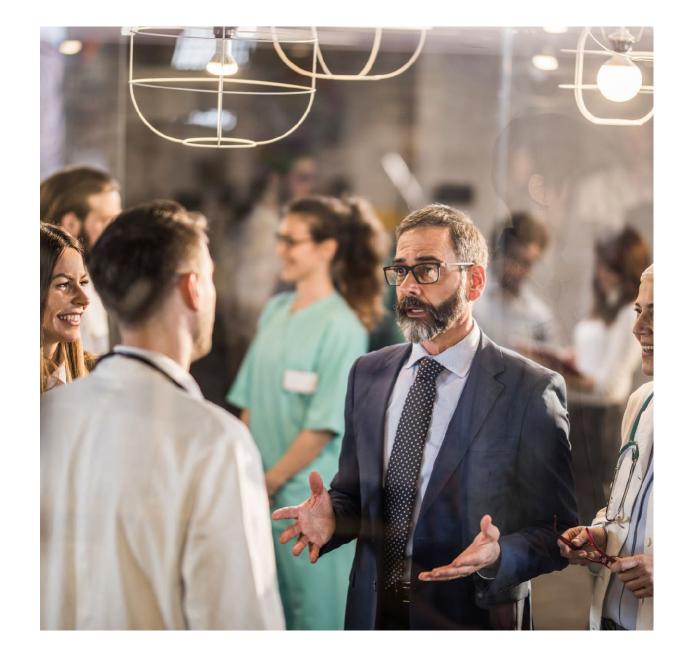






Spain ____







Agenda



1. Main issues and executive summary Spain

- a) Executive summary
- b) Key recommendations

2. Tackling the talent gap and the talent crunch in biomanufacturing in Europe

- a) Academic Ecosystem: Key Academic leaders
- b) Talent policy: Intense LifeScience Labour market
- c) Success story: TKniKa Professional Training
- d) Opportunity: Catalan Talent development ecosystem

3. Research to innovation

- a) Innovation capabilities: Diverse ecoSupportive regulatory agencies systems
- Innovation policy: Success stories: Catalonia's Emerging therapies and personalized medicine HUB
- a) Opportunities: Re-Industrialization Strategies; Cross Border initiatives

4. Business to Innovation

- a) Spanish Business ecosystem mapping
- b) Access to Finance: Dynamic Start ups, Larger Corporate Investments
- c) Success stories: HIPRA

5. Conclusion & recommendations

- a) Conclusion & next steps
- b) EIT Health members and partners' Biomanufacturing radar
- c) References















Part II

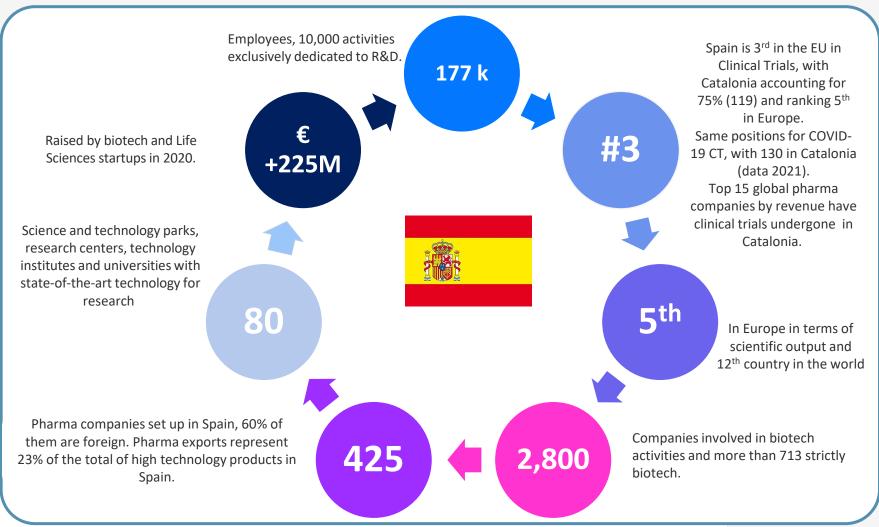
Main issues and executive summary Spain ____

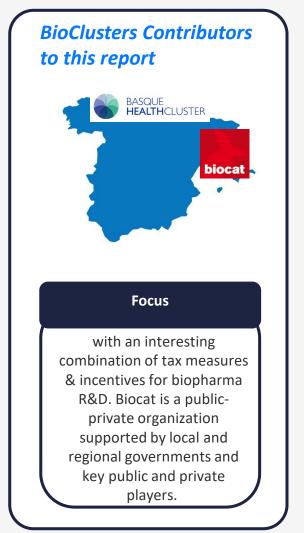




Spain

"The Spanish R&D model is characterized by a talented research and innovation ecosystem, with strong regional ecosystems, in biomanufacturing especially located in Catalonia, the Basque country and Madrid area."













Spain



Education

Pain points

Success stories

Opportunities

- To meet demand for capacities in light of the changes in the life sciences and healthcare System
- Attracting and retaining talent
- To boost the critical mass of executive talent to scale up the life sciences and healthcare ecosystem
- Centro Tknika is a centre promoted by the Deputy Ministry of Vocational Education and Training of the Education Department of the Basque Government.
- Scale-up of the success story (Centro Tknika, Basque Region)
- Co-development of new training and education modules for Biomanufacturing

Innovation

- Attracting and retaining talent
- Funding for Companies to suport scale-up in research
- Catalan Advanced Therapies Hub:
 - Emerging therapies and personalized medicine HUB, currently being developed with the support of Biocat.
- Re-industrialisation strategy
- Territorial balance policies for competitive industries
- NextGen EU funds
- Regional Hubs

Business

- Fragmented funding
- High competition to reach funds for smaller companies
- Lack of large investments / equity investors (early stage)
- <u>Viralgen</u> is a CDMO JV between Askbio and Columbus, Venture Partners with service offerings to the gene therapy market.
- Institutional CAR-T development in the Andalusian network for the Research and Transfer of Advanced Therapies.
- Policy support to keep the decision power in Spain/Europe (i.e Viralgen)
- New initiatives such as the Catalan Advanced Biotherapies Hub
- Spanish government offers funding, low interest loans during the startup and growth phases, along with incentives and tax deductions that drive growth in the industry.









Contributions

Contributors to the Report



Consulted Bodies and industrial players:









fenin

- 2 BioClusters supported in the elaboration of this landscaping
 - **Biocat** (BioRegion of Catalonia) +1,200 companies and the full value chain: 12 universities, 12 top global pharma corporations, +1000 SMEs (mainly biotech, medtech and Digital Health), 43 research and tech centers, 18 university hospitals and 3 large infrastructures. € +200M raised by biotech and Life Sciences startups in 2020.
 - Basque Health Cluster +90 members and main areas of work Health biotechnology (59% of the activities, invluding animal health), eHealth, Medical technologies.

















Part II.A

Tackling the talent gap and the talent crunch in biomanufacturing in Europe





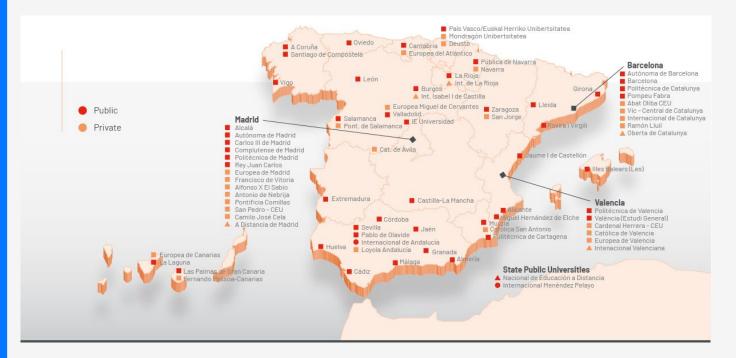






Spain has strong academics forces

Spain has World-class Academic & research centers









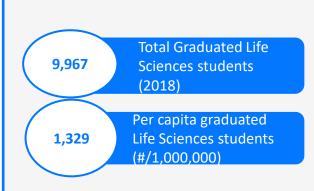
Global MBA Ranking 2021 | European Business School



Ranking 2021	European Business School	Country
1	Insead	France / Singapur
2	London Business School	UK
3	lese Business School	Spain
4	HEC Paris	France
5	SDA Bocconi	Italy
6	University of Cambridge: Judge	UK
7	University of Oxford: Saïd	UK
8	IMD	Switzerland
9	Esade Business School	Spain
10	Alliance Manchester Business School	UK
11	Warwick Business School	UK
12	IE Business School	Spain

The exemple of the BioRegion of Catalunya









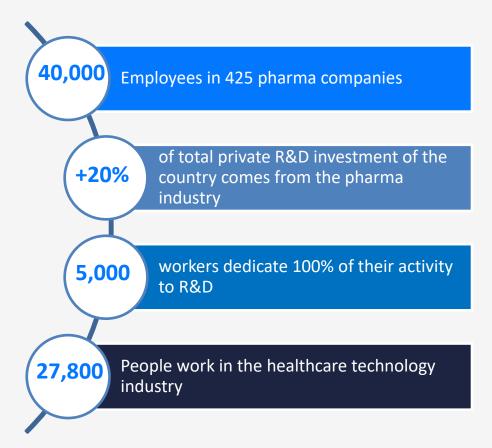
Spain labour market in Life Sciences

The pharmaceutical and biotechnology industry in Spain has become one of the most dynamic and competitive globally.

The **biotechnology industry** specifically, has grown hand-in-hand with the pharmaceutical industry. It has now, after two decades, achieved a stage of consolidation as an emerging industry.

A number of major industry multinationals have chosen Spain as the destination for investment, not only to distribute their products, but to establish their R&D, production and service centers.

3,000 biotechnology companies form an industry in which innovation and R&D are key. Half of these (50%) lead the healthcare industry with the launch of innovative new products in diagnostics and therapeutics.













Concrete innovative Education example





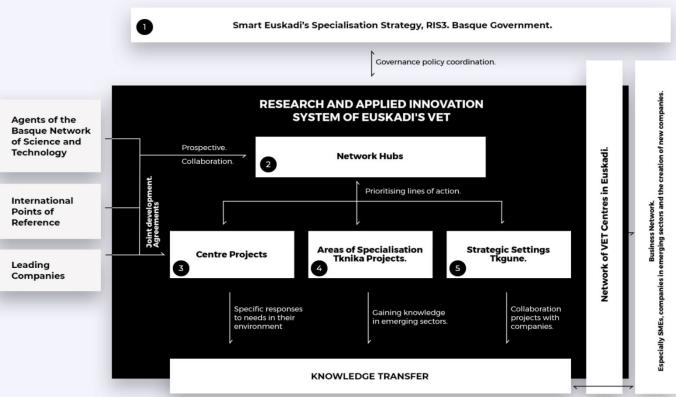
Centro Tknika, Basque Region

Tknika is a centre promoted by the Deputy Ministry of Vocatio Education and Training of the Education Department of the Basc Government.



The growing demand and evolution of the manufacturing proces along with the integration of the new technologies of Industry into the market, with the Additive Manufacturing as one of fundamental pillars, provide the machine tool industry and its us with a wide range of design and production possibilities













Concrete innovative Education example

Master in Manufacturing of Advanced Therapy Medicinal Products

Offered by the University of Granada in collaboration with the andalusian network for the design and translation of advanced therapies, and sponsored by the International Society of Cell & Gene Therapy and Miltenyi Biotec.









andaLusian network For the design a translation of Junta de Andalucía aduanced therapies



















Concrete talents and human resources programmes and KPIs





by Active Spinoffs of:

University of Barcelona

€191.5 M / 24 Spinoffs

ICREA

€122.7 M / 22

Universitat Autònoma de Barcelona

€40.4 M / 15

Institute for Research in Biomedicine

€38.4 M / 5

Hospital Clínic de Barcelona

€21 M / 6

IrsiCaixa AIDS Research Institute

€17.2 M / 2

Universitat Politècnica de Catalunya

€16.2 M / 10

IDIBAPS

€11.9 M / 8

Vall d'Hebron Institute of Oncology

€11.1 M / 2

Pompeu Fabra University

€9.7 M / 9

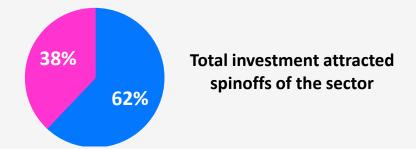




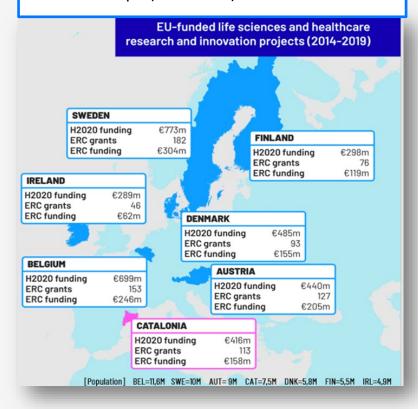
58 Catalan institutions (44 research centers and 11 universities, 1 business school, ICREA and AGAUR) have been awarded with the Excellence in Research and HR European seal.

ICREA (talent program) co-founded startups are capturing +62% of total biotech & therapeutic investment in the BioRegion of Catalonia. The 22 ICREA spin-offs have raised over 122 M€





Catalonia hosts 113 ERC grantees in the life sciences and healthcare, one of the highest ratios in Europe (2020 data).













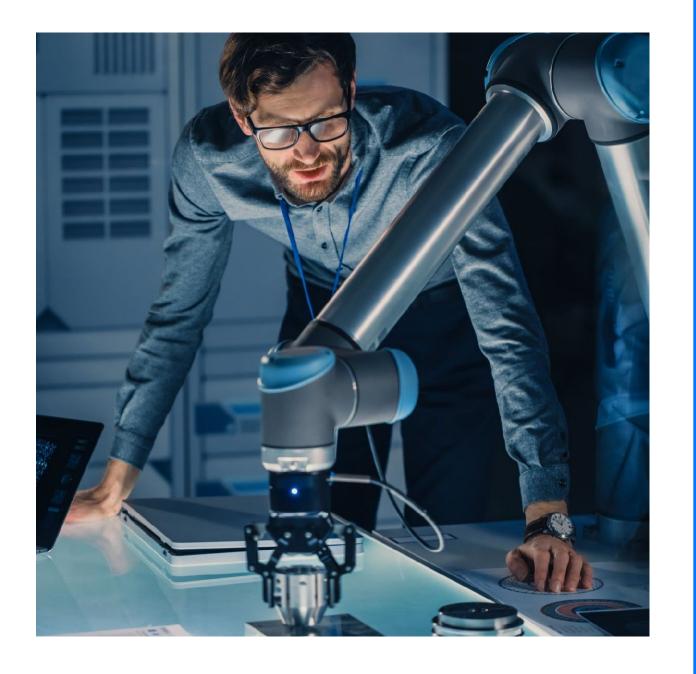
Part II.B

Research to

Innovation 🖫 🔤









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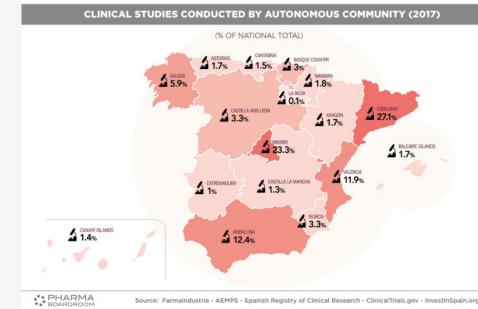
Spain, and the research ecosystem

Workforce in the life sciences innovative industry in Spain:



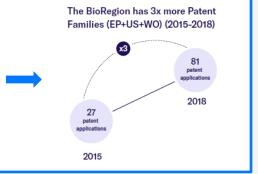
There is a diverse ecosystem of industries and research centres active in the Biomanufacturing field

- Pharmaceutical industries (corporates, SMEs) developing their own innovative biopharmaceuticals
- Contract development and manufacturing organizations (CDMO)
- Products and services in molecular and cellular biology to optimize bioproduction
- **Products and services companies** in engineering and digital technologies to design the bioprocesses and plan
- General support companies



BioRegion of Catalonia:

Biotechnology and pharma patent applications families (EP+US+WO) has been x3 between 2015 and 2018











A Rich Ecosystem within Walking Distance

The Barcelona Metropolitan Area is the most well-established ecosystem in Catalonia, with 98% of the life sciences and healthcare industry.

Barcelona, One of the Top Life Sciences Hubs in Europe



Mapping Key Players in the Greater-Barcelona Ecosystem ↗

- Investors
- Hubs & Ecosystem Supporters
- Research Centers
- Hospitals & Institutes
- Multinationals
- Science & Technology Parks
- Universities
- Business Schools



Bellaterra 47 49



- 1. Alta Life Sciences
- 2. Asabys Partners
- 3. Caixa Capital Risc
- 4. Inveready
- 5. Invivo Ventures
- 6. Nina Capital
- 7. Ysios Capital **Partners**

Hubs & **Ecosystem** Supporters

- 8. AQuAS
- 9. Barcelona Health
- 10. Barcelona Tech City
- 11. Blocat
- 12. CataloniaBio & HealthTech
- 13. Mobile World Capital Barcelona
- 14. WeLab

Research Centers

- 15. Barcelona Supercomputing Center (BSC-CNS)
- 16. Centre for Genomic Regulation (CRG)
- 17. EURECAT **Technology Centre** of Catalonia
- 18. ICFO
- 19. Institute for Bioengineering of Catalonia (IBEC)
- 20. Institute for Research In Biomedicine (IRB Barcelona)
- 21. IrsiCaixa AIDS Research Institute

- 22. Josep Carreras Leukaemia Research Institute (IJC)
 - Hospitals

& Research Institutes

- 23. Bellvitge University Hospital (including IDIBELL and ICO L'Hospitalet)
- 24. Germans Trias i Pujol University Hospital (including IGTP)
- 25. Hospital Clínic de Barcelona (including IDIBAPS)
- 26. Hospital de la Santa Creu i Sant Pau (including IIB and IR Sant Pau)
- 27. Hospital del Mar (including IMIM)
- 28. Institut Guttmann
- 29. SJD Barcelona Children's Hospital (SJD)
- 30. Vall d'Hebron Barcelona Hospital Campus (including VHIO, VHIR)

Multinationals

- 31. Almirall
- 32. Amgen
- 33. Boehringer Ingelheim
- 34. Esteve
- 35. Ferrer
- 36. Grifols
- 37. Nestlé Health Science Innovation Center
- 38. Novartis

- 39. Relg Jofré
- 40. Sanofl
- Siemens Innovation Center

Science & **Technology Parks**

- . Barcelona **Biomedical** Research Park (PRBB)
- 43. Barcelona Science Park (PCB)
- 44. Barcelona Synchrotron Park
- 45. Parc de Recerca I Innovació de la UPC (Parc UPC)
- 46. Parc Tecnològic del Vallès (PTV)
- 47. UAB Research Park (PRUAB)

Universities

- 48. Pompeu Fabra University (UPF)
- 49. Universitat Autònoma de Barcelona (UAB)
- . Universitat Politècnica de Catalunva (UPC)
- University of Barcelona (UB)

Business Schools

- 52. ESADE
- 53. IESE











- An outstanding position in clinical trials



Spain is the 3rd country in Europe in clinical trials, where the BioRegion of Catalonia accounts for 75% of the total

Supportive Regulatory agency Catalonia is #2 in clinical trials per capita(2017) and #5 in Europe for Covid-19 clinical trials (116). All world top 15 pharma by revenue have clinical trials underway in Catalonia.



Barcelona: Excellent output in biomedicine, 9th Nature Index Science City in Europe













- Spinoff from academia (BioRegion of Catalonia)



Startup

Public-Private consortium

Investors

















AELIX Therapeutics is a clinical stage biotechnology company based in Barcelona, Spain, focused on the development of a therapeutic HIV vaccine to be used in cure/eradication strategies.

AELIX Therapeutics is a spin-off of HIVACAT, a Catalan public-private consortium conducting cutting-edge research in the field of AIDS. The HIVACAT programme, which aims to develop strategies to prevent and cure HIV and AIDS, is led by IrsiCaixa Aids Research Institute and the Infectious Diseases and AIDS Unit of the Hospital Clínic of Barcelona. The HIVACAT consortium licensed the HTI technology to AELIX Therapeutics for its global development and commercialization.

The company was incorporated in November 2015 and completed a €11.5M (\$12.5M) Series A funding shortly thereafter through funds managed by Ysios Capital, a Spanish investment firm, Johnson & Johnson - JJDC, Inc., and Caixa Capital Risc, the venture capital division of Spain's leading group, "la Caixa".)





AB-Biotics was founded in 2004 as a spinoff of the Autonomous University of Barcelona (UAB) launched by Miguel Angel Bonachera and Sergi Audivert, currently executive directors and members of the company's Board of Directors. Now it is a leading biotechnology company, with an international vocation, and it divides its activities into these two main business areas (probiotics & precision medicine)

Peptomyc is a company focused on the development of a new generation of cell penetrating peptides (CPPs) targeting the Myc oncoprotein for cancer treatment. The company was founded in December 2014 and it is based on Dr. Soucek's scientific research in Omomyc (the best direct Myc inhibitor known to date) over the last twenty years.





Minoryx is a clinical stage biotech company focused on the discovery and development of novel therapies for severe, orphan genetic diseases of the central nervous system (CNS) with high unmet medical need.









Success in Advanced Therapies Development: CAR-T



Barcelona, Catalonia

February 10 2021

AEMPS authorises Hospital Clínic's CAR-T ARI-0001 for patients with acute lymphoblastic leukaemia

The Spanish Agency of Medicines and Medical Devices (AEMPS) has approved CAR-T ARI-0001, developed by Hospital Clínic, as and advanced therapy drug of non-industrial production for its use in patients over 25 years of age with lymphoblastic leukaemia that is resistant to conventional treatments. It is the first CAR-T developed entirely in Europe to be approved by a regulatory agency.

Madrid, Community of Madrid

El Gregorio Marañón compra la CART Kymriah, de Novartis, por 2,8 millones

El Boletín Oficial de la Comunidad de Madrid publica la formalización del contrato entre el centro y la compañía

CAR T Capacity in Madrid

The Regional Helath Services of Madrid, Hospital Gregorio Marañon, acquired in 2019 the first CART therapy approved in Spain and is leading the Spanish Plan for advanced therapies

Andalucía

Investigadores andaluces recurren a la ingeniería genética para tratar leucemia y linfomas

Científicos de los centros GENYO (Granada) e IMIBIC (Córdoba) han puesto en marcha un proyecto de investigación con el fin de crear un compuesto anticancerígeno a partir de células CAR-T (EXO-CAR-T) procedentes de donantes sanos

CAR T Project

This project of Public Procurement of Innovation is 80% co-financed by the European Union through the ERDF's Smart Growth Operational Program (2014-2020), aid granted by the Ministry of Science and Innovation through the FID program "Fomento de la Innovación from the Demand

The overall objective of the project consists of the preclinical and clinical development, up to phase 1 included, of a new Advanced Therapy Drug (ATMP) consisting of a CAR-T directed against lymphoid neoplasms, more effective and less toxic than those currently available in the market and at a lower cost.





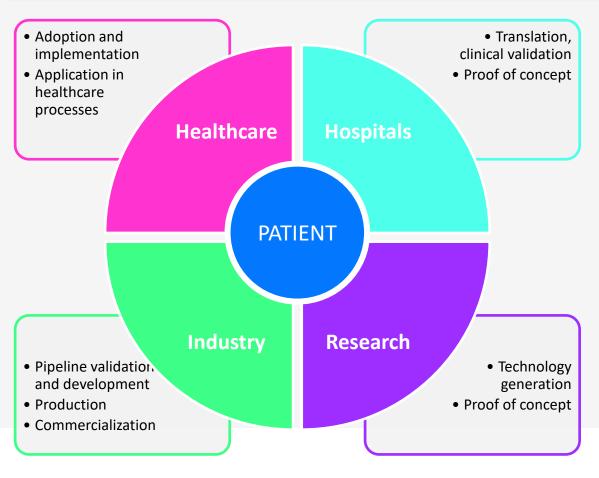




(atalonia's Emerging therapies and personalized medicine HUB)

(in development)

ADVANCED THERAPIES AND PERSONALIZED MEDICINE HUB



Advanced therapies

Tissue engineering and 3D (bio)printing

Cell and gene therapies

Regenerative medicine

Digital technologies

Personalized medicine

Genomic and other omics

Precision imaging

Patient data

Patient background and environment

Fields of application:

Oncology, minority and metabolic diseases, sophisticated transplants, infectious diseases, emerging diseases









Re-Industrialization Strategy

Becton Dickinson produce en Fraga las

jeringuillas elegidas por EE.UU, Inglaterra o España para vacunar contra la covid La planta aragonesa ya ha fabricado más de 500 millones de unidades, entre ellas, 25 encargadas por el

Gobierno de España y varias comunidades autónomas.





According to the Spanish Federation of Healthcare Companies (FENIN), the BioManufacturing sector is working towards implementing the 2030 strategy with one of its key pilars being re-industrialization, namely:

- Intramural digitalisation
- Robotization of their manufactures

Examples:

- **Becton Dickinson Iberia** (Important Investment in the Fraga (Huesca) Manufacturing site
- Reig Jofré announcement of starting vaccine production for Janesse
- Hipra enters Human Health with its own COVID-19 vaccine and is ready to produce for others
- **Boosting of Digital Innovation Hubs** like DIH4CAT in the BioRegion of Catalonia to support Health sector among others

Spain to produce at least four Covid-19 vaccines as Moderna supplies dry up

The Local ews@thelocal.es 6 February 2021 12:06 CET

coronavirus vaccine

re this article













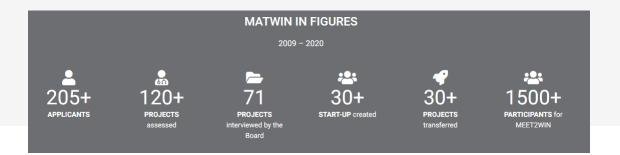
- Cross-Border Initiatives

Clusters of the Health sectors around 3 regions across Borders

- Nouvelle Aquitaine
- Basque Country
- Navarra



Embeded in the Matwin Meet2Win event













Unique in Europe, MATWIN (Maturation & Accelerating
Translation With INdustry)
is an open-innovation platform that aims at developing
translational research in oncology
and accelerating innovation transfer from bench to the
bedside

Yearly meeting to promote the cross border collaboration











Part II.C

Business

Innovation











Spain has one of the world's highest density of Advanced Therapy Companies



Life Sciences

"Around 60% of pharmaceutical companies in Spain are foreign. There are more than 425 companies employing over 40,000 people"

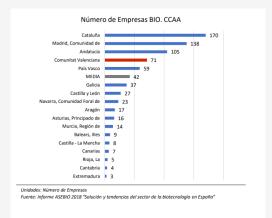
The pharmaceutical and biotechnology industry in Spain has become one of the most dynamic and competitive globally.

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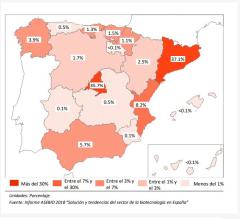
This industry employs 5,000 workers who dedicate 100% of their activity to R&D. This figure represents 25% of the employment in R&D in Spanish industry as a whole.

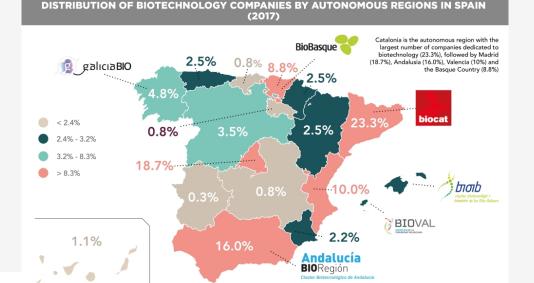
3,000 biotechnology companies form an industry in which innovation and R&D are key. Half of these (50%) **lead the healthcare industry** with the launch of innovative new products in diagnostics and therapeutics.

Innovation in healthcare technology in Spain offers great potential for development, mainly due to the large size of the market. Spain is one of Europe's principal markets, with over 1,000 companies, 500 of them manufacturers. Over 27,800 people work in the industry.



PHARMA













With Strong Corporate Presence



Pharmaceutical industries developing their own innovative biopharmaceuticals

GRIFOLS







Boehringer Ingelheim



























And SMEs developing their own innovative biopharmaceuticals















































CMOs & CDMOs: Strategic service providers for pharma & biotech SMEs













Key CDMOs in Spain



Lonza (Galicia, Spain)

Lonza is an integrated solution provider that creates value throughout Healthcare continuum[®].

They were founded in 1897 in the Swiss Alps and today have more than 100 plants and offices and approximately 15,500 full-time employees worldwide, including Spain (**Porriño**).

They have a long portfolio of products and services, including advanced intermediates, recombinant proteins, cell therapy, conjugates, vaccines, peptides, oligonucleotides, fine chemicals...

Lonza



3P Biopharmaceuticals (Navarra, Spain)

3P Biopharmaceuticals is a leading Spanish contract development and manufacturing organization (CDMO) specialized in the development of GMP-type processes and manufacturing of biopharmaceuticals and cell therapy products.

They dedicate much of their effort to the development of the, as they consider this step to be the most important part of **mammalian cell line** the development program.

3P Biopharmaceuticals focuses on working with:

- New biological entities (NBEs)
- Biosimilars and biobetters
- Advanced therapy products (ATs), specifically products belonging to cell therapies and tissue engineering.













Key CDMOs in Spain



LeanBio (Barcelona, Spain)

CDMO that focuses on the development of biopharmaceutical products. It provides customized products and services produced in mammalian cell lines, plants, yeast and bacteria. The company harnesses its technological platforms including strain and cell line development platform; process platform; analytical and formulation platforms for developing and manufacturing biotherapeutics products. It serves biopharma, cosmetics, pharma, and agro-food sectors. Leanbio is headquartered in PCB, Barcelona, Spain and its main services are:

- Strain and cell line development platform
- Process development platforms:
 - **USP** activities
 - DSP activities
- Analytical and formulation development platform
- DS/DP Manufacturing Platform

GMP activities are currently transferred to a partner.











mAbxcience (León, Spain)

Biopharmaceutical company based in Spain. It processes, scales and produces monoclonal antibodies and biosimilar recombinant proteins. The company offers services that include research and development laboratory, cGMP manufacturing, QA/QC/regulatory and training center.

Biosimilar maker and CDMO mAbxience will install an ABEC 4,000 L CSR bioreactor at its site in León, Spain.

mAbxience, the biologics division of Spain's Insud Pharma group, claims its León plant is "the biggest biologic plant in Spain and the first in Europe with fully integrated single-use technology in most processes."

The firm has several biosimilars approved across global markets. It launched its version of Roche's Mabthera (rituximab) in 2014, while a version of Roche's Avastin (bevacizumab) was launched in Latin America in 2016.

The manufacturing site was owned by The Genhelix Group till 2014, when mAbxience acquired it 100%.







Access to Finance



"A number of major industry multinationals have chosen Spain as the destination for investment, not only to distribute their products, but to establish their **R&D**, **production and service centers.**"

In the field of Life Sciences, **the pharmaceutical industry** is the industrial leader by volume of spending on research, and accounts for over 20% of total private R&D investment in the country.

Top 5 European Countries by reported Start-up fundraising deal volume in 2019

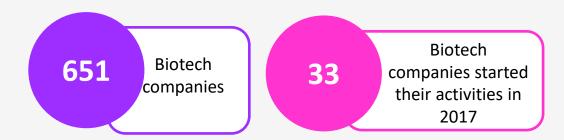


Source: Crunchbase.news

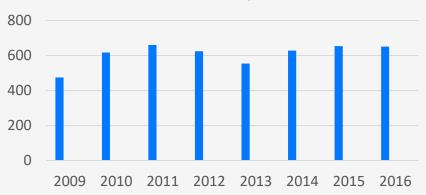








Biotech companies



If you look at the Spanish biotech sector in 2017, according to Asebio, the Spanish biotech association, the industry was dominated by Catalonia with 23.3% of all biotech companies, followed by Madrid at 18.7%, and Andalusia with 16% of the market share. Furthermore, in 2016, 66.8% of all biotech companies had a focus on healthcare, the largest sector by a significant margin (second position was the Food Industry with 23.5%, and third, Animal Health and Aquaculture with



4

Success story: Hipra



Our **experience** in the development of vaccines against **coronavirus** has allowed us to start **2 lines of research**: one on our own based on a **recombinant protein**, and another in collaboration with the Hospital Clínic of Barcelona based on **RNA messenger**

The biotechnology on which these projects are based:

In our own line of research, we are developing a vaccine based on a **recombinant protein** designed to induce a powerful **neutralizing immune response** to the Covid-19 virus and capable of providing high levels of safety.

It will be kept between +2 and +8°C, which will facilitate its logistics and distribution.

The vaccination strategy contemplates the different scenarios: primary vaccination, **effectiveness against different variants** of the virus and the **revaccination** dose, as it is not an Adenovirus vector vaccine

Relevant aspects of these projects:

- •Productive Capacity: 400 million doses estimated for 2022 and 1,200 million doses for 2023.
- •Availability: Production would begin in October and at the end of 2021 it could begin to be commercialized.
- •Versatility: It will offer protection against various variants of the virus.
- •Conservation: The vaccine may be stored between +2 and +8 ^oC, which will facilitate its logistics and distribution.
- •AEMPS support: This project has the support of the Spanish Agency for Medicines and Health Products (AEMPS) as well as the Spanish Ministries of Health, Science and Innovation





Spain expects to launch a COVID-19 vaccine before the end of the year, according to Prime Minister Pedro Sánchez, who described Spanish pharmaceutical firm Hipra's vaccine candidate as one of Europe's most promising to end the pandemic, EURACTIV's partner EFE reported.

Hipra started clinical trials of its vaccine candidate this summer and expects to produce 400 million doses by 2022.











Conclusions and Next steps

«The Spanish R&D model is characterized by a talented research and innovation ecosystem, with strong regional ecosystems, in biomanufacturing especially located in Catalonia, the Basque country and Madrid area.»

- <u>Supportive regional governments</u> with an interesting combination of tax measures & incentives for biopharma R&D. Biocat is a public-private organization supported by local and regional governments and key public and private players.
- <u>Supportive Regulatory agency</u> Catalonia is #2 in clinical trials per capita(2017) and #5 in Europe for Covid-19 clinical trials (116). All world top 15 pharma by revenue have clinical trials underway in Catalonia.

Next steps are:

- To develop further and scale up specific profesional/vocational training to feed the demand
- To support the interaction between industry and technology suppliers
- To Tackle possible barriers to competitiveness in attracting innovative and executive talent
- To push for more governmental support for mid to large CDMOs and related, to ensure expansion, not only at the Company's risks









EIT Health footprint radar

EIT Health Spanish Network Footprint



- 1. Industry
- 2. CDMO
- 3. Academic
- 4. Innovation
- 5. Start-ups & Investors

Scoring - Partners engagement with EIT Health

Neutral High



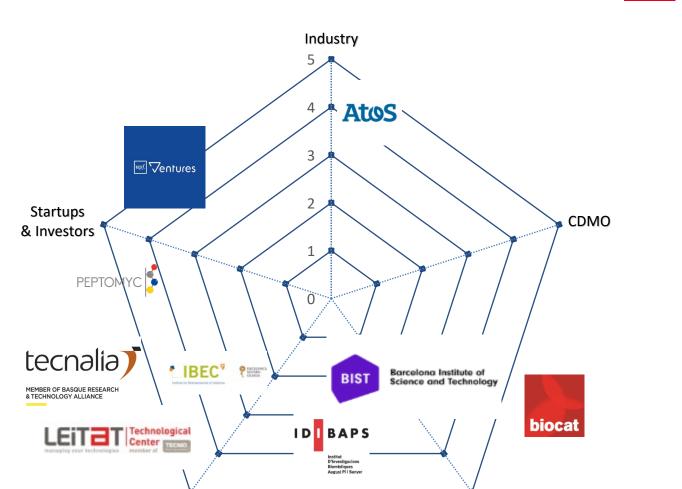






Innovation

Spain radar



IDIBELL



Academic

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- Eurostat
- PharmaBoardRoom Country reports







