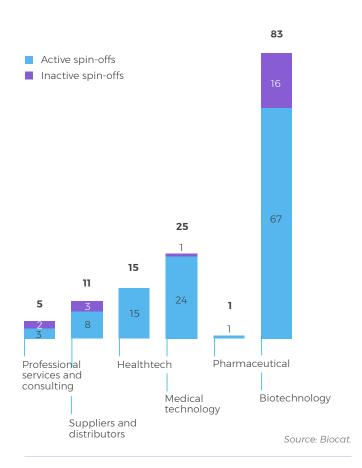
Researcher	Affiliations	Category
Pablo Alonso Coello	IIB Sant Pau	Social sciences, general
Elias Campo	IDIBAPS / UB	Clinical medicine
Joan Bladé	IDIBAPS	Clinical medicine
Jordi Bruix	UB	Clinical medicine
Josep Tabernero	VHIO	Clinical medicine
Josep Peñuelas	CREAF-CSIC	Environmental sciences/ Ecology
Josep M. Llobet	IDIBAPS / Mt. Sinai Sch Med, USA	Clinical medicine
Roderic Guigó	CRG / UPF	Molecular biology and genetics

Source: Highly Cited Researchers (2016).

GRAPH 40. Spin-offs active in the BioRegion of Catalonia, by entity of origin (2017)



GRAPH 41. Companies created (active and inactive) in the BioRegion of Catalonia, by sector (1992-2017)



publications in biomedicine are done in collaboration with authors from other countries, the highest internationalization rate in the country. With regard to the relative weight of biomedical production versus total scientific production, the proportion for Catalonia (41.5%) is slightly higher than that of the Community of Madrid (38.3%).

On the other hand, the presence of Catalan research bodies on international bibliometric rankings is noteworthy. So, the CWTS Leiden Ranking (2002-2015)⁶⁵ for the fields of biomedicine and health sciences and life and earth sciences put the UB and UAB among the top 200 universities in the world. Pompeu Fabra University (UPF) is among the top 100 for the PP indicator (top 10%).

The life sciences section of the Nature Index ranking (March 2016-February 2017)⁶⁶ also puts Catalan entities among the top 200 in the world, including the Barcelona Institute of Science and Technology (BIST) and the UB.

The 2016 Highly Cited Researchers⁶⁷ ranking highlights 3,265 researchers from around the world, 15 of which work at Catalan bodies and, more specifically, 8 in areas of interest to the BioRegion (Table 21). This ranking also features world-renowned Catalan researchers working abroad like, for example, Valentí Fuster (Mount Sinai Heart – Clinical Medicine) and Josep Baselga (through September 2018, Director of the Memorial Sloan Kettering Cancer Center – Clinical Medicine).

SPIN-OFFS

Since 1992, Catalan research organizations have created 140 spin-offs in the healthcare and life sciences sector, most of which (124) have been created since 2005. In fact, one in five companies (21%) created in the healthcare and life sciences sector in Catalonia since 2005 was promoted by a research institution. Today, 118 of these companies (84.3%) are still in business. By type of organization of origin (there may be more than one per company) (Graph 40), most of the 118 active spin-offs come from universities (43%), followed by those from research centers (18%) and healthcare research institutes (13%).

By sector of activity (Graph 41), the majority of the 128 spin-offs specialize in biotechnology (83) and medical technology (25).

In 2016, the Government of Catalonia kicked off the Knowledge Industry Program⁶⁸ in order to bring knowledge generated at universities and research centers to the productive sector. In this regard, the program aims to promote the development of new science-based companies derived from the research.

The program expects to leverage some €30 million over 5 years, over which time it will grant financial and non-financial aid to nearly 300 business projects based on the research in order to accompany the projects from the initial prototyping phase through to market launch (it also includes a training and mentoring program). The first calls mainly funded projects in ICT and healthcare and life sciences.

TABLE 22. RRI projects under SWAFS 2016-2017 (H2020)

	Num. Tot	Num. Total projects		oordinates	Funds raised (M€)
	ES	CAT	ES	CAT	ES CAT
TOTAL	15	8	5	3	6.33 3.16
% CAT of ES		53.33		60	50
% CAT of UE		16		6	3.07

Source: Compiled internally based on data from the European Commission.

THE BIOREGION AND RESPONSIBLE RESEARCH AND INNOVATION (RRI)

Responsible research and innovation (RRI) means having society participate in all phases of research and innovation processes to make sure their values better address society's needs and expectations. The concept of RRI includes different political agendas that can be grouped into five priorities: open access, gender equality, ethics, citizen participation and science education. RRI is an emerging issue promoted by the European Commission and being incorporated transversely throughout the Horizon 2020 framework program, based on the "three Os": open innovation, open science and opening up to the world.

From 2015 to 2017, 14 organizations in the BioRegion were part of 17 RRI projects. Of these, 7 projects were coordinated from Catalonia and attracted a total of €5.6 million in funding. These projects make up 44% of all projects in this arena in Spain and 39% of the funds received. Under the H2020 Science with and for Society (SWAFS) program, agreements were signed with 24 projects from around the EU (€46 million) in 2017. Catalan organizations participate in 7 of these projects, which attracted more than €3 million and make up half of all the funds received in Spain and 6.65% of the whole EU.

The activity of the following bodies, among others, was particularly noteworthy: Center for Genomic Regulation, "la Caixa" Banking Foundation, Institute for AIDS Research (IrsiCaixa), IRB Barcelona, ISGlobal and Pompeu Fabra University. Some noteworthy projects include:

- Inspires, coordinated by IsGlobal with seven other participating bodies, promoting research and innovation with more participation from society through science shops, with a bottom-up and demand-driven approach.
- 2. HEIRRI, coordinated by the UPF, in which the "la Caixa" Banking Foundation and the Catalan Association of Public Universities, among others, are also participating. This project focuses on promoting open research and knowledge on various levels and types of education.
- 3. ORION, coordinated by CRG with participation of eight other bodies, aims to foster open science and RRI at research-associ-

ated institutions through co-creation experiments involving various stakeholders.

Plus, under the framework of RIS3CAT, the Catlabs program kicked off in November 2016 in Catalonia to set up a digital, social and collaborative innovation network, using the quadruple helix model (administration, R&D+i system, enterprise and civil society). This program hopes to increase the number of stakeholders, users and innovations that address society's challenges through ICT and the Internet.

RESEARCH AGENTS

The BioRegion of Catalonia has 89 research bodies and facilities: 40 research centers, 12 universities with healthcare and life sciences degrees, 18 university hospitals, 3 large-scale facilities, 2 technology centers and 14 science and technology parks working in the healthcare and life sciences sector. Additionally, there are 780 research groups recognized by the Government of Catalonia working in healthcare and life sciences, 47% of all those in the 2014-2016 call.⁶⁹

RESEARCH CENTERS

There are 40 research centers in Catalonia working in healthcare and life sciences or related subjects (Table 23), 32 of which are part of the CERCA Institution, which oversees centers that receive direct support from the Government of Catalonia. Three of these (Center for Research in Agricultural Genomics, CRAG; Catalan Institute of Cardiovascular Sciences, ICCC; and the Catalan Institute of Nanoscience and Nanotechnology, ICN2), are also CSIC institutes. This national research body has 22 institutes in Catalonia, 11 of which work in the healthcare and life sciences sector or associated fields.

The CERCA centers are research bodies in Catalonia that are managed autonomously and devoted exclusively to research. According to figures from the CERCA Institution, the 41 research centers (32 with ties to the healthcare and life sciences sector) have a yearly budget of approximately €400 million, 9,000 researchers and 74 spin-offs.⁷⁰ The yearly contribution of the Government of Catalonia to the CERCA centers, despite the financial crisis and difficulties in recent years, has stayed relatively stable: €100 million (2012), €98 million (2013), €97 million (2014), €98 million (2015), and, finally,

TABLE 23. Research centers in the healthcare and life sciences sector or associated disciplines (Catalonia, 2017)

Research center	CERCA	CSIC	ISCIII	Severo Ochoa	Maria de Maeztu
Center for Demographic Studies (CED)	Х				
Center of Regenerative Medicine in Barcelona (CMRB)	Х				
Center for Research in Agricultural Genomics (CRAG)	Х	X		Х	
Centre de Recerca en Agrotecnologia (Agrotecnio)	Х				
Centre de Recerca Matemàtica (CRM)	Х				
Center for Genomic Regulation (CRG)	Х			Х	
Computer Vision Center (CVC)	Х				
International Center for Numerical Methods in Engineering (CIMNE)	Х				
Institute of Chemical Research of Catalonia (ICIQ)	Х			Х	
Catalan Institute of Cardiovascular Sciences (ICCC)	Х	X			
Catalan Institute of Nanoscience and Nanotechnology (ICN2)	Х	X		Х	
Catalan Institute for Water Research (ICRA)	Х				
Bellvitge Biomedical Research Institute (IDIBELL)	Х		X		
Girona Biomedical Research Institute (IDIBGI)	Х				
Biomedical Research Institute Sant Pau (IIB Sant Pau)	Х		X		
Institute for Health Science Research Germans Trias i Pujol (IGTP)	Х		Х		
Institut d'Investigació en Intel·ligència Artificial (IIIA-CSIC)		X			
Pere Virgili Institute (IISPV)	Х				
August Pi i Sunyer Biomedical Research Institute (IDIBAPS)	Х		X		
Institute for Bioengineering of Catalonia (IBEC)	Х			Х	
Institute of Evolutionary Biology (IBE)		X			
Molecular Biology Institute of Barcelona (IBMB)		X			Х
Institute of Material Science of Barcelona (ICMAB-CSIC)		×		X	
Institute of Photonic Sciences (ICFO)	Х				
Institute of Environmental Assessment and Water Research (IDAEA-CSIC)		Х			
Institute for High Energy Physics (IFAE)	Х			Х	
Barcelona Microelectronics Institute. National Microelectronics		V			
Center (IMB-CNM-CSIC)		Х			
Institute for Advanced Chemistry of Catalonia (IQAC-CSIC)		Х			
Barcelona Institute for Research in Biomedicine (IRB Barcelona)	Х			X	
Lleida Institute for Research in Biomedicine (IRB Lleida)	Х		Х		
Josep Carreras Leukemia Research Institute (IJC)	Х				
AIDS Research Institute (Irsi-Caixa)	Х				
Catalonia Institute for Energy Research (IREC)	Х				
Institute for Food and Agricultural Research and Technology (IRTA)	Х				
Institut de Robòtica i Informàtica Industrial (IRII-CSIC)		Х			Х
Barcelona Institute for Global Health (ISGlobal)	Х				
Hospital del Mar Research Institute (IMIM)	Х		Х		
Internet Research Center (i2CAT)	Х				
Vall d'Hebron Institute of Oncology (VHIO)	Х				
Vall d'Hebron Research Institute (VHIR)	Х		Х		

Source: Biocat.

Note: CERCA = Research centers in the CERCA system. CSIC = CSIC centers. ISCIII = Healthcare Research Institute accredited by the ISCIII.

Severo Ochoa = Severo Ochoa Center of Excellence (MINECO). María de Maeztu = María de Maeztu Unit of Excellence (MINECO).

€102 million (2016).

As a whole, the scientific staff at the 40 CERCA and CSIC centers for research in the healthcare and life sciences sector is made up of nearly 13,000 workers, 6,500 of which are researchers. Only 9 Catalan centers have more than 300 researchers. In this regard, the lack of critical mass is an important hurdle to overcome in this highly competitive global environment. So, the CERCA Centers Integration Program (SUMA)⁷¹ has begun a merging and convergence process to reduce the number of active centers in order to establish economies of scale in management and facilities, as well as boosting critical mass and research resources.

Within this framework, since the 2015 Biocat Report was published, the Center for Research in Environmental Epidemiology (CREAL) has been absorbed by the Barcelona Institute for Global Health (ISGlobal), and the Institute of Predictive and Personalized Medicine of Cancer (IMPPC) has been integrated into the Institute for Health Science Research Germans Trias i Pujol (IGTP), creating the new Program of Predictive and Personalized Medicine of Cancer of the Institute of Research Germans Trias I Pujol (PMPPC-IGTP). Furthermore, projects are underway to integrate the Catalan Institute of Cardiovascular Sciences (ICCC) into the Biomedical Research Institute Sant Pau (IIB Sant Pau); conduct a feasibility study to set up a single body merging the August Pi i Sunyer Biomedical Research Institute (IDIBAPS) and the Clinic Foundation for Biomedical Research (FCRB); and, finally, create the PCB-PRBB Animal Facility Alliance, which expands the technology on offer and aims to increase their respective strategic and competitive advantages.

In the same line of pooling efforts to foster mergers and strategic alignment among different research centers, the Barcelona Institute of Science and Technology (BIST)⁷² is a scientific initiative of seven of the main centers of excellence in Catalonia that was created in mid-2015. The BIST members are: Center for Genomic Regulation (CRG), Institute of Photonic Sciences (ICFO), Institute of Chemical Research of Catalonia (ICIQ), ICN2, Institute for High Energy Physics (IFAE), Institute for Research in Biomedicine (IRB Barcelona) and, since June 2017, Institute for Bioengineering of Catalonia (IBEC).

According to data from early 2017, BIST has approximately 1,400 researchers in 159 research groups, who publish more than 1,000 scientific papers a year and have created 19 spin-offs (active). Under the Marie Skłodowska-Curie Co-fund (2016) call, the H2020 program has approved the PREBIST and PROBIST programs, which will receive €10 million over the coming five years to fund 89 predoc and postdoc grants. Plus, in 2017 the Ignite call was created to foster collaboration among the BIST centers.

Catalan research in healthcare and life sciences also stands out in terms of national indicators. So, Catalonia has 10 institutes accredited as Severo Ochoa⁷³ centers of excellence, which is 40% of the 25 total in Spain. Of these 10, there are 9 working in the healthcare and life sciences sector or associated disciplines (Table 23), plus the Barcelona Supercomputing Center (BSC).

Plus, Catalonia has three María de Maeztu units of excellence in the healthcare and life sciences sector: Department of Experimental and Health Sciences (DCEXS, UPF), Structural Biology Unit (SBU, CSIC-IMBM) and the Institut de Robòtica i Informàtica industrial (IRII, CSIC-UPC).

In terms of scientific production, research centers participated in one in five papers in healthcare and life sciences with at least one author in Catalonia published between 2012 and 2016, according to the study Biocat commissioned to the Research Group on Bibliometrics (BAC). The impact of the publications generated by the research centers in this arena was 14.2% above the global average (RCI 1.142), with three times the expected 1% of publications of excellence (RHCP 3.052). The Barcelona Institute for Global Health (ISGlobal) and the Center for Genomic Regulation have the most publications (1,368 and 969, respectively).

LARGE-SCALE SCIENCE FACILITIES

In Catalonia, national and international researchers have three large-scale research facilities that have been recognized as Unique Scientific and Technical Infrastructures (ICTS) by the Spanish government.

The ALBA Synchrotron (CELLS) has eight working beam lines for scientific research and three more under construction. Furthermore, the Barcelona Supercomputing Center (BSC) has four scientific departments, one of which is focused on the life sciences. Finally, the Infrastructure for OMICS Technologies (IOT) is an initiative that encompasses the Centre Nacional d'Anàlisi Genòmica (CNAG-CRG) and the Center for Omic Sciences (COS) to provide biomolecular analysis tools for holistic capture of biological processes.

Given their impact on health, it is also considered strategic that one of the two nodes of the European Genome-Phenome Archive (EGA), managed by the CRG, is located in Catalonia.

Today, Catalonia has 13 biobanks with collections of standardized, classified biological samples and their corresponding clinical data. These collections come from a wide range of lines of biomedical research and help promote, facilitate and carry out collaborative research.

Additionally, animal facilities are a key part of the pre-clinical phases of the biomedical research pipeline and transfer to clinical research. They are common meeting places for medical device companies, research staff and healthcare providers that truly promote the development of new medical technology and its transfer to clinical practice.⁷⁴

The animal facilities of the Barcelona Biomedical Research Park (PRBB) and the Barcelona Science Park (PCB) signed the SUMA agreement in 2015 to promote the PCB-PRBB Animal Facility Alliance in order to boost their respective strategic and competitive advantages. This alliance means that, between the two facilities, there is a total of 7,000 m² of space (with the option for an additional 2,000 m²), 60 employees and 600 users.

UNIVERSITIES

The 12 Catalan universities offer undergraduate and master's degrees in the healthcare and life sciences field, with 52,500 students enrolled and 10,538 students in 2015-2016 graduating class. Regarding undergraduate students, there were 47,485 enrolled (16.7% of the Spanish total) and 7,759 in the graduating class (17.4%). Additionally, there were 5,015 students enrolled in the master's program (19.8%) and 2,779 graduates (18.9%). However, the percentage is even higher if we look at the 3,849 PhD students in the healthcare and life sciences field at Catalan universities, 22.4% of the national total, clearly showing the high quality teaching and specialization of the university system.

According to the Catalan Association of Public Universities (ACUP),⁷⁶ the funds raised by the eight Catalan public universities for research and innovation in 2015 was up significantly, turning around the downward trend seen in recent years for an overall total of €266.8 million, which is €80 million more than in 2013. This improvement is mainly due to a clear increase in the competitive funds (€193 million in 2015 versus €121 million in 2013), making up 72% of all resources, compared to 28% for non-competitive funds. Of the competitive funds, 66.2% are from the autonomous community or national level, while those from Europe and international sources make up 33.8%, with a clear upward trend.

Catalan public universities contribute to the Catalan economy with 1.4% of the GDP, according to data from the ACUP.⁷⁷ Specifically, in 2015 the Catalan public university system (SiCUP) had a joint turnover of €4.545 billion and GDP of €2.955 billion, both direct (€1.804 billion) and indirect or induced (€1.151 billion). If we include data from the public research system, the contribution to the Catalan GDP rises to 1.7% and the number of jobs created, to over 60,000.

With regard to human resources, the SiCUP and its associated stakeholders contributed to creating/maintaining a total of 44,776 full-time-equivalent jobs in 2015, 27,804 directly and 16,972 indirectly or induced, according to data from the ACUP. If we look only at human resources working at universities in the healthcare and life sciences arena, for the 2015-2016 school year there were 4,962 professors on the teaching and research staff (TRS) at the centers belonging to Catalan public universities working in these areas.⁷⁸ This figure makes up 31.1% of the total Catalan TRS and 18% of that in Spain working in the healthcare and life sciences sector.

Regarding the employed research staff (ERS), the 12 Catalan universities have 3,321 researchers in all areas of knowledge, 19% of the Spanish total. Nearly half of these researchers (1,623) come from competitive public calls (predoc or postdoc), while the other half (1,638) are hired by research projects and groups through article 83 of the Spanish universities act (LOU). Finally, there are 60 researchers hired via other paths.

The scientific production of Catalan public universities in 2015 continued to lead that of Catalan institutions, making up 54.8% of the total.79 Moreover, these publications, measured in terms of impact, show better results than previous years and put Catalan universities

among the best in the Spanish university system. In this regard, the average number of publications per FTE researcher in 2015 (1.37 publications) is 71% higher than at public universities in the rest of the country (0.80).

If we look only at scientific production in the healthcare and life sciences field, universities took part in one in four papers with at least one Catalan author published between 2012 and 2016, according to the study Biocat commissioned to the Research Group on Bibliometrics (BAC). The impact of the publications generated by the university sector in this arena was 14% above the global average (RCI 1.140), with nearly three times the expected 1% of publications of excellence (RHCP 2.712).

The University of Barcelona had the most publications and the highest impact (13,146 between 2012 and 2016, with RCI of 1.178), followed by the Anonymous University of Barcelona (8,568 publications and RCI 1.117) and Pompeu Fabra University (3,694 publications and RCI 1.121).

In 2015, 2,832 PhD dissertations were read in Catalonia (19.2% of the Spanish total). Of these, 961 were in the healthcare and life sciences field, which is 33.9% of the Catalan total and 23.2% of all theses in this arena in Spain.

As a whole, Catalan universities generate nearly 25% of all revenue from knowledge transfer activities, which is \leqslant 3 million for all universities in Spain. In the knowledge transfer and university-business collaboration arena, it is worth noting that revenue from non-competitive funds raised by public universities and related bodies since 2013 has been rising gradually, with the cumulative total in 2015 of \leqslant 90.5 million.

HOSPITALS

According to the Catalan Ministry of Health, the Catalan system has 103 hospitals (65 public and 38 private) and 199 community health and mental health centers. All of these centers together employ 92,720 workers.

If we include the whole Idescat category of healthcare activities, which ranges from hospitals to medical centers and dental clinics, the figure rises to 170,000 workers that generate €13.285 billion (2014), 3.8% of the Catalan GDP.⁸⁰ For more macroeconomic information, see Table 9: Macroeconomic data and ratios on the BioRegion of Catalonia (2016).

Catalonia now has 18 university hospitals, with 10 associated health-care research institutes, plus the University Institute for Primary Care Research Jordi Gol (IDIAP Jordi Gol), with ties to the primary care centers. In total, Catalonia has 11 healthcare research institutes, 7 of which are accredited by the Carlos III Health Institute (ISCIII) (Table 23).

With regard to human resources, according to the latest edition of the AQuAS Research Results Center,⁸¹ the 11 institutes and 9 biomedical research centers not associated with healthcare institu-

tions had 7,013 (2013), 5,754 (2014) and 6,487 (2015) FTE employees associated directly or indirectly with research activity. In 2015, 47% of staff were research doctors or researchers in training.

In terms of financial resources, in 2015 the Government of Catalonia awarded the 20 institutes and centers a total of €60.25 million in direct subsidies, up 3.5% from the previous year. That same year, the institutes and centers saw their ability to attract competitive funds rise 26% (€149.93 million) and an increase of 10% in the non-competitive funds brought in €90.77 million. Therefore, AQuAS highlights that the multiplying factor for public subsidies compared to funds (competitive or non-competitive) has improved from 3.5 (2014) to 4 (2015). In the latest ISCIII call for Health research projects (2016), Catalonia was awarded €19.6 million, 32.1% of the national total.⁸²

The scientific production of the 20 institutes and centers totaled 7,217 publications (original articles, revisions and proceedings) in 2015, up 4% from 2014.83 Of these publications, 64% were in first-quartile journals (Q1). Furthermore, Catalonia ranks very highly in terms of document citation compared to other countries and above the European and global averages. Regarding highly cited papers, those among the most cited 1% in the world (for the same discipline over the same period), the positive progression is clear: 203 (2013), 236 (2014) and 256 (2015).

According to the study Biocat commissioned to the Research Group on Bibliometrics (BAC), the healthcare sector participated in one in four papers with at least one Catalan author published between 2012 and 2016. The impact of the publications in the Catalan healthcare sector was 19.7% above the global average (RCI 1.197), with 3.5 times more than the expected excellence by volume of publications in Catalonia (RHCP 3.546). These two indicators are the highest of any for Catalan biomedical publications.

The biomedical research institutes and hospitals themselves were the most active centers in publishing in the healthcare sector, a fact that further strengthens the excellence of the Catalan healthcare system and the hospital-healthcare research center tandem. Hospital complexes were ranked third, although their publications have the highest impact rating in the sector. The biomedical research institutes and hospitals, likewise, had excellence and impact indicators above those for the sector as a whole.

Hospital Clinic (7,611 publications), Hospital de Sant Pau (2,672), Hospital del Mar (2,430) and Bellvitge University Hospital (2,179) are the most active and their impact is between 18% and 28% above the global average.

With regard to transfer, if we compare data from 2015 to that for 2014, the upward trend is noteworthy, although the figures are still modest. So, according to the Research Results Center. Institutes and centers: 2014-2015 AQuAS data, hospital research institutes licensed/transferred 40 patents in 2015, up 25% from the previous year. The most noteworthy growth was at IMIM, VHIR and IGTP.

Furthermore, hospital research institutes had 4,634 active clinical trials in 2015, 10% more than the previous year according to the aforementioned AQuAS report. Especially noteworthy is the increase at IRHSCSP, with 47% more trials than the previous year, above all in blood diseases and cancer. The IGTP also did 47% more clinical trials, above all in infectious diseases and cancer, while the increase at IDIBIGI was 25%. Cancer continues to be the main focus of clinical trials at all of the institutes except IDIAP Jordi Gol, which focuses mainly on endocrine diseases.

Despite the general increase in the number of clinical trials, participation in Clinical practice guidelines (CPG), which had increased between 2012 and 2014, has dropped 26.4% (134 guidelines in total in 2015).

Specifically referring to clinical trials, the XXIII Informe BEST (December 2017) is a valuable source of information showing Catalonia's leading position in Spain.⁸⁴ This is a strategic project that brings together 45 pharmaceutical laboratories and 59 hospitals to create a platform of excellence in clinical drug research. So, the Clinical Research Ethics Committees of reference are Catalan in 1,479 of the 2,871 trials (51.5%). Plus, Catalan centers had a total of 5,744 participations (27.1% of the Spanish total) and the 33,971 patients from Catalonia make up 28.6% of the total.

Another valuable source of information on innovative activity of Catalan hospitals is the Plataforma de Innovación en Tecnologías Médicas y Sanitarias (ITEMAS), promoted by ISCIII and co-funded by ERDF. The core of the platform is made up of 31 associated innovation units, which collect data to obtain indicators and measurements on innovation in healthcare technology. Table 24 shows the most significant aggregate data for the 10 Catalan units that are ITEMAS members: Fundació Parc Taulí, Fundació Sant Joan de Déu, IBB Sant Pau, IDIBAPS, IDIBELL, IGTP, IMIM, Institut Guttmann, IRB Lleida and VHIR.

As can be seen in the table (data from 2016), the 10 Catalan ITEMAS units, despite making up only one third of the platform members, attract half (49.7%) of all funds from international projects awarded and 42.1% of revenue for clinical trials. With regard to intellectual property, the 10 Catalan units make up 39.8% of all patent applications and 44.1% of all patents granted to ITEMAS. Furthermore, the 10 Catalan ITEMAS units have helped create technology-based companies, 24 of which are still active (53.3% of the total for the platform), that attracted €7.63 million (71.6% of the total).

In January 2017, German company Fresenius acquired Quirónsalud, a group that owns 43 hospitals including Clínica Teknon and Hospital Universitari Quirón-Dexeus in Barcelona. The operation, valued at €5.76 billion, created the largest private operator in Europe and illustrates the growing trend of consolidation in the private hospital sector. In this sector, concentration allows groups to round out their business and medical areas but, above all, it gives them the size to better negotiate policies with insurance companies.

TABLE 24. ITEMAS indicators for the BioRegion of Catalonia (2016)

Resources	Totals	Weight within Spain
Research staff	5,249	30.7%
National projects granted (amount)	279 (29.3 M€)	24.3% (27.3%)
International projects granted (amount)	38 (9.9 M€)	24.3% (49.7%)
Clinical trials signed (revenue)	963 (34.9 M€)	40.4% (42.1%)
Processes		
Ideas in fund-raising phase	181	25.3%
Ideas in assessment phase	142	28.9%
Ideas in development phase	229	37.4%
Ideas in transfer phase	152	33.1%
Ideas in market phase	155	36.8%
Results		
Articles published in JCR journals	5,150	37.8%
Innovation projects awarded (amount)	70 (8.3 M€)	24.6%
Contracts signed	274 (9.8 M€)	15.0%
Patent applications	217	39.8%
Patents granted	165	44.1%
Patent families	154	42.1%
Patent families exploited (revenue)	88 (0.5 M€)	28.2% (51.8%)
Active technology-based companies (funds raised)	24 (7.6 M€)	53.3% (71.6%)

Source: ITEMAS.

RESEARCH GROUPS

The Government of Catalonia has recognized 780 research groups in the healthcare and life sciences sector. This figure makes up 47% of the 1,652 total consolidated research groups recognized in the 2014-16 team call, managed by the Agency for Management of University and Research Grants (AGAUR).⁸⁶

Most of the research groups specializing in the healthcare and life sciences field are associated with universities (43%), research centers (29%) and hospitals and healthcare research institutes (24%).

TECHNOLOGY CENTERS

Since 2015, the merger of technology centers into the Eurecat Foundation has created a large technology center that is a benchmark for the Catalan business sector. Eurecat has gradually incorporated more technology centers in order to become more efficient and gain critical mass, with the goal of better serving the Catalan business sector and being able to successfully compete on an international level.

Eurecat brings together more than 450 professionals (nearly 200 are researchers), generating total annual turnover of €45 million and serving more than 1,000 companies and organizations. Eurecat participates in approximately 160 national and international R&D&i consortium projects, holds 73 patents and 8 spin-offs. The Eurecat technology services are broken down into three large areas of knowledge: industry (including sustainability), digital (including healthtech) and biotechnology (nutrition and health).

Plus, in late 2016, Eurecat and Leitat signed an agreement to be permanently linked in order to take advantage of the synergies between the two bodies, boost efficiency and gain critical mass in business volume. Leitat is a technology center based in Terrassa, which had 155 national and European R&D projects underway in 2015. Its R&D areas include, among others, materials, biotechnology, energy and the environment. In September 2017, the Government of Catalonia authorized a €20-million subsidy for Eurecat, €4 million of which will go to Leitat..

This process, led by ACCIÓ, the Government of Catalonia Agency for Business Competitiveness, has brought the number of technology centers in Catalonia down to just two. ACCIÓ has also transformed

TABLE 25. Science and technology parks with activities associated with the healthcare and life sciences (Catalonia, 2017)

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Science and technology parks	PO	V. \ <6	4	70 A	o' o'	\$r.\ 40	40	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	\$ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\	4	, We
22@Barcelona	Х								Х	Х	x
Barcelona Synchrotron Park Parc de l'Alba)		Х	Х	х					Х	Х	
Esade Creapolis		Х				Х					
a Salle Technova Barcelona						Х					Х
Barcelona Science Park PCB)	Х	Х	Х	Х						Х	Х
leida Agrifood Science and Technology Park PCiTAL)	X	Х				Х	X		Х	Х	
University of Girona Science and Technology Park	Х	Х						Х		Х	
Science and Technology Park of Terrassa (Orbital.40)					Х	Х	Х				
Barcelona Biomedical Research Park (PRBB)		Х	Х								X
JAB Research Park		Х		Х			Х		Х	Х	
Barcelona Activa Technology Park									Х		Х
Parc Tecnològic del Vallès, S.A.		Х							Х	Х	
JPC Park	Х			Х	Х				Х		
TecnoCampus Mataró- Maresme (TCM)				Х							

Source: Biocat and XPCAT.

the TECNIO program,⁸⁷ which is no longer a network of technology services centers. Now TECNIO is a seal to identify where to find unique Catalan technology, public and private suppliers that offer it (59 developers, including technology centers, research groups and centers, and companies) and those who facilitate knowledge and technology transfer (10 commercialization units at universities and research centers).

With this change, the TECNIO program has opened up to private institutions and companies, and to services associated with knowl-

edge transfer, from intellectual property managers to investment fund managers. In short, it is an effort to improve the innovative capacity and competitiveness of companies, especially SMEs. Of the 69 stakeholders with the TECNIO seal, 39 (56.5%) work in areas associated with the healthcare and life sciences.

SCIENCE AND TECHNOLOGY PARKS

The Network of Science and Technology Parks of Catalonia (XPCAT) brings together 16 large-scale spaces for the production, transfer,

dissemination and use of knowledge and acts as a bridge between the research and innovation communities.⁸⁸ This ecosystem integrates university groups, research and technology centers, business incubators, large corporations with their R&D centers, companies focused on innovation and new knowledge-based start-ups.

In total, 14 of the 16 parks carry out activities associated with the healthcare and life sciences field (Table 25), in a wide variety of areas: agrifood, biotechnology and the life sciences, pharmacy, nanobioengineering and nanotechnology, optics and photonics, health, nutrition and food safety, food technology, energy technology, environmental technology and, finally, medical technology.

Of the 163 companies in the healthcare and life sciences sector currently located at science and technology parks, 56% are biopharmaceutical companies, 11% medical technology businesses and 6% healthtech firms. The Barcelona Science Park is home to the most companies (35%), followed in a distant second by Parc Tecnològic del Vallés (12%), the UAB Research Park, the Science and Technology Part of the UdG and TecnoCampus Mataró-Maresme (the final three with 8% each).

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Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Success stories in technology transfer in the BioRegion of Catalonia



PREDICTING KIDNEY TRANSPLANT REJECTION

www.idibell.cat



O) PROJECT LEADER

Oriol Bestard



START YEAR

2016



PARTICIPATING ORGANIZATIONS

IDIBELL, Oxford Immunotech

PROJECT AIMS

To incorporate a new analysis technique to predict rejection by measuring the anti-HLA antibodies secreted by memory B cells against those antigens. This type of rejection is one of the most frequent causes of loss of kidney grafts.

COLLABORATION FRAMEWORK

Dr. Bestard's research group (IDIBELL) has contributed its clinical experience and expertise in kidney transplants, from which satisfactory results have been obtained indicating the capacity to predict when a transplanted kidney will be rejected. These results have led to one patent application. The international corporation Oxford Immunotech (United Kingdom) has collaborated in co-developing the kit derived from this technology.

MOST SIGNIFICANT CHALLENGES

The key challenge in this project has been technical. To overcome it, the group has developed a sensitive easy-to-apply assay to assess B cells in the blood after in vitro activation.

RESULTS

IDIBELL has licensed a patent associated with predictive detection of kidney-transplant rejection to the company Oxford Immunotech, which is in the national phases in Europe and the United States. Plus, several collaboration agreements have been signed with this company and IDIBELL has been granted a €750,597 European competitive project for this research. Currently, Oxford Immunotech is working on technical development of the predictive kit and will be in charge of marketing it.

TREATMENT FOR X-LINKED ADRENOLEU-**KODYSTROPHY (X-ALD)**

www.idibell.cat



O) PROJECT LEADER

Aurora Pujol



START YEAR

2017



PARTICIPATING ORGANIZATIONS

IDIBELL, SOM Biotech

PROJECT AIMS

Providing a treatment for the hereditary neurometabolic disease X-linked adrenoleukodystrophy (X-ALD) based on repositioning commercial drugs indicated for other diseases. X-ALD is a rare disease that currently has no treatment, with an incidence rate of 1:17,000 in newborns, although poor diagnosis means the real number may actually be higher. Patients with X-ALD, which is more common in men than women, undergo progressive destruction of myelin, the substance that insulates nerves in the brain and bone marrow.

COLLABORATION FRAMEWORK

Dr. Pujol's research group (IDIBELL) has contributed satisfactory results from experiments treating X-ALD in animal models. These have been the basis for 4 patent applications. On the other hand, Catalan company SOM Biotech is collaboration to co-develop some of these drugs to take them to market as a therapy.

MOST SIGNIFICANT CHALLENGES

One of the most important challenges this project has had to face is the pharmaceutical industry's lack of interest in this type of diseases. The fact that it is a rare disease means it takes a lot of investment in R&D to market a treatment, while the return on that investment is quite low.

RESULTS

IDIBELL has licensed three of the four patents on repositioned drugs to treat X-ALD to SOM Biotech. They have signed a collaboration agreement to fund the project and a first-view contract, through which SOM Biotech will have first priority in seeing any new technology developed by Dr. Pujol's research group for this disease. Two of the three drugs are now about to move into phase II/III clinical trials and, if completed successfully, may hit the market in 2 to 3 years.

ADVANCE(CAT)

www.advancecat.net



O) PROJECT LEADER

Josep M. Canals



START YEAR

2016



PARTICIPATING ORGANIZATIONS

UB, Ferrer, BST, BMF, Bioibérica, Butler Scientifics, CMRB, FBiG, FCB, VHIR, IBEC, IGTP, (FIR-HSCSP), FLeitat, IDIBAPS, IDIBELL, Qrem, UAB, Acció, Biocat

PROJECT AIMS

To set up a network of Catalan centers involved in advanced therapies (cell therapy, gene therapy and tissue engineering) to boost research and speed up development of new products. Several innovative projects from this arena will be taken to clinical practice.

COLLABORATION FRAMEWORK

ADVANCE(CAT) is a project led by the University of Barcelona and Ferrer International, pooling the expertise of 18 organizations ranging from large pharmaceutical corporations to clinical research start-ups and even a soccer team (Fútbol Club Barcelona). Plus, the project is open to new collaborations. ADVANCE(CAT) is part of the NEXTHEALTH community, coordinated by Biocat and co-funded by the Government of Catalonia through ACCIÓ (Agencia para la Competitividad de la Empresa) and the European Union, under the framework of the ERDF (European Regional Development Fund) Catalonia 2014-2020 program, as part of the RIS3CAT strategy.

MOST SIGNIFICANT CHALLENGES

Most advanced therapies are in the early stages and it is important to join forces to speed up development and transfer to clinical practice and industry. The main challenge this project faced in its first year was to build a fast-acting, effective structure to promote collaborations among partners and allow for precise monitoring of the results. Additionally, the diseases to tackle are very different.

The main challenge for the future is to ensure the continuity of the consortium after the community project is finished and to get the funding needed to move forward with the project and its collateral projects.

RESULTS

There are 5 clinical trials underway on advanced therapies, including an ARI trial for lymphoma and acute lymphoblastic leukemia and an HIV vaccine. Advances have been made in tissue engineering therapies, including the use of mesenchymal stem cells from adipose tissue and umbilical cord blood for myocardial regeneration.

So far, more than €1.8 million has been raised in research projects from sources like H2020, GenCat, ISCIII and MINECO and 10 scientific papers have been published in prestigious international journals.

AELIX THERAPEUTICS

www.aelixtherapeutics.com



O) PROJECT LEADER

Bonaventura Clotet, Christian Brander, Jordi Naval



START YEAR



PARTICIPATING ORGANIZATIONS

IrsiCaixa, Laboratoris Esteve, Ysios Capital, J&J Innovation - JJDC, Caixa Capital Risc

PROJECT AIM

To develop a therapeutic HIV vaccine to be used in cure/eradication strategies. This vaccine program is based on an innovative T-cell vaccine immunogen design that directs the body's immune system to the most vulnerable parts of the virus. AELIX hopes to be instrumental in developing the first therapeutic vaccine regimen to cure HIV infection.

COLLABORATION FRAMEWORK

AELIX Therapeutics is a spin-off of IrsiCaixa and the HIVACAT program, a Catalan public-private consortium conducting cutting-edge research in the field of AIDS and related diseases. HIVACAT has received funds from the "la Caixa" Foundation and Laboratorios Esteve, as well as public research funding. The company was incorporated in November 2015 and shortly after completed a €11.5 million (\$12.5 million) series-A round of funding led by Ysios Capital, Johnson & Johnson Innovation - JJDC, Inc., and Caixa Capital Risc.

MOST IMPORTANT CHALLENGES

Before setting up the company, the most significant challenge was to define a joint project that all involved could agree on. Plus, the associated intellectual property was being used at that time for other research projects, which made it necessary to ensure this was compatible with commercial development. Currently, management of the manufacturing process is complex, as the company works with CMOs in England, Germany and Italy, which is an operational challenge.

RESULTS

The design of the immunogen, called 'HTI', is driven by immune data from nearly 1,000 individuals living with HIV from four cohorts on three continents. Preclinical data shows that mice and macaques immunized with HTI have a strong, broadly directed T-cell response that has been associated with HIV-1 control in previous human studies.

Clinical trial products have already been manufactured. A first-in-human (FIH) phase I study with HIV-infected individuals began in August 2017, the primary focus of which is to assess the safety and immunogenicity of the vaccine. The trial is taking place at Germans Trias i Pujol Hospital (HUGTIP) in Badalona. Results are expected in 2018.

The series-A funding will also go towards a phase II proof-of-concept efficacy trial in HIV-infected individuals who will undergo a therapeutic, heterologous prime-boost vaccination regimen.

ANILING

www.aniling.com



O) PROJECT LEADER

Llorenç Coll



START YEAR

2014



PARTICIPATING ORGANIZATIONS

IMPPC

PROJECT AIMS

Aniling is a company that is working to make precision medicine possible using the epigenomics revolution, developing a new standard for genetic analysis globally, with technology that can analyze the genome and epigenome simultaneously.

COLLABORATION FRAMEWORK

Aniling was created as a spin-off of the Institute of Predictive and Personalized Medicine of Cancer (IMPPC), through an agreement that granted Aniling the exclusive license to a patent protecting this technology. The founders of the project were Llorenç Coll (CEO) and Miguel Angel Peinado (CSO), with Jaume Amat as their strategic adviser. The company also has a scientific advisory board with experts like Elías Campo, Manel Esteller, Ivo Gut and Susan Clark.

MOST SIGNIFICANT CHALLENGES

From the beginning, one of Aniling's strategic focal points has been to create a robust, flexible, well-balanced team. Additionally, defining the market was also a challenge in the early stages, given the significant innovative component of the technology. The next phase for Aniling is to take the prototype to market and, to do so, the company is working with international opinion leaders. This requires additional investment to validate the product on the market. The company is currently working to raise more funds, from both public and private sources.

RESULTS

So far, Aniling has invested more than €1 million in developing a prototype for advanced users in the oncology arena. This funding has been obtained from various sources, including Caixa Capital Risc and ACCIÓ. Aniling has recently launched an Advanced User Program internationally. In Catalonia, groups are participating from institutions like ICO, Hospital Clinic, VHIR (AMMIC project under RIS3CAT) and the ADN GCAT-Genomes for Life DNA biobank. In the first phase, roughly 200 samples will be analyzed to validate the market for the company's first kit. According to Aniling, the technology will save time, money and sample size, analyzing the genome and epigenome simultaneously for the first time, increasing sensitivity and reducing error rates 10- to 100-fold over current standards.

GALGO MEDICAL

www.galgomedical.com



O) PROJECT LEADER

Antoni Riu



START YEAR

2013



PARTICIPATING ORGANIZATIONS

Galgo Medical, Hospital Clínic de Barcelona, Universitat Pompeu Fahra

PROJECT AIMS

To develop and patent post-processing software that can automatically detect electrical conduction channels from high-resolution 3D magnetic resonance images to help electrophysiologists plan and guide ablation throughout their surgeries.

COLLABORATION FRAMEWORK

Pompeu Fabra University (UPF) and Hospital Clinic Barcelona collaborated to develop different types of technology that led to a portfolio of patents. A group of entrepreneurs, six engineers with different backgrounds, decided to crystallize the technology in a start-up, creating Galgo Medical.

MOST SIGNIFICANT CHALLENGES

Transforming possible product ideas from a group of researchers into a salable product of interest to the international clinical community has been a challenge in many ways. The most important challenge was to find the funding to move forward with the projects and keep them alive in the first and successive years. The first financial aid was two Torres-Quevedo grants to hire doctors, a Retos-Colaboración project, a Eurostars project and an ENISA line of credit. Getting the prototype was relatively simple, but it took 5 more years to complete the product and get it ready for market.

RESULTS

The result of the collaboration is the product ADAS3D, which characterizes the myocardial substrate as well as the electric conduction channels using an MRI, in order to identify and plan the best ablation strategy (endo, epi, combined), either ventricular or auricular. ADAS3D has been granted CE marking, presented at the top international conferences in electrophysiology, used in more than 400 surgeries and is being assessed at the top electrophysiology centers in the world. The product is now ready for market. Galgo Medical has two other products: one geared towards orthopedics in osteoporosis (3D-SHAPER) and the other for planning brain aneurysm operations (ANKYRAS). The company's technology is protected by seven patents.

GOODGUT

www.goodgut.eu



O) PROJECT LEADERS

Jesús Garcia-Gil, Xavier Aldeguer, Mariona Serra



START YEAR

2014



PARTICIPATING ORGANIZATIONS

University of Girona (UdG), Girona Biomedical Research Institute (IDIBGI)

PROJECT AIMS

To develop support systems for diagnosing and treating digestive diseases through the study of the intestinal microbiota. The company has three product lines: RAID-CRC (early detection of colorectal cancer), RAID-CD (diagnosing irritable bowel, Crohn's disease and ulcerative colitis) and PREVIPECT (prebiotic to treat digestive diseases).

COLLABORATION FRAMEWORK

From the University of Girona, Professor of Microbiology Jesús Garcia-Gil has contributed expertise in microbiology of ecosystems. Additionally, from the Girona Biomedical Research Institute (IDIBGI), Dr. Xavier Aldeguer, head of the Digestive System Unit at Hospital Doctor Josep Trueta, has contributed clinical knowledge of digestive diseases.

MOST SIGNIFICANT CHALLENGES

The most important challenge of GoodGut has been to not lose sight of the market when developing products, as they tend to take more than a year of development and, over this time, the market and regulatory issues can change. The team highlights the need to "plan to improvise", meaning you have to think of all possible scenarios to minimize the risk associated with developing your projects. Planning the project from beginning to market launch has been key to tackling the changes that have popped up, as has revising that plan periodically.

RESULTS

GoodGut has received funding from several sources: the NEOTEC program from the Center for the Development of Industrial Technology (CDTI), the Ministry of the Economy and Competitiveness Retos program, MERCAT grants from the Agency for Administration of University and Research Grants (AGAUR), IFEM microloans from the Catalan Institute of Finance (ICF), the Girona Regional Council and Industrial doctorates.

GoodGut has currently submitted 5 patent applications for its 3 products. The company will begin a clinical validation study in Germany with 2,800 patients on RAID-CRC (early detection of colorectal cancer), which will allow it to hit the market sometime in 2019. With regard to RAID-CD (diagnosing irritable bowel, Crohn's disease and ulcerative colitis), the company is finishing up clinical studies that will allow it to get CE marking by the end of 2018. For PREVIPECT (prebiotic to treat digestive diseases), the company has finished proof of concept and is starting toxicity studies prior to the clinical trial.

HEMOPHOTONICS

www.hemophotonics.com



O) PROJECT LEADER

Udo Weigel



START YEAR

2013



PARTICIPATING ORGANIZATIONS

ICFO, HemoPhotonics

PROJECT AIMS

To develop and market medical devices based on non-invasive photonic technology to monitor blood flow and oxygenation levels in microvessels in different types of human tissue in real time. Under the framework of the European BabyLux project, a new optical system has been developed that can measure blood flow and oxygenation levels in microvessels in the brains of premature babies, which helps reduce the risks associated with brain damage caused by insufficient oxygen supply.

COLLABORATION FRAMEWORK

HemoPhotonics is a spin-off of the Institute of Photonic Sciences (ICFO). Specifically, the company came out of the ICFO Medical Optics group, led by ICREA professor Turgut Durduran, who is an expert in diffuse optical imaging and monitoring techniques. Under the framework of the BabyLux project, HemoPhotonics and ICFO have joined forces with the other seven partners from four European countries: Politecnico di Milano, Capital Region of Denmark, Fraunhofer IPT, PicoQuant, Loop, Fondazione IRCCS Ca' Granda and Fondazione Politecnico di Milano. The members of the consortium have extensive experience, both academic and industrial, in diffuse optical imaging, industrial design and clinical research in neonatology.

MOST SIGNIFICANT CHALLENGES

From a technical standpoint, the project has combined two types of photonic technology in near-infrared spectroscopy for the first time (TRS and DCS), which has posed a challenge in terms of designing and building the integrated system. The main challenge, however, was the limitation on including new developments or improvements to the device due to the characteristics of the call.

Most of the funding for the project came from the European Commission's ICT Policy Support Program, under the Competitiveness and Innovation Framework Program (CIP) 2007-2013 (FP7). The challenges still pending for this project include certification for the device, which is the most intensive in terms of funding needs.

RESULTS

After an initial validation in the laboratory, the two Babylux neuromonitors were moved to neonatal ICUs in Milan and Copenhagen, where 60 measurements were conducted on 35 babies. In the results of these tests, Babylux shows less variability than commercial devices currently in use and has also been proven to be safe in terms of acute adverse reactions. The measurement campaigns are ongoing in both cities in order to consolidate preclinical research and foster future use of the device in care settings.

Although BabyLux is geared towards pediatric neurology, the technology developed can also find applications in other clinical areas, like vascular medicine, oncology, endocrinology, anesthesiology and sports medicine, which opens up potential lines of business that HemoPhotonics is currently exploring.

NEW THERAPEUTIC MOLECULES FOR CANCER METASTASIS

www.becbarcelona.eu



O) PROJECT LEADER

Xavier Trepat



START YEAR

2016



PARTICIPATING ORGANIZATIONS

IBEC, Mind The Byte, Ferrer

PROJECT AIMS

To develop new therapies for cancer metastasis based on the discovery of Dr. Xavier Trepat, of the Institute for Bioengineering of Catalonia (IBEC) and ICREA professor (Catalan Institution for Research and Advanced Studies), who has identified how the interaction of certain proteins on the cell surface that play a key role in adhesion, cadherins, plays a part in metastasis.

COLLABORATION FRAMEWORK

The company Mind the Byte contributes computational modeling of the interactions between cadherins and the design of blocker molecules; the IBEC research center contributes expertise in mechanobiology and tests the compounds; and pharmaceutical corporation Ferrer contributes chemical, pharmacological and drug-development knowhow, and will play a key role as the industrial partner in later stages.

MOST SIGNIFICANT CHALLENGES

The decision to incorporate computational design in the early stages of the project helps cut costs and time in developing a potential drug. In the cases this project studies, it is a pharmacological target that is difficult to tackle as it involves protein-protein interactions where finding a molecule to inhibit the interaction is a challenge.

RESULTS

The project is currently in the development stage and any results obtained so far are confidential. If molecules are obtained that effectively inhibit the metastasis processes being studied, the project members expect to protect them with a patent.

ICARDIO

www.eurecat.org/icardio-electrocardiograf



O) PROJECT LEADER

Telehealth Devices



START YEAR

2016



PARTICIPATING ORGANIZATIONS

Telehealth Devices, Eurecat

PROJECT AIMS

To develop the 2.0 version of the portable electrocardiograph device iCardio, useful in preventing heart disease, remote monitoring and predicting worsening conditions. Its main characteristics are its portability and the option to send the data captured to a cloud computer system. The project seeks a quick, personalized, low-cost solution for end users in line with current healthcare needs.

COLLABORATION FRAMEWORK

Eurecat has provided the support necessary to tackle the technological challenge of improving the hardware and software, technological guidance to find funding through joint participation in public calls and technical support in the certification phase, one of the most important in the creation of a medical device.

MOST SIGNIFICANT CHALLENGES

From a technical standpoint, Eurecat has coordinated a multidisciplinary applied-technology research team, made up of the Functional Printing and Embedded Devices and eHealthresearch units, that has made it possible to overcome the main technological challenges and complete a full product analysis. The most important organizational challenge has been to coordinate these teams and, from a regulatory standpoint, the most noteworthy has been adapting the device to UNE-EN 60601 and UNE-EN 62366 regulations.

RESULTS

The iCardio device is expected to hit the market in spring 2018, after the final certification testing is completed in the first quarter of the year. The target market for iCardio is global, and the company Telehealth expects to provide service and support worldwide.

The project was funded initially with capital contributed by the founding partners and a private venture capitalist. Eurecat has helped apply several public funding options to be submitted soon (SME Instrument).

SEROLOGICAL TEST TO **MONITOR TRANSMISSION OF MALARIA DURING PREGNANCY IN ERADICATION SCENARIOS**

www.isglobal.org



O) PROJECT LEADER

Alfredo Mayor



START YEAR

2017



PARTICIPATING ORGANIZATIONS

ISGlobal, Foundation for Innovative New Diagnostics (FIND)

PROJECT AIMS

To develop a serological test to monitor recent exposure of pregnant women to the Plasmodium falciparum parasite, which causes malaria. Use of this serological test will help measure the impact of eradication efforts to completely interrupt transmission of the parasite.

COLLABORATION FRAMEWORK

ISGlobal has investigated the use of serological tests in malaria and the potential of using pregnant women as a sentinel group in malaria vigilance, as there is evidence that the prevalence of malaria in these cases is comparable to the prevalence in the population of children in a community. The Foundation for Innovative New Diagnostics (FIND) is processing and funding the patent application, submitted in the United States in June 2017, and the PCT, expected to come one year later, with exclusive sublicensing rights.

MOST SIGNIFICANT CHALLENGES

It is quite a challenge to get the product to market and this will require the involvement of international stakeholders in global health, including WHO, PATH, USAID, Global Fund to Fight AIDS, TB and Malaria and the Bill and Melinda Gates Foundation, as well as the private sector. With this aim, ISGlobal and FIND have agreed to draft a preliminary business plan to start contact with the international diagnostics industry and gage commercial interest in the test while applying for the patent.

RESULTS

The proof of concept has yielded positive results, but no clinical trials have yet been done. One patent application has been submitted. One element that sets this serological test apart is its application in prenatal appointments, which cuts the cost of implementing epidemiological vigilance systems that are more complex to organize and fund, as well as national malaria surveys.

In terms of exploitation, it is expected to be rolled out in both the public and private sectors in low-income endemic countries.

LEUKOS BIOTECH

www.leukosbiotech.com



O) PROJECT LEADER

Ruth M. Risueño



START YEAR



PARTICIPATING ORGANIZATIONS

Josep Carreras Leukemia Foundation, Josep Carreras Leukemia Research Institute

PROJECT AIMS

To develop a new class of drugs around a therapeutic target that selectively destroys leukemia stem cells. This discovery opens the doors to a new therapeutic strategy to treat recurring cancer.

COLLABORATION FRAMEWORK

Leukos Biotech was founded in October 2015 by the Josep Carreras Leukemia Research Institute and Dr. Ruth M. Risueño. The Josep Carreras Leukemia Foundation has funded the company's first phases of development. In July 2016, the Inveready investment group joined the project, leading the first round of funding. Dr. Enrique Llaudet joined the company as partner and CEO in February 2016.

MOST SIGNIFICANT CHALLENGES

Thanks to its partners, Leukos was able to overcome the liquidity problems common in the first years of any biotech company. Like the majority of companies in the sector, some of the main challenges this spin-off has faced were in the regulatory arena, as it is essential to prove that product development complies with quality and benefit requirements in order to start a clinical trial with patients. From a commercial standpoint, the main difficulty is to generate a product profile that attracts the interest of pharmaceutical corporations willing to acquire a license to its patent.

RESULTS

Leukos Biotech closed a first round of investment led by Inveready, as well as public grants valued at more than €500,000.

In terms of product development, a phase II clinical trial is expected for mid-2018 with LMA patients and a new diagnosis kit for LMA has been developed and is currently in the clinical validation phase. The company has applied for 3 patents.

NEXTCARE

www.nextcarecat.cat



O) PROJECT LEADER

Felip Miralles and Josep Roca



START YEAR

2016



PARTICIPATING ORGANIZATIONS

Eurecat, Hospital Clínic, IDIBAPS, Atos, Wordline, Costaisa Group, SI-Sinf, SONMEDICA, Nabelia, TicSalut, Philips, Esteve Teijin Healthcare, AQuAS, CHV, BRN, BIB, ISGlobal, HealthTech Cluster, MWC, IBEC, CRG, CREB-UPC, FBiG, ACCIÓ, Biocat

PROJECT AIMS

To develop a comprehensive care model to manage complex chronic patients based on the concept of 4P medicine (predictive, preventative, personalized and participative) in order to support professionals in managing personalized clinical histories, monitoring the status and activities of patients, giving patients recommendations on how to manage their disease themselves and improve their quality of life, and reducing the risk of getting sick.

COLLABORATION FRAMEWORK

Nextcare is being developed around five actions with important synergies between them, for which 23 organizations are being coordinated, from multinational ICT corporations to clinical research bodies. It is led by Eurecat and Barcelona Hospital Clínic i Provincial. Plus, the project is open to new collaborations. This project is part of the NEXTHEALTH community, coordinated by Biocat and co-funded by the Government of Catalonia through ACCIÓ (Agencia para la Competitividad de la Empresa) and the European Union, under the framework of the ERDF (European Regional Development Fund) Catalonia 2014-2020 program, as part of the RIS3CAT strategy.

MOST SIGNIFICANT CHALLENGES

The project is facing key challenges associated with regulatory aspects of managing and integrating large databases. Additionally, the technological results achieved must be transferred to real management of chronic patients, generally by implementing tools generated for outpatient care and transactional health programs.

RESULTS

In its first year, the project reached an agreement with the Programa público de analítica de datos para la investigación y la innovación en salud (PADRIS) to integrate clinical data and has completed a study on outpatient care. It has also advanced in interoperability needs with Cat@Salut La Meva Salut for self-management tools, among others.

The project has consolidated the Rehabilitation Unit at Hospital Clinic under the framework of promoting healthy lifestyles and is assessing the forced spirometry test as a primary-care diagnostic tool.

Two scientific papers have been published in specialized journals and project proposals are expected to be submitted to H2020 and EIT Health in spring 2018.

NOSTRUM BIODISCOVERY

www.nostrumbiodiscovery.com



O) PROJECT LEADER

Modesto Orozco



START YEAR

2015



PARTICIPATING ORGANIZATIONS

IRB Barcelona, BSC-CNS, UB, ICREA, Nostrum BioDiscovery (NDB) i Fundación Botín (FB)

PROJECT AIMS

To facilitate launch to market of new biotechnology drugs and molecules through computer simulation. The company has cutting-edge bioinformatics and modeling technology to accelerate and drive down the cost of designing new drugs, which are increasingly complex and costly, and advanced towards precision medicine. The advantages could save up to €40 million for each new drug, a 15% - 20% cost reduction in the initial phase.

COLLABORATION FRAMEWORK

Nostrum BioDiscovery is the result of the synergy between IRB Barcelona and BSC-CNS, two research centers of excellence in Barcelona with powerful research teams developing experimental and in silico technology. Nostrum BioDiscovery has cutting-edge bioinformatics and modeling technology developed by researchers Modesto Orozco and Víctor Guallar (IRB Barcelona and BSC, respectively), with support from the University of Barcelona and the Catalan Institution for Research and Advanced Studies (ICREA), which is why they are shareholders in the spin-off. The Botín Foundation has participated as a catalyst for technology transfer, as well as providing €500,000 in seed capital through the Mind the Gap program.

MOST SIGNIFICANT CHALLENGES

Nostrum BioDiscovery was created at a time of transformation in the pharmaceutical industry, which is moving from in-house drug discovery to a model in which research and development programs are being partially outsourced. This opened doors for the first spinoff to come out of collaboration among four institutions with very different characteristics. The most important difficulty has been to design the right collaboration and transfer framework, coordinating the different legal requirements of each of the institutions. This has been possible thanks to the drive of the entrepreneurs and the transfer departments at each institution, plus the help of the Botín Foundation.

RESULTS

The first round of funding for Nostrum BioDiscovery, led by the Botín Foundation, raised €500,000. Plus, the company has recently been awarded a CDTI Neotec grant, recognizing its level of excellence.

Just one year after being founded, Nostrum BioDiscovery is already working for some of the largest pharmaceutical and biotechnology companies on the international scene, includina AstraZeneca.

Plus, the tools the company uses have been applied to new targets for various diseases including cancer, cardiovascular conditions and anti-infection drugs. Alliances have been forged with groups at research centers and hospitals: the company has applied its technology to these targets while the academic collaborators work on validating them.

PEPTOMYC

www.peptomyc.com



O) PROJECT LEADER

Laura Soucek



START YEAR

2016



PARTICIPATING ORGANIZATIONS

VHIO, ICREA, Peptomyc

PROJECT AIMS

To develop a new generation of peptides targeting the Myc oncoprotein, for oncology treatments. Myc is a central transcription factor that coordinates cell growth and proliferation, the expression of which is unregulated in most human cancers. To inhibit it, Dr. Laura Soucek has designed a Myc dominant negative called Omomyc. The company's mission is to maximize the therapeutic potential of Omomyc, developing it to treats glioblastoma (GBM), non-small cell lung cancer (NSCLC) and triple-negative breast cancer (TNBC) intravenously.

COLLABORATION FRAMEWORK

Peptomyc is a biopharmaceutical spin-off of the Vall d'Hebron Institute of Oncology (VHIO) and the Catalan Institution for Research and Advanced Studies (ICREA). The company was founded in Barcelona in December 2014 based on research led by Dr. Laura Soucek over the past 20 years. A licensing agreement has been signed regulating transfer of the technology.

MOST SIGNIFICANT CHALLENGES

The main challenge this spin-off has faced has been transferring the fruit of 20 years of research to market. The facilities the VHIO and ICREA have given have made it possible for the company to not have transfer difficulties. On the regulatory front, Peptomyc will soon conduct non-regulatory preclinical experiments and coordinate execution of regulatory experiments needed to take Omomyc to the clinical-trial phase (phase I/II).

RESULTS

Peptomyc has one patent in progress in Spain to protect the use of peptides derived from Omomyc for oncology. A second patent application has been submitted and PCT to protect new variants of Omomyc. Both patents fall under the framework of the licensing deal signed with VHIO.

In July 2017, Peptomyc closed a series-A round of funding, with participation from ALTA Life Sciences, as well as investors from the seed round (Healthequity and a group of business angels). The company raised €5.2 million in these rounds, including more than €2 million in public funds leveraged from sources like the Ministry of the Economy and Competitiveness Retos program, Neotec-CDTI and Phase I SME Instrument (European Commission).

RETINOPATHY SCREENING APP (RETIPROGRAM)

www.iispv.cat/recerca/arees de recerca/31/ grup-de-recerca-en-oftalmologia-retiprogram



O) PROJECT LEADER

Pere Romero Aroca



START YEAR

2015



PARTICIPATING ORGANIZATIONS

Pere Virgili Institute (IISPV), Rovira i Virgili University (URV)

PROJECT AIMS

To develop a support system for clinical diagnosis based on using artificial intelligence and computer-vision techniques to classify patients by their risk of developing diabetic retinopathy (DR), one of the most common comorbidities and the main cause of blindness.

COLLABORATION FRAMEWORK

RETIPROGRAM is led by the Ophthalmology Research Group-HUSJR-IISPV (Pere Virgili Institute) headed up by Dr. Pere Romero, with collaboration from the ITAKA Research Group (Intelligent Technologies for Advanced Knowledge Acquisition) headed up by Dr. Antoni Moreno and Dr. Aïda Valls, and the IRCV Research Group (Intelligent Robotics and Computer Vision) headed up by Dr. Domènec Puig, both at Rovira i Virgili University. The project came out of two projects funded by the Institute of Health Carlos III.

MOST SIGNIFICANT CHALLENGES

The initial challenge of RETIPROGRAM was to find funding to subcontract the IRCV and ITAKA research groups for computer development, as well as seeking collaborations with industry. In terms of the transfer of the project to clinical practice, the challenges were to boost the cost/efficacy of the current DR screening system, improve care of patients at high risk of developing the disease and to decrease the number of unnecessary referrals through early detection, lowering the social and healthcare burden.

RESULTS

Screening with non-mydriatic retinal cameras in primary care centers has helped improve detection of DR. According to the Catalan Health Service (ICS), eye exams should be given to people with type-2 diabetes when they are diagnosed and at least once a year after that. The RETIPROGRAM study on 28,000 diabetics followed over 8 years has proven more effective with one screening every 2.5 years. Nevertheless, there's no comparison for its effectiveness if it can be applied periodically according to the patient's personalized needs.

The project expects to apply the new system by making it compatible with computer clinical history systems in the Camp de Tarragona Healthcare Region. Plus, and automatic image-reading system will be incorporated to classify DR by its seriousness. The software has been registered and the project has been sent to the Innòbics platform for assessment.

THEIA

www.bist.eu/theia



PROJECT LEADER

José Antonio Garrido, Pablo Loza-Álvarez, Mokhtar Chmeissani and Jeroni Nadal



START YEAR

2017



PARTICIPATING ORGANIZATIONS

ICFO, ICN2, IFAE, Barraquer Ophthalmology Center and Barcelona Institute of Science and Technology (BIST)

PROJECT AIMS

To develop a graphene implant to help people with retinitis pigmentosa, which affects 1 in 3,700 people, see again. This implant is based on using a multi-electrode array (MEA) biochip as a retina prosthesis. Using graphene is an improvement on current chips, which are limited by the number of electrodes that can be implanted. Plus, graphene is more flexible, biocompatible and transparent.

COLLABORATION FRAMEWORK

THEIA is the result of an alliance between three of the seven Catalan research centers that make up BIST, with Barraquer Ophthalmology Center. ICN2 is responsible for implementing the graphene-based MEA; IFAE, for integrating the electronic MEA controller; and ICFO, for the microscopy experiments to test proper stimulation of the photoreceptors in the retina. Barraquer will implement a proof of concept for this new chip in three years. THEIA falls under the framework of the Ignite Program promoted by BIST to foster multidisciplinary research, which has already funded 8 projects.

MOST SIGNIFICANT CHALLENGES

The initial challenges facing THEIA are imminently technical. As a multidisciplinary project, it faces important challenges in biology (genetic encoding of calcium indicators in the retina, resection and retina imaging), materials technology and science (manufacturing graphene-based MEAs) and electronics (implementing customized stimulation electronics). In terms of funding, the project requires significant efforts beyond the funds earmarked from the BIST Ignite Program.

RESULTS

THEIA has successfully proven its ability to obtain in vitro images with high spatial resolution of the electric activity of retinas using genetically encoded calcium indicators and local stimulation with graphene micro-electrode matrices. The next steps include identifying the best micro-electrode designs for effective focal stimulation and designing more flexible MEA devices, assessing their efficacy for in vivo stimulation.

To tackle these phases, THEIA has been awarded a second round of funding under the BIST Ignite Program and is searching for new funding opportunities.

TRANSPLANT BIOMEDICALS

www.transplantbiomed.com



O) PROJECT LEADER

Ignasi Heras Vila and Carmen Peralta Uroz



START YEAR

2014



PARTICIPATING ORGANIZATIONS

IDIBAPS, Transplant Biomedicals

PROJECT AIMS

To develop a new device to conserve and transport organs to be transplanted (TB1) integrating conservation technology developed at the August Pi i Sunyer Biomedical Research Institute (IDIBAPS). The device aims to improve post-transplant and make the most of organs donated.

COLLABORATION FRAMEWORK

The TB1 project is the result of the relationship that brings together the science of excellence contributed by IDIBAPS, the spin-off created by the same institution and the development of a healthcare product by Transplant Biomedicals through to real use in hospitals. IDIBAPS and Transplant Biomedicals signed an exclusive licensing deal for the patent to

MOST SIGNIFICANT CHALLENGES

One of the initial challenges, during the pre-clinical validation of the technology, was to develop animal models as similar as possible to common clinical practice. After the pre-clinical validation, the greatest technological challenge was to scale up the technology to a clinical prototype adapted to human organs.

The most important challenge, however, has been to go from disruptive technology to a product that can be produced at an industrial scale, which is fully adapted to healthcare personnel and that international transplant centers will be interested in acquiring.

RESULTS

TB1 has currently completed pre-clinical validation for kidney and liver transplants. The results have shown the potential for reducing the injury organs experience in the ischemic phase between donor and receiver, an increase in post-transplant survival rates and the ability to take advantage of organs that are currently discarded.

The company has raised a cumulative €6.5 million in funding. They closed the first investment in 2017 for a medical device in Spain, with €2.5 million to complete development of the device and start a first-in-human clinical study in benchmark transplant hospitals in Catalonia in the second quarter of 2018: Hospital Clinic Barcelona, Hospital Bellvitge and Hospital Vall d'Hebron. The company expects to get CE marking by the end of 2018 and begin marketing the product in 2019.

In the future, Transplant Biomedicals hopes to diversify the technology and develop a TB1 to preserve livers and hearts for transplant over the next 2 years. To fund the next steps, they are considering series-B funding.

AUTOMATIC BLADDER IRRIGATION

www.vhir.org



O) PROJECT LEADER

Montserrat Llinàs



START YEAR

2015



PARTICIPATING ORGANIZATIONS

HUVH, VHIR, Vecmedical Spain

PROJECT AIMS

To develop new equipment to automate bladder irrigation in urology patients. This process is currently done manually. Automating it would substantially reduce most complications (obstruction of the system, vesicle perforation, urinary tract infection), as well as cutting costs and increasing quality of care.

COLLABORATION FRAMEWORK

The project is the result of a collaboration between Vecmedical, a company that specializes in developing medical devices, and the Vall d'Hebron Research Institute (VHIR). Vecmedical develops medical devices and VHIR leads the clinical trials to validate the technology and gain approval in regulatory processes.

MOST SIGNIFICANT CHALLENGES

The main hurdle in developing medical devices within the framework of a public institution is the lack of financial resources. Collaboration with a company in the healthcare-device manufacturing sector has made it possible to obtain public grants from the Carlos III Institute of Health in 2015 and the CDTI in 2017.

An additional challenge has been defining the regulatory path to obtain the necessary approval before hitting the market. Finally, one of the most important challenges is taking the product to market, getting the Catalan healthcare sector to adopt the technology coming out of its own hospitals and research centers. In this regard, innovative public procurement initiatives may be key.

RESULTS

National funding and working with an industrial collaborator have allowed us to move forward with proof of concept, developing a functional prototype, production strategy and regulatory path. The first clinical trial is expected to begin in late 2018.

ZECLINICS

www.zeclinics.com



O) PROJECT LEADER

Davide D'Amico, Javier Terriente, Simone Calzolari and Ignasi Sahún



START YEAR



PARTICIPATING ORGANIZATIONS

ZeClinics, UPF, PRBB

PROJECT AIMS

To provide scientific services of excellence in the drug-discovery arena using zebrafish as an animal model. This model provides highly relevant information in the optimization phase for possible drugs, as it is 72% genetically homologous with humans (80% for some diseases). Plus, its larvae are transparent, grow quickly and easily (5 days) and are easy to handle.

COLLABORATION FRAMEWORK

ZeClinics is a 100% private initiative, with 4 founding partners who have contributed value in the form of knowledge, with help from two main stakeholders: Pompeu Fabra University (UPF), which has helped from the beginning providing structural support, training and mentoring; and the Barcelona Biomedical Research Park (PRBB), which has given them access to scientific and technical services of excellence.

MOST SIGNIFICANT CHALLENGES

ZeClinics has had to tackle the challenges facing any company that starts from scratch, like searching for initial funding, difficulties in setting up company structures, lack of business training and the complexity of explaining and transforming an idea into a product or service. To tackle these challenges, all of the founders did training in various disciplines in order to become professional entrepreneurs. The company has chosen to do R&D tailored to each client, which has allowed them to generate innovative and disruptive services, has funneled a lot of effort into being at all of the most important international events in the sector and on social media, working to convey the image of a modern, active company.

RESULTS

ZeClinics successfully closed the largest crowdfunding campaign in biomedicine in 2015, raising €100,000 to move forward with a personalized medicine project called ZeOncoTest. In late 2016, the company was granted a Phase 2 SME Instrument valued at €1.8 million to develop one of its products, ZeCardio, software to assess cardiovascular parameters in an innovative way that it is currently in the process of protecting with a patent. Plus, the company is completing a specialized toxicology platform for cosmetics and phytosanitary

ZeClinics expects to set up a holding company in 2018, with a CRO service company and a new company devoted to drug discovery, generating new molecules for use in oncology, cardiology, central nervous system and GMO models.

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Acknowledgments



ACKNOWLEDGMENTS

The 2017 Biocat Report was overseen by Biocat Director of Communications, Marketing and Strategic Relations Sílvia Labé. It is the result of collaboration among everyone on the Biocat team, but especially CEO Jordi Naval, Head of Science Policy and External Relations Montse Daban, Head of Knowledge Management Mònica Montero, CRM Manager Marta Malé, Head of Media Relations and Content Núria Peláez and Head of Research and Scientific Debate Marta Soler. We would also like to mention the collaboration of Llorenç Arguimbau, who developed part of the cumulative data for these past two years.

We particularly appreciate the collaboration of all the companies and organizations that agreed to share their experience in technology transfer.

As for all the editions, we would like to thank the professionals from public and private, national and international organizations who chose to participate, contributing updated data and information to complement the analysis we are presenting:

- Francesc Abad and Montse Solé, from the Government of Catalonia Secretariat of Universities and Research.
- Roger Cabezas and Lluís Rovira, from the CERCA Institution.
- The team from the ACCIÓ Strategy and Competitive Intelligence Unit, in particular Giulia Diamante and Inma Rodríguez.
- Elsa Alonso, Cristina Borràs and Aïda Díaz Sáez, from the Agency for Management of University and Research Grants (AGAUR).
- Salvador Cassany, from the Servei de Control Farmacèutic i Productes Sanitaris.
- Lorena Cussó and Laura Sampietro-Colom, for the data provided from the Medical Technology Innovation Platform (ITEMAS) (PTI3/0006/0001) promoted by the Carlos III Health Institute and the Sub-Directorate General for Research Assessment and Promotion under the National R+D+I Plan. Project funded jointly by the ERDF.
- Lucía Arévalo, from EURECAT.
- Raúl Méndez and Eduard Suñén, from the BAC (Research Group on Bibliometrics).
- Pascual Segura, from the University of Barcelona Patent Center, and Gian-Lluís Ribechini, chairman of the Comissió de Gestió Empresarial del Col·legi d'Enginyers Industrials de Catalunya, for their help and knowledge on patents.
- Marta Codina. SABI consultant at Informa.
- Nieves Cuadrado, from the Spanish Statistical Office.
- Fèlix Bosch, from the Esteve Foundation, and Ricard Valls, for their data on philanthropy in Catalonia.

- Rosina Malagrida, head of the IrsiCaixa Health Living Lab.

We would also like to thank all the investors that provided data on funding, as well as the nearly 200 companies that answered the internationalization survey, helping give us an increasingly realistic view of the BioRegion.

Thanks, as well, to all the organizations and professionals that, with their contributions and comments, have helped us day by day to compile this report.

We also want to thank the following entities for the cession of the images that illustrate the covers of the chapters of this report

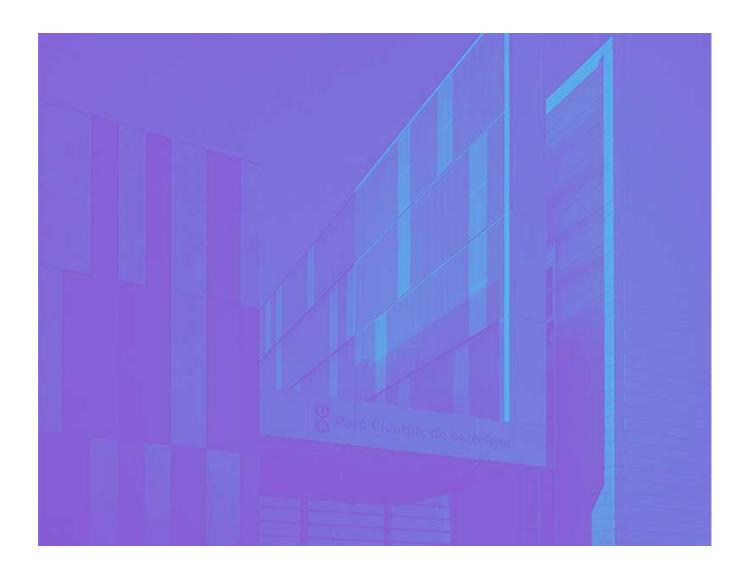
- BSC-CNS (Barcelona Supercomputing Center)
- -Hospital de la Santa Creu i Sant Pau.
- -PCB (Parc Científic de Barcelona).
- -PRBB (Barcelona Biomedical Research Park).
- -ALBA Synchrotron.

Finally, our sincerest thanks to Amgen for their commitment and financial support for this report.

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Methodology



The data on which the analyses of the BioRegion of Catalonia are based is from the Biocat Directory, a database that is available at http://www.catalanlifesciences.com. It compiles information on the companies and organizations operating in Catalonia in the healthcare and life sciences arena and is managed in collaboration with Venture Valuation, the owners of Biotechgate, the most complete international database in this arena. The companies are classified according to the same criteria that is used for all the bioregions that are part of the global platform, http://www.biotechgate.com/, which currently has information on more than 50,000 organizations around the world,89 including 16,000 biotech companies, over 2,600 pharmaceutical corporations, 5,600 medtech firms and more than 1,300 in the emerging healthtech sector. Having a standardized classification 90 gives a much more comprehensive snapshot of each bioregion and shows which are the most active clusters in certain areas, although, clearly, not all countries are covered or updated⁹¹ equally.

Biocat cross references data from the Directory with data from its internal system, a CRM with over 9,000 entries and nearly 28,000 contacts generated through Biocat's activities and the projects it promotes or participates in, with precise details on Catalan companies. This results in highly accurate indicators that provide a snapshot of the BioRegion at a specific time. For this report, the data compiled covers the period through December 30 2017, unless it is specifically indicated. So, both the new companies detected and rounds of investment included are those Biocat was aware of as of the time this chapter was drafted.

In order to provide a very clear snapshot of the BioRegion, this edition of the Report uses a new method for grouping companies that makes it much easier to visualize the sectors. Since the 2013 Biocat Report, when the BioRegion joined the Biotechgate global directory, all of the graphs broken down by core sectors (biotech, pharma, medtech) were shown using the classification in the Directory. This representation, however, had a handicap: it separated companies that conducted research from those that only distributed and/or marketed products or services. This differentiation is correct and necessary (and this is how it is done in the Directory online), but it doesn't provide an overview of the global weight of each sector, because it separates an important part of companies into the generic category of "Providers", which puts, for example, service providers alongside important subsidiaries of multinational corporations. In the 2017 Biocat Report, we have chosen to show all the companies in each sector in the graphs, including for the first time this year healthtech, giving a more realistic view of the sum of companies in the biotechnology, pharmaceutical, medical technology or emerging digital health sector, which already has its own category in the Directory. The graphs in this Report and those generated automatically on the Directory site, therefore, aren't directly comparable as they apply different criteria.

Another methodological change in this edition that should be noted is that the graphs showing the evolution of the number of companies in the BioRegion had previously been compiled using the number of companies in the Directory as of the date of closing the report. But Biocat is always working to locate companies not

included and update the database, not only with newly created companies. Comparing each new edition of the report with a different base doesn't give a clear picture of the real evolution of the sector, because it must take into account this difference. Starting from this edition, therefore, in order to provide a view that reflects reality as faithfully as possible, the base to show the evolution of the companies and analyze this aspect (turnover, size, number of employees) is the same for all the years in the comparison.

For the section on the companies' turnover and employment, calculations use the SABI database (Iberian Balance Sheet Analysis System), which gets its information from the business registry. It must be noted that complete information for all of the companies is not available in this section, as some that have been created more recently have not yet submitted their accounts; there are companies that have never submitted their accounts; and, additionally, a small percentage of companies are in the Biocat Directory because they operate in Catalonia but don't have their business headquarters in the country, so they are not counted either.

The information on the therapeutic areas of Catalan biotechnology companies was provided by the companies themselves or is available on their websites. Regarding the pipeline, this Report references data from the Biocat database, contrasting the information with ClinicalTrials.gov. It does not include pharmaceutical industry or large companies, but exclusively the innovation emerged from the academy.

To understand the data in the Biocat Report, is important to take into account the difference between the sector's organic growth, which can be seen in graph 2.1.3 and counts the number of companies created in the BioRegion, and the incorporation of companies into the Biocat Directory, the result of ongoing work to located companies and update the database that has driven up the number of companies year after year.

In terms of the data on funding and investment, it is worth noting that it includes capital funding for emerging or innovative Catalan companies, whether public or private, through formal investment vehicles or instruments. This means that, of all the companies established in Catalonia working in the healthcare and life sciences arena over the period in question, the graphs on investment only show entrepreneurship-based companies focusing on research or products. Normally, companies with more than 10 years of history are excluded, and the external investment received is counted from the time the company was set up, not including the capital raised beforehand as a research group. Companies that do not have their business headquarters in Catalonia, consultancy firms, subsidiaries or distributors, are not counted. Companies that have changed their business headquarters and left Catalonia are only included through the year they were officially based in Catalonia or, exceptionally, if they have a significant part of their R&D or the bulk of their infrastructure and personnel in Catalonia.

With regard to investors, a wide range of bodies are included, from national and international venture capital funds to corporate investment, business angels, accelerators, public capital funds and investors or participating loan vehicles (but not co-investment). This also includes public subsidies and grants (Spain and Europe), and crowdfunding campaigns.

In situations like licensing deals, bank leveraging and participating loans, the amounts invested are counted towards the total for the year of the agreement or, if this information is not available, when the company or investor announced it publicly. This means that investment commitments are also counted, not only money actually invested.

The data comes from the company itself and/or public sources (press releases, investors, VC reports, press, etc.). Through the 2015 Biocat Report, a list of the investments was included. Starting in 2017, however, in order to include rounds of funding that are significant but that companies wish to keep private, only a total aggregate figure is given.

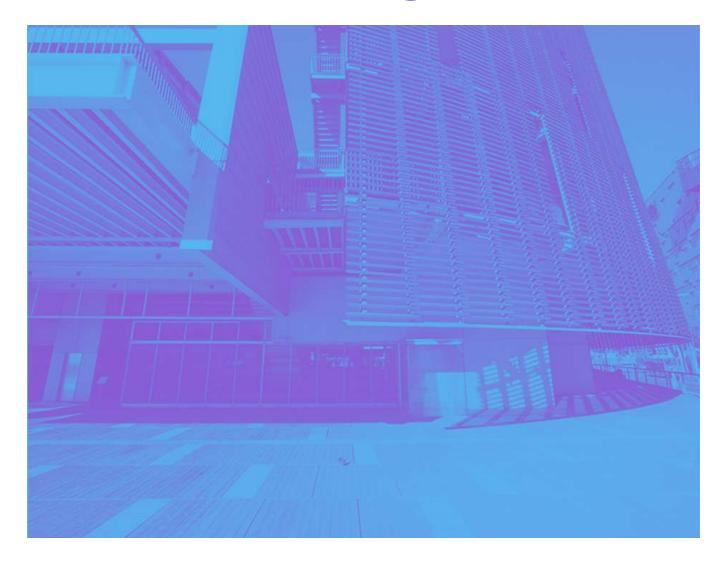
Notes

- ⁸⁹ Biotechgate Company Database. Countries covered. [http://www.biotechgate.com/web/cms/index.php/covered_countries.html].
- ⁹⁰ Biotechgate Company Database. Definitions. [https://www.biotechgate.com/web/cms/index.php/covered_industry_sectors.html#definitions].
- ⁹¹ Biotechgate Company Database. Industry sectors covered. [http://www.biotechgate.com/web/cms/index.php/covered_industry_sectors.html].

Biocat Report 2017

Scaling-up the BioRegion of Catalonia

Abbreviations and acronyms



ABBREVIATIONS AND ACRONYMS

4YFN	4 Years From Now	CPG	Clinical practice guidelines
ACUP	Catalan Association of Public Universities	H2020	Horizon 2020
AGAUR	Agency for Management of University and	EMR	Electronic medical records
	Research Grants	IBEC	Institute for Bioengineering of Catalonia
AQuAS	Agency for Health Quality and Assessment of	ICCC	Catalan Institute of Cardiovascular Sciences
	Catalonia	ICF	Catalan Institute of Finance
ASCRI	Spanish Venture Capital & Private Equity	ICFO	Institute of Photonic Sciences
ASCIN	Association	ICIQ.	Institute of Chemical Research of Catalonia
ASEBIO	Spanish Bioindustry Association	ICN2	Catalan Institute of Nanoscience and
BAC	Research Group on Bibliometrics	ICIVZ	Nanotechnology
BIB	Bioinformatics Barcelona	ICREA	Catalan Institution for Research and Advanced
BIST		ICREA	Studies
	Barcelona Institute of Science and Technology	ICT	
BSC	Barcelona Supercomputing Center	ICT	Information and Communication Technology
CALTECH	California Institute of Technology	ICTS	Unique Scientific and Technical Infrastructures
CATALONIABIO	Catalan Association of Biotechnology Companies	IDIAP Jordi Gol	University Institute for Primary Care Research Jordi Gol
CDTI	Center for the Development of Industrial	IDIBAPS	August Pi i Sunyer Biomedical Research
	Technology		Institute
CELLS	ALBA Synchrotron	IESE	Graduate Business School of the University of
CIMTI	Center for the Integration of Medicine and		Navarra
	Innovative Technologies in Catalonia	IFAE	Institute for High Energy Physics
CNAG-CRG	Centre Nacional d'Anàlisi Genòmica	IGTP	Institute for Health Science Research Germans
COS	Center for Omic Sciences		Trias i Pujol
IPC	International Patent Classification	IIB Sant Pau	Biomedical Research Institute Sant Pau
CRAG	Center for Research in Agricultural Genomics	IMI	Innovative Medicines Initiative
CREAL	Center for Research in Environmental	IMPPC	Institute of Predictive and Personalized
CITE/TE	Epidemiology	11.11 1 0	Medicine of Cancer
CRG	Center for Genomic Regulation	INE	Spanish Statistical Office
CRO	Contract Research Organization	IOT	Infrastructure for OMICS Technologies
CRUE	Conferencia de Rectores de las Universidades	IPO	Initial Public Offering
CRUE		NPO	9
0010	Españolas		Non-profit organizations
CSIC	Spanish National Research Council	IRB Barcelona	Institute for Research in Biomedicine
DCEXS	Department of Experimental and Health	IRII	Institut de Robòtica i Informàtica Industrial
	Sciences	ISCIII	Carlos III Health Institute
EdRIP	Edmond de Rothschild Investment Partners	ISGlobal	Barcelona Institute for Global Health
EGA	European Genome-Phenome Archive	ITEMAS	Plataforma de Innovación en Tecnologías
FTE	Full-time equivalent		Médicas y Sanitarias
EIC	European Innovation Council	LOU	Spanish universities act
EMA	European Medicines Agency	M&A	Mergers and Acquisitions
EMBL	European Molecular Biology Laboratory	€M	Millions of euros
ENISA	Empresa Nacional de Innovación	\$M	Millions of dollars
EPFIA	European Federation of Pharmaceutical	MAB	Alternative Equity Market
	Industries and Associations	MSCA	Marie Skłodowska-Curie Actions
EPO	European Patent Office	MWC	Mobile World Congress
ERA	European Research Area	NMBP	Nanotechnology, Advanced Materials,
ERC	European Research Council		Advanced Manufacturing and Processing, and
USA	United States of America		Biotechnology
FARMAINDUSTRI	A National Trade Association of the Spanish-	OECD	Organization for Economic Co-operation and
	based Pharmaceutical Industry		Development
FCRB	Clinic Foundation for Biomedical Research	PADRIS	Public Data Analysis for Health Research and
FECYT	Spanish Foundation for Science and		Innovation Program
Technology		PCB	Barcelona Science Park
FENIN	Federación Española de Empresas de	PCT	Patent Cooperation Treaty
	Tecnología Sanitaria	TRS	Teaching and research staff
FERO	Oncology Research Foundation	ERS	Employed research staff
GEM	Global Entrepreneurship Monitor	PERIS	Strategic Plan for Health Research and
	1	-	5

ABBREVIATIONS AND ACRONYMS

Innovation

GDP Gross domestic product FP Framework program

PMPPC-IGTP Program of Predictive and Personalized

Medicine of Cancer of the Institute of

Research Germans Trias I Pujol

PRBB Barcelona Biomedical Research Park

R&D Research and development

RRI Responsible research and innovation

SBU Structural Biology Unit

SISCAT Integrated Public Health System of Catalonia

SUMA CERCA Centers Integration Program

ICT Information and communication technology

UAB Autonomous University of Barcelona

UB University of Barcelona EU European union

UPF Pompeu Fabra University

GVA Gross value added

VHIR Vall d'Hebron Research Institute

WIPO World Intellectual Property Organization

WoS Web of Science

XPCAT Network of Science and Technology Parks of

Catalonia



In collaboration with:

