

ASEBIO REPORT 2019

PREPARED FOR THE SPAIN OF TOMORROW



Edited by the Spanish Association of Bioenterprises (AseBio)

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Spanish Association of Bioenterprises

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THANKS TO THE COLLABORATORS





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Letter from Ana Polanco

Our current situation is unprecedented: a healthcare and economic emergency that requires us to take a hard look at the tools that will help us pull out of this crisis better and faster, which have put the spotlight on knowledge in science and technology. Today, more than ever, science and innovation are a driving force for economic and social prosperity and the foundation for rebuilding the country after Covid-19.

After overcoming the initial phases of the crisis, it is time to learn from the lessons Covid-19 has left us and start to think about what we want to be as a country and how we want to rebuild our society and our economy. At AseBio, we want to put biotechnology and the life sciences at the heart of Spain's reconstruction strategy in order to better protect ourselves against future healthcare emergencies and spur on new economic growth that is greener and more sustainable. And we've expressed this to the parliamentary Committee for the social and economic reconstruction of our country by participating in the Workgroup on Public Health and Healthcare.

With the 2030 Agenda and the European Green Deal, our country has a new roadmap for growth and will have to make decisions that will allow us to promote a new, sustainable economic model that creates jobs with high value added in strategic, knowledge-intensive sectors. To do so, we have to keep working with society as a whole to get the social backing to mobilize broad support for legislators and public decision-makers. To this end, it is essential to build bridges between science and society so citizens perceive the benefits of investment in R&D and the better overall working of the system. This is the only way we can make science and innovation part of the country we want to build.

At AseBio, we've called for a joint effort, countrywide, to promote and renew Spain's commitment to science and innovation, in strategic areas with the capacity to transform and have an important impact on people's lives, such as biotechnology and the life sciences. So, it is time to once again give biotechnology the push it needs to allow the country to lead the transition to a more sustainable future and to drive our science and innovation system and align it with challenges like ageing, protecting society against emerging illnesses, sustainable eating, the just transition and the climate emergency.

We want to make science and innovation part of the vision of the country we want to build, because they should be assets shared by the private and public sectors to generate social well-being. And at AseBio, we have a deep commitment to raising visibility of our sector and giving our members a voice, as they are the driving force of the association, to valorize all their capacities and the transversal nature of their activity on all levels.

We have to look to our shared values as a society because they are the foundation that will allow us to take firm steps in rebuilding the country. Trust in science and technology is a value that unites and defines our society. Together, let's make this value one of the founding pillars of the new economic model that our country needs to tackle today's challenges.

Ana Polanco, president of AseBio

Letter from Ion Arocena

As we sat down to put together this report, alarm bells started going off around the world from the Covid-19 healthcare emergency, which has had devastating effects on personal health and an impact on the economy that is not yet clear.

As we received the new indicators and put together the graphs, we saw that, once again this year, the sector had made a firm commitment to R&D, with nearly €770 million, up 13% from the previous year. This figure shows the sector's commitment to science and innovation, which has become more important than ever, taking into account this healthcare crisis. In the same line, most of the indicators reflect the dynamic nature of the biotechnology sector and its renewed commitment to investing in the future.

2019 was the 20th anniversary of AseBio. In November, we celebrated it with a Manifesto for Biotechnology and the Life Sciences for a healthier, safer society and a more sustainable planet. With it, we hoped to renew our country's commitment to science and innovation, and to our sector in particular, so we called for a Spanish Strategy for Biotechnology and the Life Sciences as a strategic sector for the country. Months later, we've seen how the content of this Manifesto is more important now than ever. Not only to protect us against emerging illnesses like Covid-19, but also to generate green, sustainable economic growth to pull out of the economic crisis caused by SARS-CoV-2.

In fact, we finished 2019 by participating actively in the Climate Summit held in Madrid last December. There, with our members, we explained how biotechnology is key not only in providing solutions to climate change, but also in protecting us against emerging diseases like the one that would paralyze the world just a few months later.

There is no question that 2019 was a key year and turning point for our Association. In 2019, we inaugurated a new strategic plan with the vision of getting Spanish society to commit to science and innovation as a driving force for social wellness and development, because we believe this is the only way biotechnology will be recognized as a key tool for tackling the social and environmental challenges the future will bring. So, we've worked to tell a new story about our sector and, above all, to align our members' work with the country's social and political agenda.

Our commitment to science has inspired us to work to improve our system of R&D incentives. In this regard, 2019 was also the year the Association put the shortcomings of an underfunded, loan-based science and innovation system on the political and media agenda. This model impedes execution of the public budget earmarked for R&D, which then loses its ability to leverage private investment and, in short, puts our companies at a disadvantage compared to their European and US counterparts.

We firmly believe we are catalysts for public-private partnership and collaboration among companies. So, in 2019, we continued to act as a meeting point for companies large and small, investment funds and public research centers. In this line, we have continued working to turn science into biotechnology innovations that improve people's lives, acting as a platform to connect organizations of various sizes and natures, through events like the AseBio Investor Day and Agrobiotechnology Forum.

We've kicked off 2020 with our homework done, thanks to the 2019-21 Strategic Plan that guides our strategic priorities and lines of action. The indicators show the sector is prepared to give its all, thanks to the firm commitment to R&D and its talent. So, we are sure this is our time to shine, the moment when science and innovation will be put front and center in the strategy for the country's future. We have so much knowledge to share and so many ideas to contribute to rebuild the country on a stronger, more sustainable foundation.

Ion Arocena, CEO of AseBio

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METHODOLOGY





The 2019 AseBio Report, considered the benchmark publication in the biotechnology sector since 2003, is published annually by the Spanish Bioindustry Association to provide a snapshot of the biotechnology sector in Spain. Its mission is to analyze every area that makes up the situation in which biotechnology is being developed in our country today, and how it is evolving.

As it does every year, this Report provides a general overview of the status of the biotech sector, with several analyses of R&D investment, the most important financial operations, the sector's economic impact, the talent working in the sector, and the biotechnology ecosystem in Spain, as well as studies on how science and biotechnology are perceived, and scientific and technological production measured in publications, patents, and products and services launched to market. Plus, for the first time, the 2019 AseBio Report aims to promote biotechnology by analyzing how it is helping address the goals laid out in the 2030 Agenda, thanks to its transversal nature and transformative, innovative capacity.

This Report is mainly geared towards those who, for their professional (businesspeople, public officials, legislators, professionals at financial institutions, media outlets, scientists and bioentrepreneurs, among others) or personal interest, would like a clear snapshot of biotechnology in Spain.

Contents

The 2019 AseBio Report has 10 sections. Each of its chapters takes a closer look at the most important issues affecting the Spanish biotechnology sector:

- Introduction and executive summary (chapters 1 and 2): introduce the Report, its scope and main goals, plus a brief summary of its overall content.
- R&D investment (chapter 3): covers R&D investment in the sector, how it has evolved and a comparison to other sectors.
- Funding (chapter 4): describes the main financial operations, venture capital activity in 2019 and how it has evolved, and the public administration's support for the sector.
- Talent and diversity (chapter 5): shows the number of researchers in the sector and female participation in R&D activities.
- Business fabric (chapter 6): analyzes the number of companies that make up the sector and how it has evolved. It also provides information on what these companies are like and where they are located.
- Environmental conditions (chapter 7): assesses how society perceives science and innovation and how the biotechnology sector perceives its environment.
- Results of collaborations (chapter 8): includes the main advances in the sector, and quantifies the scientific publications, patents, products and services launched to market, alliances established in 2019 and companies' internationalization.

- Impact (chapter 9): analyzes the biotechnology sector's impact on the economy and employment, as well as production in the sector.
- 2030 Agenda and the climate emergency (chapter 10): includes examples of how biotechnology is helping achieve the goals on the 2030 Agenda and address the climate emergency.
- Who's who: features information on members of the AseBio Board of Directors, Work Committees and members.

Thanks

AseBio would like to thank all our collaborators for their support. Without their help, this Report would not have been possible. And, especially:

- MERCK, main collaborator, and Amgen, Ayming, Bayer, Bioiberica, Bionet, BTI, CNIO, Euronext, Ingenasa, MSD and Zeclinics, whose contributions have made it possible to publish the AseBio Report.
- All our members who have contributed the information needed to draft the contents.
- The National Statistics Institute (INE) and the Economic Forecasting Center (CEPREDE) for their help in compiling the statistics on the sector.
- The Spanish Foundation for Science and Technology (FECYT) for the information contributed for the section of scientific production.
- The Madrid Science Park and ClarkeModet for their analysis of patents applied for and granted in 2019.
- All the organizations that helped identify companies established in 2019.
- The State Research Agency (AEI), the Center for the Development of Industrial Technology (CDTI), the National Innovation Company (ENISA) and the Spanish Venture Capital and Private Equity Association (ASCRI) for their collaboration on the chapter on funding.





R&D INVESTMENT

R&D investment is up in the biotechnology sector

In 2018, the biotechnology sector invested nearly €770 million in R&D, 71% from biotech companies.

According to previous data, biotech companies were ranked first in 2018 for R&D investment in industrial sectors, surpassing the pharmaceutical sector for the first time. In terms of the increase in R&D investment by biotechnology companies, in 2018 the year-on-year growth was 13%, putting it among the five fastest-growing sectors in R&D investment.

Looking at where this money goes, 43% of investment by biotech companies went to salaries for R&D staff in 2018.

FUNDING

Private capital increases and venture capital have become the main funding tools

2019 saw a new record in both number of operations (32) and volume of resources attracted (€103 million) by companies in the sector through private capital increases. Complementary funding through loans and equity shares held by business development bodies were up from 2018, but didn't reach the levels of 2017. Plus, crowdfunding has become a consolidated funding tool in the Spanish biotechnology sector, with €10 million invested.

Investment paid out and committed by venture capitalists that invest in Spanish biotechnology companies rose in 2019, with over €74 million throughout 2019.

TALENT AND DIVERSISITY

Biotechnology is a sector with a high percentage of researchers and of women.

The sector is increasingly attracting young talent. The number of students enrolled in university studies in biotechnology rose every year from 2015 to 2019, to nearly 7,000 students the past academic year, 60% of which were women.

The biotechnology sector hires many researchers, above the spanish average. Therefore, biotech companies are ranked second in percentage of researchers to total employees in the sector.

In terms of women participating in the sector, nearly 60% of all employees involved in R&D activities at biotechnology companies are women, surpassed only by healthcare and social services and pharmacy.

BUSINESS FABRIC

The number of companies in the biotechnology sector is growing

In 2018, the number of companies carrying out biotechnology activities rebounded slightly, with 2,969 companies in total, 751 of which are biotech firms.

Over 47% of biotech firms work in human health, followed those

focused on food applications, which make up 38% of these companies. Plus, 65% are micro-SMEs, with fewer than 10 employees.

In terms of geographic breakdown, Catalonia, Madrid, Andalusia and the Basque Country are home to the highest concentration of companies.

ENVIRONMENTAL CONDITIONS

Society's perception of science has improved, although recent years point to a less optimistic trend in terms of technological innovation

Over the past decade, people's perception of science and technology has improved. Of those asked in the FECYT Social Perception of Science and Technology in Spain survey, 60% said science and technology have more benefits than drawbacks.

In terms of innovation, Spanish society has a positive view. Nevertheless, the percentage of people with a positive opinion of innovation has dropped the past two years, from 89% in 2017 to 73% in 2019.

The sector rates employee training and availability very highly, while the cost of innovation continues to be the main roadblock to the sector's development.

RESULTS OF COLLABORATIONS

The science produced by the Spanish biotechnology sector is excellent and it holds more and more international patents

Regarding production of scientific knowledge, Spanish biotechnology makes up 2.8% of global production and is cited 30% more than the global average in this area. Spain is ranked 9th in scientific production in biotechnology and has the highest percentage of scientific papers in high-impact journals of any country: 83.3%.

The biotech sector is protecting its innovations more and more internationally, mainly through the European Patent Office (42%) and PCT patents (32%).

Companies in the biotechnology sector have international aspirations. Currently, 35 AseBio member companies are present in 43 markets on all continents.

Biotechnology is committed to collaboration. 68% of all alliances are forged with international partners. Plus, 74 of the 155 alliances identified included a partner from the public arena and, in terms of the purpose of the collaboration, 85 of these alliances were set up to carry out R&D activities.

IMPACT

The economic impact of the sector on the GDP is growing

Biotech companies posted a total joint turnover equal to 0.8% of the GDP with an impact of over €8.2 billion in income, roughly 0.7% of the national total. Furthermore, biotech companies contributed 0.3% of the GDP in taxes and account for 105,000 jobs, 0.6% of national employment.

Biotechnology activities are at the top of rankings on production growth of economic activities for 2018, up 10.1%.

Productivity and salary per employee at biotech firms was three

times higher than for the economy as a whole.

2030 AGENDA AND CLIMATE EMERGENCY

Biotechnology is part of eleven of the seventeen Sustainable Development Goals on the 2030 Agenda

Our sector's innovative capacity has allowed biotechnology to offer up ways to protect ourselves against healthcare emergencies, like the one caused by Covid-19, with vaccines, treatments and diagnostic solutions. But beyond that, biotechnology also has innovative solutions to challenges like ageing, curing diseases, food safety, curbing greenhouse gases and achieving more sustainable agriculture.

The 2030 Agenda poses new global challenges for the biotechnology sector that require comprehensive, innovative solutions and biotechnology is an essential tool for 11 of the 17 Sustainable Development Goals.

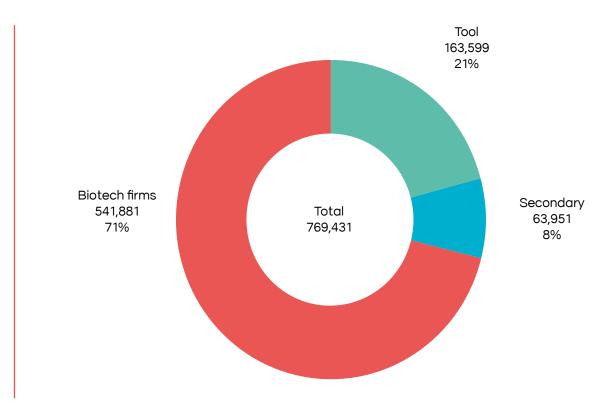






Biotechnology companies invested €770 million in R&D in 2018

In 2018, the biotechnology sector invested nearly €770 million in R&D, with strictly biotechnology firms (biotech companies) making up most of that investment, 71% of the total, followed by companies that use biotechnology as a production tool, which invested roughly 21% (graph 3.1).



Biotechnology companies devote most of their R&D investment to paying researchers.

Most of the R&D investment in biotechnology goes to cover operating expenses, which make up over 93% of the total with the biggest budget item being acquisition of goods and services, followed by paying researchers (table 3.1).

In terms of biotech firms, 43% of this R&D investment goes to paying researchers and technicians and assistants. 7% goes to capital expenditures, 60% of which is investment in equipment and instruments.

Most of the funds come from the company itself (63%) and the rest from funding provided by other companies (either in the same group, public or private companies, or research associations), the public administration or international funds. For biotech firms, the percentage of funds from the public administration is higher.

	Biotech	Secondary	Tool	Biotechnology Total
Internal R&D expenditure in biotechnology	541,881	63,951	163,599	769,431
A) By nature of the expenditure				
Operating expenses	502,430	60,603	156,683	719,715
 Paying researchers 	151,282	26,154	44,011	221,447
 Paying technicians and assistants 	83,753	10,469	28,587	122,809
 Other operating expenses 	267,396	23,979	84,084	375,459
Capital expenditures	39,451	3,349	6,916	49,715
 Land and buildings 	7,987	676	858	9,521
 Equipment and instruments 	22,742	2,475	5,248	30,466
 Acquisition of specific R&D software 	1,212	89	509	1,810
 Other intellectual property products specifically for R&D 	7,510	109	301	7,919
B) By source of funds				
 Internal company funds 	347.382	40.321	103.210	490.913
 Funds from other companies 	62.516	5.356	14.676	82.548
 Funds from the public administration sector 	67.645	12.905	16.259	96.809
 Funds from the higher education sector 	193	0	4	197
 Funds from private non-profit institutions 	1.422	0	3.344	4.766
 Funds from the rest of the world 	62.723	5.369	26.106	94.197

R&D investment in biotechnology companies is growing at an increasing pace, up 13% in 2018.

R&D investment in biotechnology companies has been growing steadily since 2014, at an increasing pace, reaching 13% growth in 2018. Strictly biotechnology companies (biotech firms) posted strong growth, above 21%, while the contribution of secondary businesses decreased slightly and those that use biotechnology as a production tool posted more moderate growth, around 8%.

AN EMERGING ALTERNATIVE MODEL

ZeClinics

Powering discovery with Zebrafish

In general, we could say that there are two main approaches to drug discovery. The first is more traditional, using canonical models, and the other uses innovative models, validating results and improving processes along the way.

Since it was founded in June 2013, seven years ago, ZeClinics has led the charge in this second vision, seriously putting forth the zebrafish as an alternative model for drug development in the regulatory preclinical stages. And it has done so through education, explaining the advantages of this model throughout these years and working hard to not only improve its complete portfolio of services, but also with special focus on its R&D programs to show that there is another way to do things.

At ZeClinics, we follow
European guidelines and
the recommendations we
get from ECVAM, where we
participate actively in protocolharmonization studies. This is
how we know that using zebrafish
larvae allows us to significantly
reduce the use of mammals in
research. And that isn't in vain:
the EPA (U.S. Environmental
Protection Agency) has already
officially announced that it will
eliminate all experiments with
mammals by 2035.

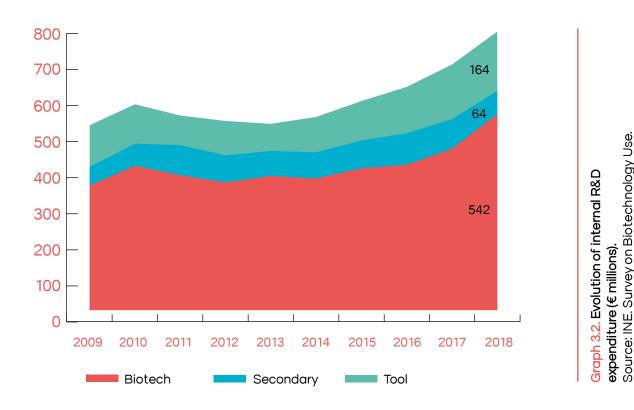
At the same time, cutting study costs and times, at ZeClinics we create scientific spaces of excellence for research into not only the big nosological classifications like Alzheimer's and Parkinson's, but also several rare diseases, which are so often overlooked.

We currently have studies underway on GRIN disorders, Dravet syndrome and Duchenne muscular dystrophy, to name just three examples.

The final result of all our work at ZeClinics has been to generate a stable niche of international clients, in over 40 countries; to fund our own pharmaceutical company, ZeCardio Therapeutics; to grow, care for and maintain our wonderful staff of 30 employees, respecting gender equality and work-life balance, creating an atmosphere of respect, equality and fairness, investing in their training, focusing on giving back to society in the form of knowledge and, thanks to all of that, with our modern R&D platforms in cardiovascular, oncology and neurology, developing all our potential in the field of biotechnology.

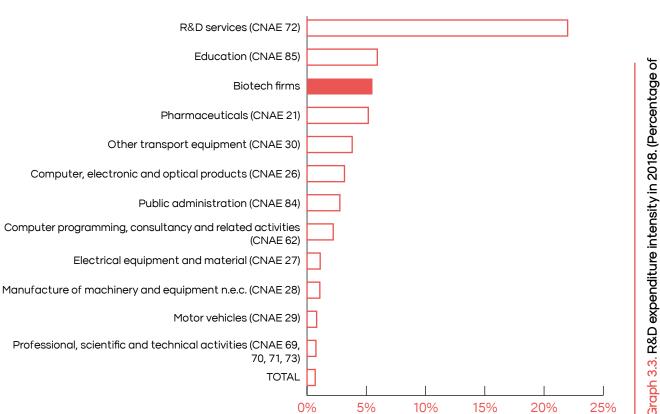
This field that, furthermore, we firmly believe is destined to lead the change we need in the 21st century society. After a global pandemic that has, officially, caused nearly 400,000 deaths

in just a few months, and isn't over yet, now is the time when all of us in the biomedical arena can do our part to transform the driving force behind our country's economy. Our weight in the economy is bigger every year, far surpassing 0.7% of the GDP and generating tens of thousands of very high-quality jobs. We know that the long-term evolution of our sector is going to be excellent. But we can't forget that we have to focus on our transcendental contribution to people's health and well-being. In short, they are the reason we do what we do and one of the main motivations behind starting the ZeClinics adventure.



Biotech companies were ranked first as a sector for R&D investment, after services and the educational sector, pulling ahead of the pharmaceutical sector for the first time.

Biotech companies invest the most in R&D relative to production, with 5.5%. They are only surpassed by the R&D services and educational sectors. (Graph 3.3). Furthermore, in 2018, biotech companies pulled ahead of the pharmaceutical sector, which has traditionally been ranked first after services and education.

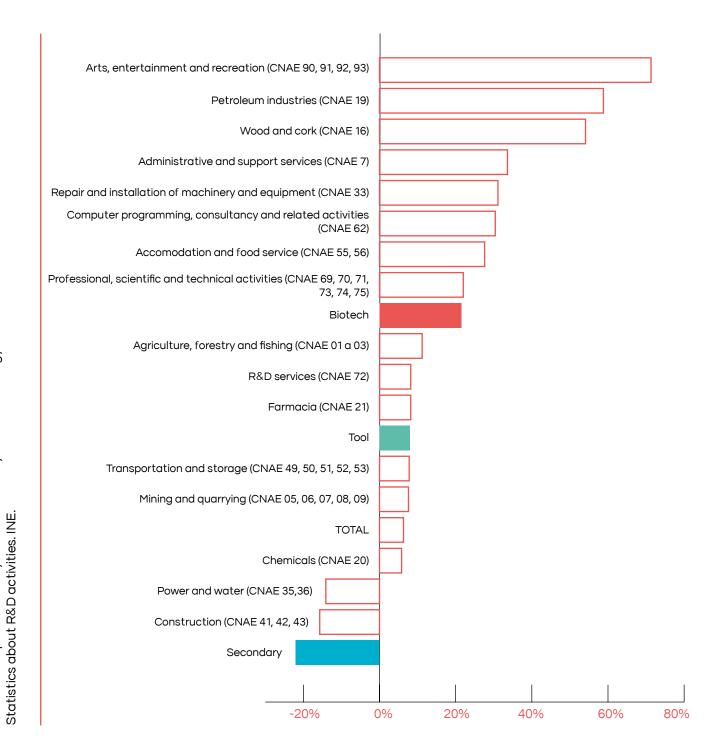


ardph 3.3. R&D expenditure intensity in 2018. (Percentage of production). Source: Compiled internally from 2018 Survey on Biotechnology Use and Statistics about R&D activities. INE.

Biotech companies are among the top 10 fastest-growing sectors in R&D investment.

Strictly biotechnology companies are ranked among the top 10 sectors in terms of growth, with triple the average national rate (graph 3.4).

With regard to other sectors, joint R&D investment for all the companies rose just over 6%, although the difference between the various areas of activity was very high, ranging from 50% growth in sectors like oil and wood to a 10% drop in power and water. The huge variation in companies with biotechnology as a secondary activity can be explained by the fact that some of them were reclassified in 2018, considering biotechnology as a tool in their processes.



PAMPLONA TO HOST TENTH EDITION OF SPAIN'S TOP BIOTECHNOLOGY EVENT: BIOSPAIN



BIOSPAIN is the main biotechnology event in Spain and one of the most important in Europe, hosted by the Spanish Bioindustry Association (AseBio) in collaboration with Sodena, the Government of Navarra's financial instrument, in this tenth edition.

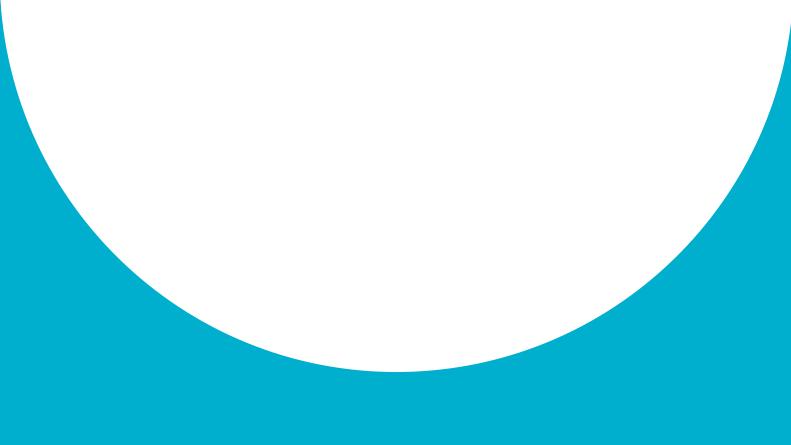
BIOSPAIN is the tool AseBio uses to create business and investment opportunities, thanks to over 17,000 one-to-one meetings held over the past 10 years. As such, AseBio has been an integral part of developing the Spanish biotechnology ecosystem.

The 10th edition of BIOSPAIN will be held from 29 September to 1 October 2021 at the Baluarte Congress Center and Auditorium of Navarra in Pamplona-Iruña. The event will feature a full program of conferences covering the main, most relevant topics, like immunotherapy, CAR-T, precision medicine, CNS, the circular economy, agrobiotechnology and artificial intelligence.

The companies that attend BIOSPAIN, mainly Spanish biotechnology SMEs, not only get lots of new business leads, but also a platform for international exposure where they can share their capacities in biotechnology first hand. So much so that the survey of participants in the 2018 edition showed that 84.81% reported identifying real business opportunities.







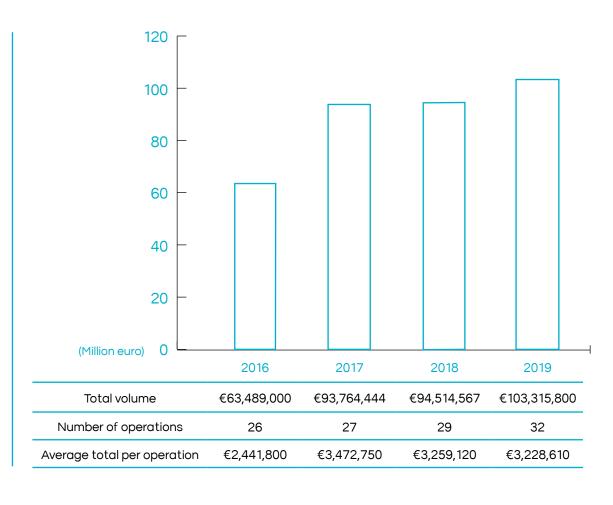


4.1 Private funding instruments

New record in private capital increases.

2019 saw a new record in both number of operations and volume of resources attracted by companies in the sector through private capital increases. There were 32 operations identified with a joint total of €103 million and an average of €3.2 million per operation.

Comparing to data from the previous year, 2018, both the number of transactions (+3) and the total volume (+ \in 8.6 million) rose. The average value of operations held steady from 2018, at \in 3.2 million.



The most noteworthy operation of the year (see table 4.1 for the full list) was the Sanifit capital increase. This company, which is searching for treatments to progressive vascular calcification disorders, raised €55 million in a round of funding, led by Caixa Capital Risc, that included Spanish funds Columbus Venture Partners, Alta Life Sciences and Ysios Capital, Dutch funds Forbion Capital Partners and Gilde Healthcare, Danish fund Lundbeckfonden Ventures and French fund Andera Partners. This increase came on the



→ heels of the one in 2018, which also included international funds, for €17.5 million.

Other noteworthy operations were those by Anaconda Biomed and SOM Biotech. In the case of Anaconda Biomed, the company that is developing catheters for mechanical thrombectomies did another capital increase for €15 million in 2019. SOM Biotech, a company that focuses on accelerated discovery of therapies for conditions with unmet needs, raised €7 million.

Organization	Participating investors	Instrument	Total investment volume committed (euros)
Sanifit	Caixa Capital Risc / Columbus Venture Part- ners / Alta Life Sciences / Lundbeckfonden Ventures / Ysios Capital / Forbion Capital Partners / Gilde Healthcare / Andera Partners	Capital increase	€55,000,000
Anaconda Biomed	Sabadell Asabys Health Innovation Investments / Ysios Capital / Omega Funds / Innogest / Sabadell Venture Capital	Capital increase	€15,000,000
SOM Biotech	Socios actuales	Capital increase	€7,000,000
Algenex	Cleon Capital / Vita Advisory / Business angels	Capital increase	€4,000,000
Vivebiotech	Inveready Biotech / Easo Ventures / So- cios actuales	Capital increase	€3,500,000
Allinky Biopharma	Family offices	Capital increase	€2,400,000
Ability Pharma	Inveready Asset Management / FiTalent	Capital increase	€2,000,000
Palobiofarma	Inveready Biotech	Capital increasel	€1,800,000
Arthrex Biotech	Invivo Ventures	Capital increase	€1,500,000
Ona Therapeutics	Asabys Partners	Capital increase	€1,500,000
Biocross	Sodical / CRB Inverbío	Capital increase	€1,121,800
Aglaris Limited	CRB Inverbío	Capital increase	€1,000,000
Amadix	Familiy offices	Capital increase	€800,000
Genbioma	Clave Mayor	Capital increase	€700,000
A4Cells	BeAble Capital	Capital increase	€650,000

Table 4.1. Private capital increases in Spanish biotechnology companies in 2019. Source: AseBio and ASCRI.

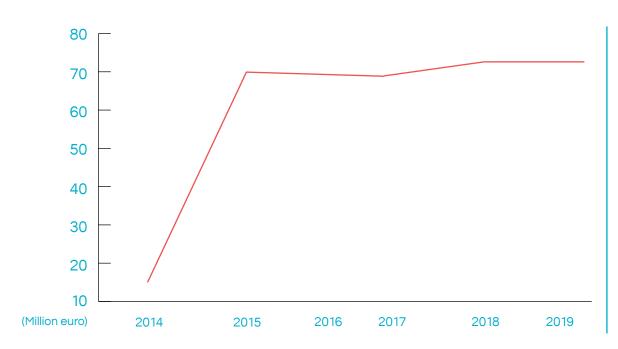
Aquilon	Laboratorios Labiana / Fondo Seguranza	Capital increase	€546,000
Ojer Pharma	Inveready / Easo Ventures / Clave Mayor	Capital increase	€540,000
Oncostellae	Fitalent / Unirisco / Xesgalicia	Capital increase	€600,000
InnoupFarma	Inveready / Sodena / Socios actuales	Capital increase	€600,000
Vytrus Biotech	Institut Català de Finances (ICF)	Capital increase	€500,000
Biolan	Socios actuales	Capital increase	€400,000
Medibiofarma	Inveready / Fitalent	Capital increase	€400,000
Neurofix	Socios actuales	Capital increase	€318,000
Osasen	Biolan / Seed Capital Bizkaia	Capital increase	€300,000
Polimerbio	Clave Mayor	Capital increase	€300,000
Spiral Therapeutics	Inveready	Capital increase	€230,000
Quibim	Clave Mayor	Capital increase	€200,000
CreatSens	Bstartup / Genesis Ventures	Capital increase	€125,000
Limno Pharma	Genesis Ventures	Loan	€125,000
Admit Therapeutics	Ship2B	Capital increase	€70,000
Droplite	Genesos Ventures	Loan	€50,000
Adan Medical	Ship2B	Follow-on loan	€40,000

Spanish biotechnology companies once again attracted international investors in 2019. In fact, the three biggest capital increases of 2019, by Sanifit, Anaconda Biomed and SOM Biotech, included international funds.

Organization	Investor	Country	Total volume committed
	Caixa Capital Risc	Spain	
	Columbus Venture Partners	Spain	
	Alta Life Sciences	Spain	
	Lundbeckfonden Ventures	Denmark	
Sanifit	Ysios Capital	Spain	€55,000,000
	Forbion Capital Partners	Netherlands	
	Gilde Healthcar	Netherlands	
	Andera Partners	France	
	Sabadell Asabys Health Innovation	Spain	
Anaconda	Ysios Capital	Spain	
Biomed	Omega Funds	USA	€15,000,000
	Innogest	Italy	•
_	Sabadell Venture Capital	Spain	•
	Cleon Capital	Spain	
Algenex	Vita Advisory	United Kingdom	€4,000,000
	Business angels	Spain	•

Table 4.2. Private capital increase operations with international investors. Source: AseBio.

The first investments by international investors in Spanish companies came in 2014 with the Oryzon capital increase. Since then, international investment has grown, hitting a total of €74 million invested in operations with international participation in 2019 (graph 4.2).



Graph 4.2. Evolution of volume of private capital increase operations with international investors (2014-2019).

FUNDING INNOVATION FOR YOUR COMPANY'S NEEDS



ayming

Companies need immediate liquidity. A good roadmap, along with the right incentives, is often key to achieving it.

To get the best return on a company's R&D investment, it is important to analyze it on a financial level and in terms of innovation, setting up a strategy that has the right combination of incentives in line with the company's economic and operational situation.

How to manage your investment in innovation. The funding that was always there.

Spain has a diverse portfolio of measures to fuel innovation, which can be combined to perfectly fit companies' financial needs and project pipelines.

For more liquidity, they can offset social security payments or apply R&D tax deductions. If this isn't enough, they can monetize up to 80% or opt for a tax equity mechanism that, with some requirements, allows companies to get the whole deduction back in a very short period.

Projects that haven't begun yet can request public aid, like the lines of credit from the CDTI, Europe or through several ministries, even for productive investments. If, on the other hand, the company is already seeing profit from its research, it can get tax breaks through Patent box.

Plus, innovative SMEs can combine these incentives, multiplying their options.

In order to optimize liquidity and the return on these incentives, it is important to consider eligibility for the mechanisms available and their compatibility, as it depends on different factors and the items eligible for funding differ with each incentive.
At Ayming, we understand the importance of optimizing funding so that no good project goes unexecuted.

Covid-19 emergency! Funding now. Our current situation has brought about changes to help resolve the Covid-19 healthcare emergency. The various bodies have launched measures associated with access to non-repayable aid and extensions of guarantees for projects related to the pandemic, as well as speeding up the deadlines and making application and repayment requirements more flexible.

Ideas for the future. The funding of tomorrow.

We advise hundreds of companies on funding their innovation each year. At Ayming we play an active role in the progress of the R&D ecosystem, collaborating and taking part in numerous associations, foundations and chambers of commerce. Together, we strive to promote innovation, fostering alignment of public policies and companies' global challenges.

The pandemic has made society more aware of the need to support and foster our public and private science systems. Plans to make sure innovative companies have the liquidity to carry out their projects must take into account the cost, in terms of opportunities lost, of not having these entrepreneurship initiatives.

With regard to the initiatives companies have a right to, we propose simplifying the requirements and facilitating access to 100% of the total deduction or allowing it to be used to offset other taxes due. In terms of the amounts, we believe that reinstating the 15% deduction for technological innovation and increasing the offset for

R&D staff to 75% would help modernize the sector and its immersion in the digital economy.

We celebrated the CDTI announcement that it will double its funds over the next three years. But we still need more non-repayable funding. Companies need liquidity without going into debt. Increasing the non-repayable portion of loans and the amount advanced would be excellent initiatives.

The challenges we are facing have highlighted the importance of R&D investment as a driving force for the economy during reconstruction. Instruments are needed to fuel structural changes in public-private partnership to help turn investment in science into innovative solutions to improve social well-being. This is the only way biotechnology will be able to harness the massive potential of the so-called twin transitions: climate neutrality and digital leadership, helping build a more sustainable production model.

Long live innovation!

Funds raised on capital markets are up 27%.

Table 4.3 shows the operations by biotechnology companies traded on either the Spanish Alternative Stock Market or Continuous Market. Throughout 2019, there were five capital increases by issuing new shares, carried out by

biotechnology companies Reig Jofre, Oryzon, Pangaea Oncology and Atrys Health, raising over €52 million, up 27% from 2018.

	2016	2017	2018	2019		
Capital increase by publicity traded companies	€20,522,889	€41,345,199	€38,200,000	€52,144,440		
2019						
Organization	Type of capital increase		Total volume committed			
Reig Jofré	Capital increase	e by issuing shares	€24,000,000			
Oryzon	Capital increase by issuing shares €20,000,000		0,000,000			
Atrys Health	Capital increase	e by issuing shares	€5,000,000			
Oryzon	Capital increase by issuing shares €1,324,500		,324,500			
Pangaea Oncology	Capital increase	e by issuing shares	es €1,819,940			

Table 4.3. Capital increases by companies traded on either the Spanish Alternative Stock Market or Continuous Market.

Acquisition operations continue at Spanish biotechnology companies.

Throughout 2019, acquisition operations continued at Spanish biotechnology companies. For most of them, the total amount is not known.

Noteworthy corporate operations include Keensight Capital acquiring 90% of 3P Biopharmaceuticals, AMSLab acquiring 51% of Laboratorios CIFGA, Kaneka acquiring 86.6% of AB-Biotics, and total takeovers of Pevesa Biotech and Igenomix by the Kerry Group and EQT, respectively.

Complementary funding through loans and equity shares held by business development bodies were up from 2018, but didn't reach the levels of 2017.

Complementary funding is that obtained by biotechnology companies through loans or equity shares held by regional or national business development bodies. These are regional financial instruments, like participation and venture capital loans, or loans granted by ENISA, a public company under the Ministry of Industry, Trade and Tourism.

Table 4.4 shows that, although the total number of operations, total volume and average volume all rose, they still were not on par with those seen in 2017. Nevertheless, compared to 2018, the volume increased 50%; the average total per operation, 22% and the number of operations, 23%.

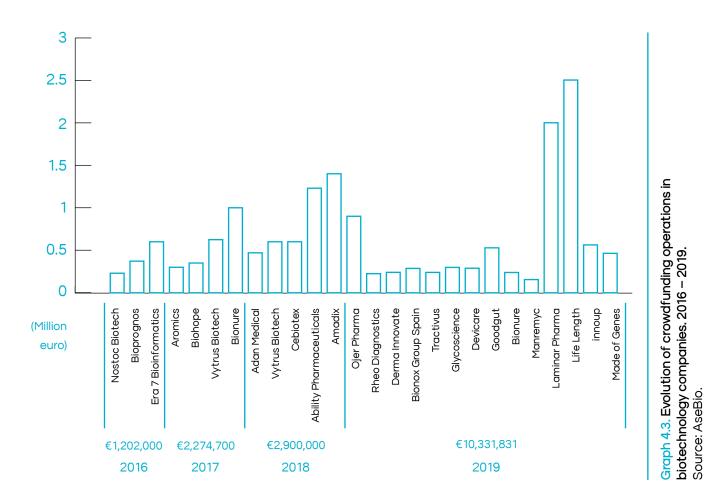
As was the case in 2018, biotechnology companies did not reach €10 million in this type of funding in 2019 either.

	2016	2017	2018	2019
Total volume	€7,695,000	€10,868,204	€3,715,155	€5,584,000
Number of operations	33	31	22	27
Average total per operation	€233,182	€350,587	€168,871	€206,815

Table 4.4. Evolution of loans granted by ENISA and by regional societies in 2019.
Source: AseBio and ENISA.

Crowdfunding has become a consolidated funding tool in the Spanish biotechnology sector.

Crowdfunding has continued to consolidate its place as a funding option for biotechnology companies, with growing weight. As we can see in graph 4.3, the number of companies turning to this type of funding and the amount they raised both hit new records in 2019. The amount of funds mobilized is now €10 million.



Venture capitalists continue banking on Spanish biotechnology companies.

The biomedical investment fund Sabadell Asabys Health Innovation Investments, managed by Asabys Partners with a target of €70 million, began with €30 million committed by its initial partners, with Banco Sabadell as its main investor. The fund will invest in 15 companies in the Spanish and international biomedical sector over the next five years.

Columbus Venture Partners, in early 2019, announced its second fund, the Columbus Life Science Fund II, FCR, had been registered with the CNMV with the goal of raising €70 million. This fund will invest in biotechnology companies working in advanced therapies and continue the activity started by the previous fund, Columbus Innvierte Life Science, which has five companies in its portfolio.

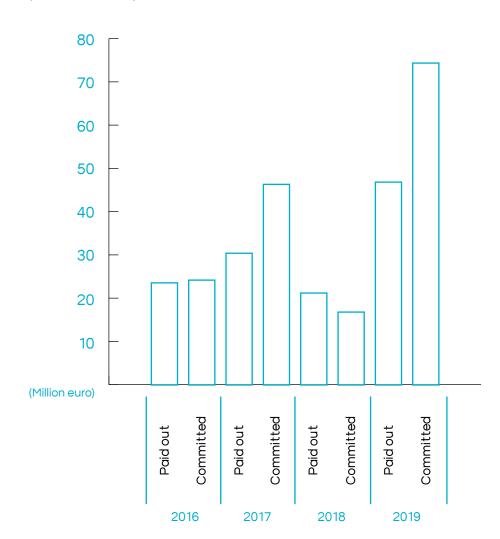
In May 2019, venture capital manager Clave Mayor kicked off its Tech Transfer Agrifood fund, with participation from the Official Credit Institute (ICO) through FONDICO Global, and the Navarra business development instrument (Sodena). The fund aims to raise €15 million and has currently put together €10.5 million. This fund will invest in companies in the agrifood sector, with investments to cover existing demand to generate technology and transfer it to the agrifood industry.

The founders of Ilana Capital launched the Abante Biotech Fund, a collective investment fund that invests in publicly traded companies and was named the most profitable health fund in Europe for 2019. In 2019, they announced that their fund focusing on investment in small biotechnology companies had reached €20 million. Now in 2020, this figure has hit €30 million, above initial expectations.

Source: AseBio.

Plus, according to the analysis AseBio has been carrying out since 2016, the amount paid out and committed by venture capitalists in Spanish biotechnology companies once again rose in 2019. These organizations, CRB, Caixa Capital Risc, Ysios Capital, Inveready,

Invivo, Clave Mayor, Columbus, Alta Life Sciences, Fitalent and Asabys, committed over €74 million throughout 2019 (up 342% from 2018), to be paid out in the future.



4.2. Public funding instruments

In addition to private instruments, the biotechnology sector also turns to public grant programs, including those run by the Center for the Development of Industrial Technology (CDTI) and the State Research Agency (AEI). Now let's look at the analysis of how CDTI grants for R&D projects have evolved in the biotechnology sector since 2012, and those awarded by the AEI State Program for Research, Development and Innovation since 2014.

R&D projects and Neotec grants supported by the CDTI in the biotechnology arena.

The CDTI supports business projects for industrial research and experimental development to create or significantly improve a production process, product or service, submitted by one or a group of companies. In the innovation arena, it supports projects close to market that help boost the company's competitiveness by incorporating emerging technology in the sector.

These projects are funded through partly repayable grants and directly awarded subsidies for Eurostars and Innoglobal.

Neotec subsidies are intended to fund new technology-based companies, which are those whose main activity is to exploit products or services that require the use of technology or knowledge developed through research activity.

In 2019, 75 projects in biotechnology were funded, including individual R&D projects, cooperative R&D; CIEN, FEMP, Eurostars and Innoglobal projects; Direct Innovation Line for 2019 and 14 projects in biotechnology under the Neotec grants from the 2018 call that were awarded in 2019.

	Number of projects	Total budget (€)	Total awarded (€)	Non-repaya- ble portion/ subsidy (€)	Repayable portion (€)
R&D projects approved in the biotechnology arena	61	43,939,547	35,292,165	8,976,247	26,315,918
Neotec grants	14	5,270,222	3,343,284	3,343,284	
Total	75	49,209,769	38,635,449	12,319,531	26,315,918

Innvierte actions in the biotechnology arena in 2019.

The CDTI, through public-private vehicles created under the Innvierte initiative, has made 79 investments in the biotechnology sector for a total of €172.72 million.

Furthermore, through the coinvestment tool Innvierte launched in the second half of 2019, €21 million have already been committed to 11 companies.

Evolution of projects funded by the CDTI in the biotechnology arena.

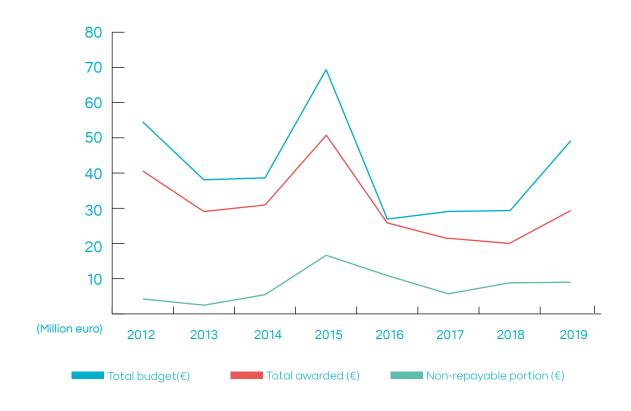
Analysis of the evolution of funding for CDTI projects between 2012 and 2019 looks at the biotechnology R&D projects approved for funding through repayable and partially repayable aid each year.

As we can see in table 4.6 and graph 4.5, the number of projects approved, the total budget and the amount granted all rose in 2019. Unlike the previous year, in 2019 the non-repayable portion fell to 23%, returning to levels from 2014.

	2012	2013	2014	2015	2016	2017	2018	2019
Total budget (€)	54,574,672	38,130,273	38,667,929	69,379,626	26,997,606	29,153,878	29,263,359	49,209,769
Total awarded (€)	40,591,923	29,090,636	30,954,425	50,701,328	25,751,881	21,382,075	20,069,625	38,635,449
Non-repayable portion (€)	4,267,112	2,524,403	5,469,468	16,543,458	10,848,637	5,719,520	8,797,848	8,976,247
Repayable portion (€)	35,555,612	25,845,101	24,634,085	34,157,869	14,903,244	15,662,555	11,271,777	26,315,918
Number of projects	72	62	44	46	29	42	57	75
% NRP vs. awarded	11%	9%	18%	33%	42%	27%	44%	23%

Table 4.6. Evolution of R&D projects approved in the biotechnology arena.

Source: CDTI.







The biotechnology talent pool: brilliant university talent with a high percentage of women.

Biotechnology has consolidated its place as a sector capable of attracting young talent. The number of students enrolled in university studies in biotechnology rose every year from 2015 to 2019, to nearly 7,000 students the past academic year.



Graph 5.1. Evolution of number of students enrolled in university studies in biotechnology (undergraduate).

Source: Compiled internally from Statistics on University Students of the Secretary of State for Universities (Ministry of Science, Innovation and Universities).

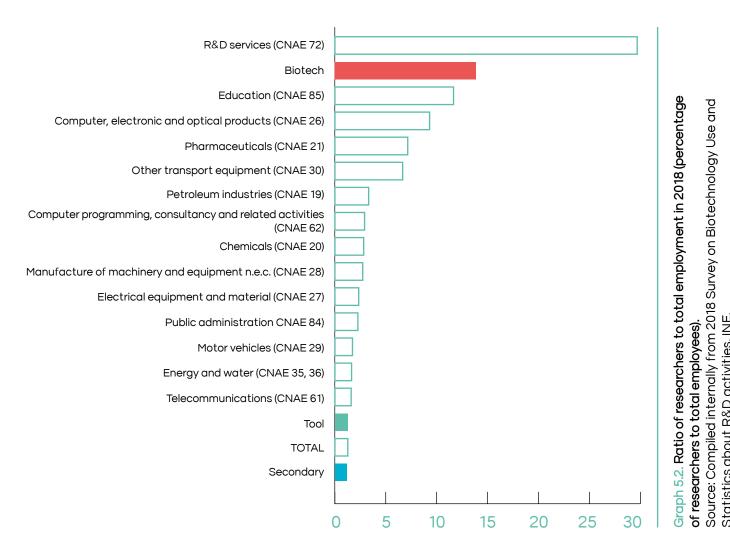
Women make up 60% of all students enrolled on these courses, well above other STEM disciplines (science, technology, engineering and mathematics) like engineering and computers, where they are only 25% and 15% of the population, respectively.

The talent pool in the biotechnology sector features brilliant upand-comers and to get into this

university degree in 2019 they needed one of the highest scores on admissions tests. At 19 of the 24 public universities that offer biotechnology, this degree is among the top 10 highest admissions scores required.

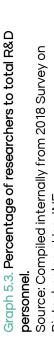
The biotechnology sector hires many researchers, above the Spanish average.

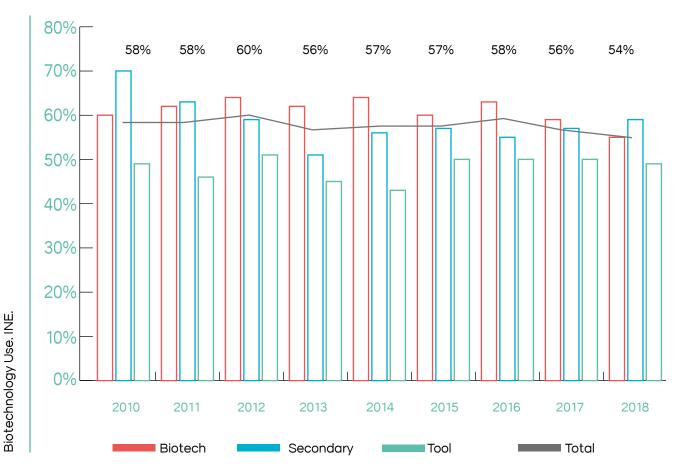
The biotechnology sector is knowledge intensive, as graph 5.2 shows. Biotech companies are ranked second in percentage of researchers to total employees in the sector, surpassed only by the research and development services sector.



If we look at this data more closely, meaning the proportion of researchers to total staff for R&D activities, we can see that the proportion has stayed above 54% since 2010 (graph 5.3). At biotech

companies, the percentage of researchers to total R&D personnel has always been above 55%.



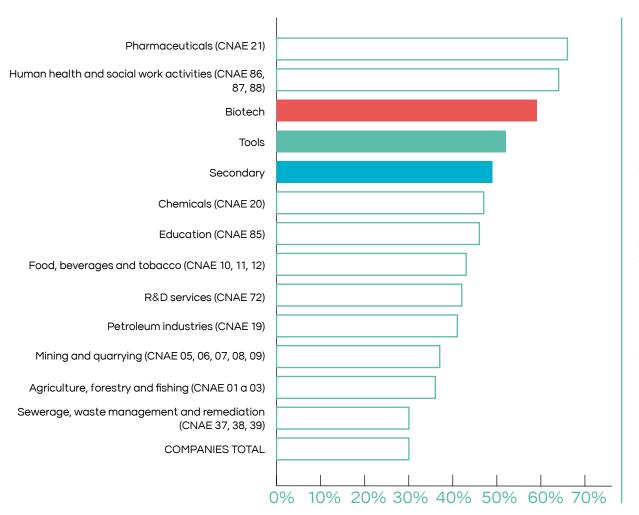


The biotechnology sector has highly qualified employees who earn above the Spanish average wage.

As we'll see later in the section on their impact on the sector, the average salary per employee at biotech companies is much higher than the Spanish average (graph 9.7 on page 108). This highlights, once again, that jobs in the biotechnology sector are held by highly qualified employees.

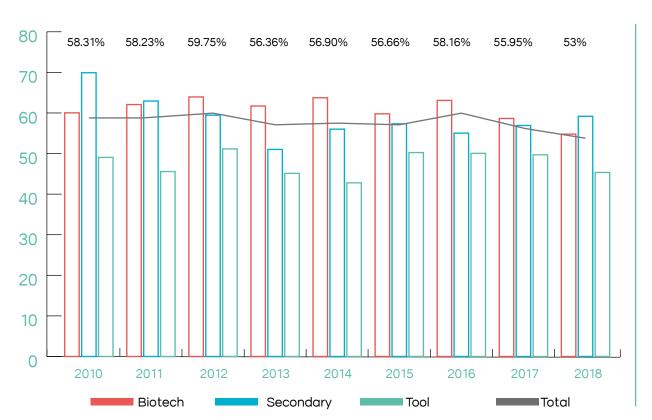
Biotech companies are leaders in employing women in R&D activities.

Biotech companies are ranked third in terms of women in R&D activities, with 59%, surpassed only by healthcare and social services and pharmacy. This percentage is well above the average for the economy as a whole, where women's participation in R&D activities is barely above 30%.



Graph 5.4. Percentage of women to total R&D personnel. Source: Compiled internally from 2018 Survey on Biotechnology Use and Statistics about R&D activities. INE.

Although the percentage of female researchers in biotechnology has dropped slightly, as graph 5.5 shows, it has always been above 53%. For biotech companies, this figure has never dropped below 55%.



Graph 5.5. Evolution of female researchers in biotechnology (percentage of women to total R&D personnel). Source: Compiled internally from 2018 Survey on

Biotechnology Use. INE.

THE IMPORTANCE OF BEING ASKED WHAT KIND OF WORLD I WANT

cnio stop cancer

In 2012, we created the CNIO Women in Science Office (WISE). An office staffed by volunteers from CNIO, which I am also part of as a researcher and director of CNIO. The goal of this office is to consolidate gender perspective as one of the hallmarks of our institution. According to Scimago and Nature Index rankings, CNIO is among the top cancer research centers in the world, and we also want to be on the forefront of gender equality. It is an urgent, important issue because, although the majority of researchers at CNIO are women, leadership positions in research groups are still mostly held by men. This inequality in the higher echelons of research is repeated at many other research centers all over the world, and it doesn't seem to be changing as quickly as we would like.

What are the roadblocks to this change?

Eight years after setting up CNIO WISE, I'm optimistic and believe we've brought about change at CNIO. The CNIO that was oblivious to the problems facing female scientists, to the difficulties of balancing work and family life for women and men, and to fostering empowerment and networking among women is far behind us. Now we are proud of our gender initiatives and we like to boast about them. The CNIO WISE seminars, which have featured writers like Rosa Montero, Elvira Sastre and Laura Ferrero; singer/songwriters like Christina Rosenvinge and Luz Casal, prosecutors like Consuelo Madrigal, and women in politics like María Teresa Fernández de la Vega and Ángeles Sinde, have been the first of

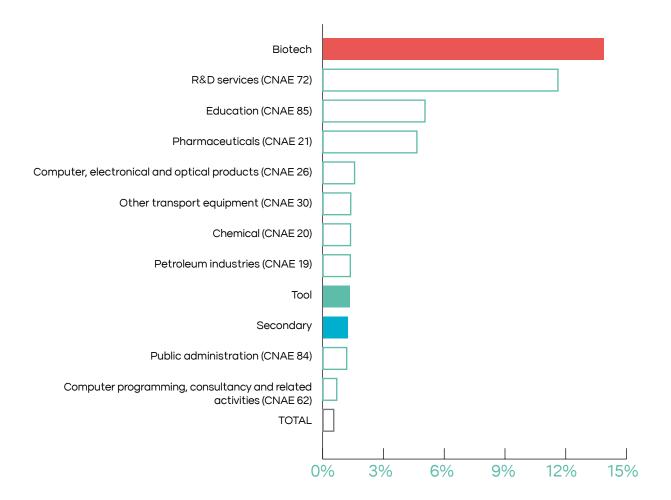
their kind at science institutions in our country. It hasn't been an easy road, nor a quick journey; we've had to be patient and self-confident, we've had to repeat the same messages over and over again and sometimes, though not most, we've had to put up with discouraging comments. But we've never given up. Luckily, we've had the support of our Board of Trustees, and of many friends in politics, science, art, music and literature who have shared their experiences and ideas with us, and above all have supported and advised us. Thanks to all of them. we've learned to be more aware of the problems facing many women in various professions and the importance of eliminating them. Plus, we wanted to open our doors to young people, boys and girls from secondary school, who have come to CNIO to share in our CNIO WISE seminars with our researchers.

I think it is important to highlight that the first CNIO WISE initiative was to call all the CNIO female researchers in and ask them what they want CNIO to be, how CNIO could help them do their job better as scientists and become leaders of their own research group, to want to be more independent. It seems obvious but it isn't. These questions have allowed us to establish shared goals that have a good chance of being achieved, and that is why I strongly recommend asking female workers what they want. The female researchers at CNIO said they didn't find the decision-making positions in science attractive. They said they wanted to bring about change in research centers, not become laboratory heads. And they were right. Science in the decision-making

and research-management levels is a world designed by men, where they are the majority, to fit men's schedules and priorities. From that meeting and many others, we came up with specific proposals on how to do it, many related to realistic schedules, balancing work and family life, supporting motherhood, and these have been put down in an ambitious equality plan, which has made CNIO a better place to work. Oddly enough, Nature published a study last year that asked female academics in the US what they would change about their institutions in order to continue advancing in their jobs. The list of requests was very similar to what we are already doing at CNIO.

Women don't want to break into a world designed by men, we want to have a world made by women and men, together. And I'm sure that this world is a better one for both women and men.

Plus, if we compare the percentage of female researchers to the total employed population (graph 5.6), biotech has a higher percentage of women in research than other areas of activity like pharmaceuticals or chemistry.



Graph 5.6. Ratio of female researchers to total employment in 2018 (percentage of women researchers to total employees).

Source: Compiled internally from 2018 Survey on Biotechnology Use and Statistics about R&D activities. INE.

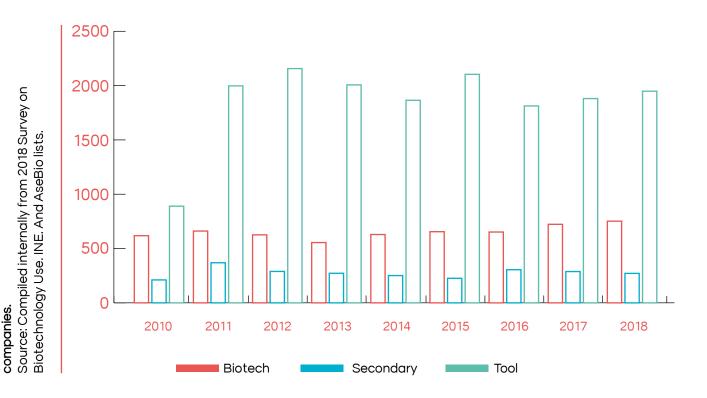




2,969 companies carried out biotechnology activities in 2018, of which 751 are biotech firms, up 4% from the previous year.

In 2018 (graph 6.1), the number of companies carrying out biotechnology activities rebounded slightly, with 2,969 companies in total, roughly back to the levels from 2015. This meant an average growth of 2.8% from the previous year, above the average growth for companies in all other activities (2.2%). Therefore, the ratio of biotechnology companies to companies in all other activities has increased to nearly two companies with biotechnology activity for every 1,000 businesses.

Strictly biotechnology companies, biotech firms (whose main task is biotechnology), posted higher growth rates, above 4% in 2018, with a total of 751 businesses.



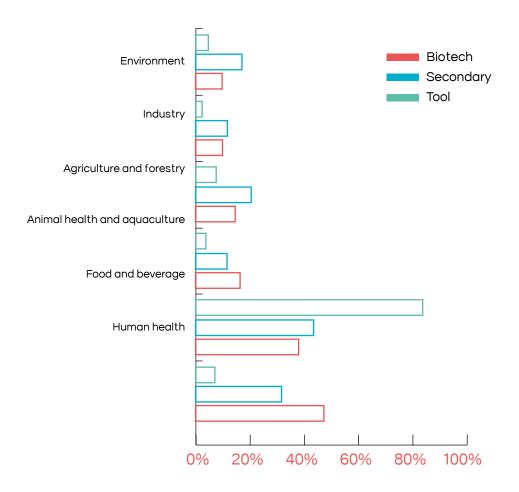
Human health and food continue to be the key work areas in the biotechnology sector.

Human health and food continue to be the predominant fields for biotechnology companies, although these results are highly conditioned by the high percentage of companies that use biotechnology as a production tool in the food sector (graph 6.2).

If we focus on companies that work exclusively in biotechnology (biotech firms), over 47% work in the field of human health, followed by those focused on food applications, which make up 38% of these companies.

Graph 6.1. Evolution of the number of biotechnology

Applications in the primary sector (aquaculture, animal health, agriculture and forestry) are further down the list, with roughly 15% of companies, and industrial or environmental applications are slightly below 10%.



55% of biotech firms are micro-SMEs, with fewer than 10 employees.

Focusing only on biotech firms, table 6.1 shows that just under 55% of these are micro-SMEs with fewer than 10 employees and 28.4% have fewer than 50 workers. Nevertheless, in terms of total turnover, over 86% of the total is created by the 87 medium-sized companies and 18 large corporations identified.

	Number of companies	% of total	Average turnover € millions	% of total turnover
Micro-SME (fewer than 10 employees)	467	54.9%	0.4	1.9%
Small (10 to 49)	179	28.4%	6.2	10.5%
Medium (50 to 249)	87	13.8%	50	40.8%
Large (more than 250)	18	2.9%	276	46.8%
TOTAL	751	100%	14.1	100%

Table 6.1. Breakdown of biotech firms by size. Source: Compiled from the information on companies collected by AseBio.

companies collected by AseBio.

Catalonia has the greatest concentration of biotech firms.

As table 6.2 shows, Catalonia, with nearly 24% of all biotech companies, is the main hub of biotechnology activity in Spain, both in number

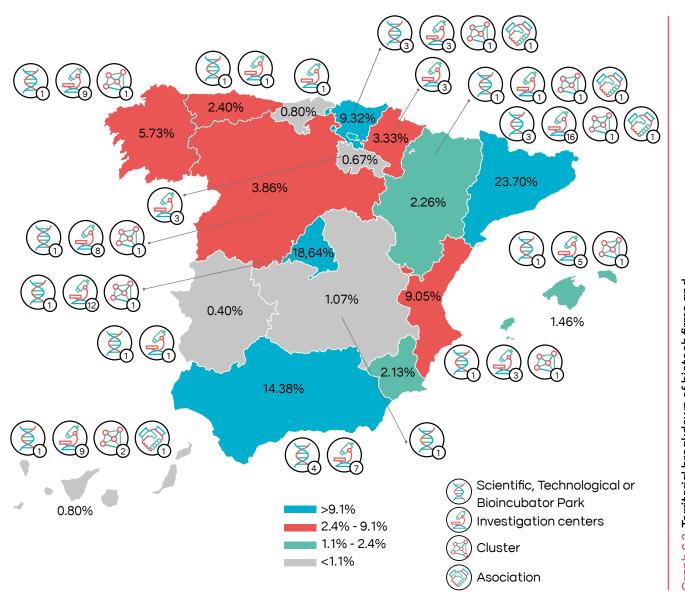
of biotech companies and in turnover, with over 50% of the joint turnover in 2018. It is followed by the Community of Madrid and Andalusia in terms of relative weight of biotech companies, with 18.6% and 14.4%, respectively. In terms of turnover, however, Madrid makes up 30% of the national total, as the average turnover per company is significantly higher.

	Number of companies	% of total	Average turnover € millions	% of total turnover	GVA in % of regional total
Andalusia	108	14.38%	4.4	4.47%	0.09%
Aragón	17	2.26%	20.3	3.25%	0.20%
Asturias	18	2.40%	0.5	0.09%	0.02%
Balearic Island	11	1.46%	0.4	0.05%	0.01%
Canary Island	6	0.80%	0.5	0.03%	0.00%
Cantabria	6	0.80%	20.0	1.13%	0.35%
Castile y León	29	3.86%	6.0	1.63%	0.13%
Castile-La Mancha	8	1.07%	7.5	0.57%	0.04%
Catalonia	178	23.70%	30.3	50.81%	0.78%
Valencian Community	68	9.05%	4.8	3.05%	0.09%
Extremadura	3	0.40%	5.3	0.15%	0.01%
Galicia	43	5.73%	8.3	3.38%	0.16%
Madrid	140	18.64%	22.3	29.42%	0.17%
Murcia	16	2.13%	1.2	0.18%	0.03%
Navarra	25	3.33%	2.4	0.56%	0.01%
Basque Country	70	9.32%	1.8	1.20%	0.08%
La Rioja	5	0.67%	0.7	0.03%	0.02%
TOTAL	751	100%	14.1	100%	0.24%

Graph 6.3 shows where biotech companies are located in Spain, by Autonomous Community. We can see that Catalonia has the largest number of companies, followed by the Community of Madrid and Andalusia.

This same graph (graph 6.3) also shows each Autonomous Community's biotechnology facilities, meaning technology parks, business associations or sector clusters, and research centers. According to this data, we can see that

Catalonia and Madrid have the richest ecosystems for biotechnology.



In 2019, 27 new biotech companies were set up.

According to the analysis AseBio carries out each year, which is a projection study on the number of companies created each year that work in biotechnology, a total of 27 new companies were identified in 2019, 13 fewer than in 2018. These companies, with their location and main activity, are listed in table 6.3.

Catalonia has the largest number of biotechnology companies created, with six, followed by the Basque Country and Galicia, with four each.

Company name	Autonomous Community	Activity
Arthex Biotech	Valencian Community	Developing RNA treatments for genetic diseases.
Actucg	Andalusia	Sequencing, analyzing and researching nucleic acids (DNA and RNA). Using artificial intelligence and databases for bioinformatic analysis of sequences.
Biorepositorio Iberia	Galicia	Specialized services in areas associated with storage and management of biological samples at low temperatures.
Breedalia	Valencian Community	Growing and commercializing medicinal cannabis B2B.
Cellia Regenerative Medicine	Basque Country	Developing medical devices for human health.
Connecta Therapeutics	Catalonia	Developing new treatments for fragile X syndrome.
Forchronic	Madrid	New generation of precision nutraceuticals.
Genbioma	Navarra	Researching the microbiome and developing new solutions in probiotics and other bioactive compounds.
Hidrosphere	Galicia	Identifying the taxonomy of benthological species and studying biological and environmental parameters that are key for monitoring the state/ecological potential of continental, transitional and coastal surface waters.
Hifas Veterinary	Galicia	Creating and commercializing raw materials, food supplements and pharmaceutical products from fungi, for farm animals and pets.
Ingeniería y Desarrollos Derivados del Carbón	Extremadura	Researching, developing and producing biotechnology solutions to improve the health and well-being of people and animals.
Inhibitec Anticuerpos	Cantabria	Developing therapeutic monoclonal antibodies for autoimmune diseases, like psoriasis.
Innovatekbi Krea	Basque Country	Developing technological products using microencapsulation.
Insectaria	La Rioja	Producing, commercializing and handling Anthocoris nemoralis for use as a biological pest-control agent.
Limno Pharma	Andalusia	Developing new therapies for age-related macular degeneration (AMD) and retinitis pigmentosa (RP).
Method Therapeutics	Madrid	Developing biotechnology and biomedical projects for untreated, potentially deadly cardiovascular conditions.
Miramoon Pharma	Basque Country	Allosteric modulator drugs to treat muscular, neurological and age-related conditions. Smart molecules for neurodegenerative and rare conditions.
NeuroHeal Biomedicals	Catalonia	Developing products to treat lesions of the central nervous system using systems biology.

Catalonia	Developing new biological therapies to fight metastatic cancer.
Basque Country	Developing antibodies for metastatic cancer.
Catalonia	Diagnostic kit based on microRNA expression profiling of peripheral blood.
Navarra	Manufacturing and commercializing animal feed products: probiotics and prebiotics.
Catalonia	Researching and producing highly efficient active ingredients and medical devices with low toxicity for cosmetic use to reduce the impact of cancer on the skin.
Navarra	Developing antimicrobial compounds based on bacteriophages and their enzymes
Andalusia	Characterizing the biological and biosafety risks of strains of bacteria and fungi for stable drying of bioinoculants and biofertilizers and to produce ecological bactericides and fungicides.
Catalonia	Drug discovery for cardiac conditions using the zebrafish model.
Galicia	CDMO services for drugs and pharmaceutical-grade probiotics.
	Basque Country Catalonia Navarra Catalonia Navarra Andalusia Catalonia

Table 6.3. Companies devoted to biotechnology that began working in 2019.

Source: AseBio, with collaboration from IDEA Agency, Axencia Galega de Innovación, Biocat, Bioga, Bioibal (Biotechnological and biomedical cluster of the Balearic Islands), BIOVAL, the Chamber of Commerce of Cantabria, CEEI Asturias, CEEI Valencia, the European Center of Business and Innovation in Navarra (CEIN), the General Directorate for Industry, Energy and Innovation of the Government of Navarra, the Directorate General of Innovation, Industry and Commerce of La Rioja, the Directorate General Research and Innovation of Aragon, the Madri+d Knowledge Foundation, Fundecyt - Science and Technology Park of Extremadura, Sodercan group, Institute for the Promotion the Region of Murcia, Oficina de Transparencia y Buen Gobierno de la Junta de Castilla La Mancha, Madrid Science Park, Albacete Science and Technology Park, SODENA, SPRI and the Canary Islands Special Zone (ZEC).

MERCK GUARANTEES INNOVATION FOR SUSTAINABLE HUMAN PROGRESS



It has now been 5 years since the signing of the United Nations 2030 agenda, with its 17 sustainable development goals (SDGs) that will allow us to grow as a global society with more respect for people and the planet. This has been one of the biggest milestones in recent history, which I admire for two reasons: for the nature of the proposal itself and because it is a plan that shows sustainability concerns and is the responsibility of all UN member countries.

At Merck, we accepted the challenge and firmly believe that the world we live in tomorrow will be determined by the choices we make today. So, we're still doing what we do best, and have done since the origins of the company more than 350 years ago: innovate.

Thanks to our position in the AseBio presidency, we are leading the development of the biotechnology ecosystem as a key element for social development and competitiveness and strive for greater recognition of the value R&D has for Spanish society and the sustainability and competitiveness of our economy.

In terms of how to proceed as a biotechnology company, our mission, vision, values and experience have led us to focus on areas where we know we can contribute to sustainability through science and technology. We research, develop,

produce and pool our efforts with partners to fuel sustainable innovation that has a real impact on society, working to find answers to some of the great challenges that affect us all.

We are helping accelerate scientific discovery with our role in providing the scientific community with tools, services and platforms that make research simpler and more precise. One example is our 23 CRISPR patents (like CRISPR/CAS9 and Proxy CRISPR) for gene editing.

Secondly, our vision for a sustainable healthcare system requires a model based on personalized health, in which prevention and treatment strategies are designed based on the patients, not the disease. This has led us to focus our pipeline on researching and developing biomarkers and targeted therapies in immuno-oncology, oncology and immunology, to provide personalized solutions to conditions that have a serious impact on patients' lives, like multiple sclerosis, lung cancer and bladder cancer.

Nevertheless, our commitment to sustainability goes beyond just SDG 3 and ensuring healthy lives and wellbeing for all people. We've also taken a step forward in the fight against scarcity of resources.

We live in a world that is using resources 50% faster than they can be replenished and, with our approach to science, we feel a

responsibility to promote high-impact innovation in this area to protect our natural habitat and reduce our mark on the environment, in line with the EU Green Deal. We are already working with the scientific community to research clean meat as a healthy, ethical, eco-friendly alternative that doesn't come from animals, developing new materials for precision agriculture and piloting photonic materials that optimize land use and guarantee crops with less agricultural resources.

In short, we are contributing to sustainable human progress through innovation in science and technology, with an approach that is focused on people, the planet, prosperity and alliances. Exactly the same core ideas as the UN SDGs.

Miguel F. Alcalde, General Manager of Merck in Spain



The Madrid Science Park Foundation (Fundación Parque Científico de Madrid - FPCM) is a project that began 19 years ago and has played a key role in transferring knowledge and technology from universities and research centers to society, through over 300 companies in the Community of Madrid. 80% of these companies have prospered thanks to the comprehensive support model, professional services and facilities the park makes available to entrepreneurs so they can compete in the best possible conditions on the market.

The FPCM board of trustees includes members from two universities with extensive experience in teaching and research in biotechnology, the Autonomous University of Madrid and the Complutense University of Madrid, plus support from CSIC, Ciemat, Banco Santander and the Madrid City Council.

In 2019, FPCM saw its peak growth, with 99% occupancy serving 95 science- and technology-based companies. Since the beginning, FPCM has been firmly committed to the biotechnology sector, as the only science park in the Community of Madrid with a turnkey laboratory to allow entrepreneurs to carry out their projects with the scientific equipment they need. This distinction led us to incubate 38 companies from the biotechnology sector in 2019.

Our biotech entrepreneurs innovate in areas that are extremely important now, like developing cellular and molecular biotechnology projects, genetic diagnostics, functional ingredients for food and cosmetics, plant biotechnology, personalized medicine, in vitro fertility, cancer or neuroscience, among others.

As a jumping off point for entrepreneurship, FPCM also collaborates with its trustees to coordinate acceleration programs to start up companies, with ample representation from the biotechnology sector. In this task, we get support from the CEOs at our biotech companies, who help us promote transfer by mentoring the projects in the program.

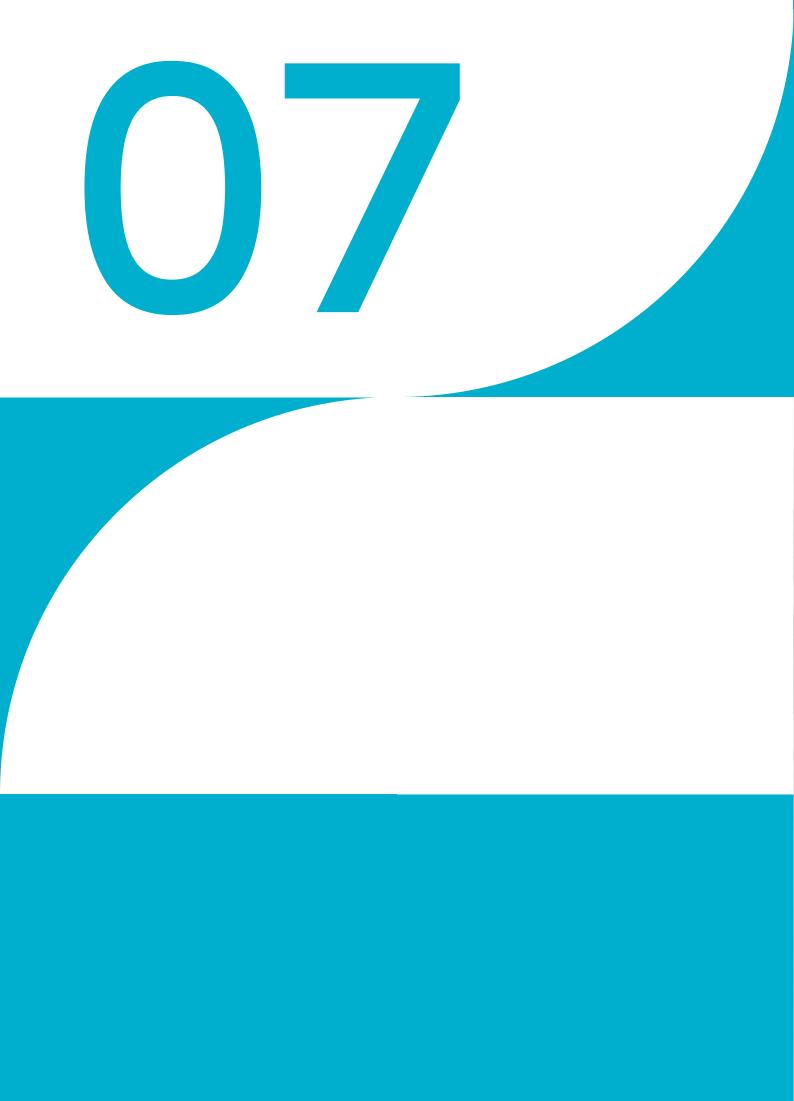
FPCM has a genomics platform through which it provides latest generation scientific services, which technology-based companies can use to carry out their normal scientific activities.

The platform's clients include research centers, hospitals and companies. Services provided to biotechnology companies make up 25% of all the activity of the Genomics Unit, in economic terms. The most in-demand service in this arena has to do with identifying biomarkers from different perspectives (oncology, microbiology, etc.) for use in precision personalized medicine.

In May 2020, FPCM, with the Autonomous University of Madrid (UAM) and the Alberto Sols Biomedical Research Institute (CSIC-UAM), received approval from the Carlos III Health Institute, which falls under the Ministry of Science and Innovation, to create a Covid-19 Diagnostic Unit using PCR tests to detect the SARS-CoV-2 coronavirus, with the capacity to do up to 500 tests per day. FPCM will collaborate on diagnostics through its Genomics Platform and has loaned a Kingfisher robot for automatically extracting RNA. This unit is currently focused on diagnosing the elderly in senior care homes in the Community of Madrid.

At FPCM we are proud to collaborate with AseBio on the annual report and to be part of the Spanish biotechnology innovation ecosystem.

Pilar Gil Ibañez, General Manager of FPCM _Spanish Association of Bioenterprises





7.1. How society sees our work: The public value of science, innovation and biotechnology

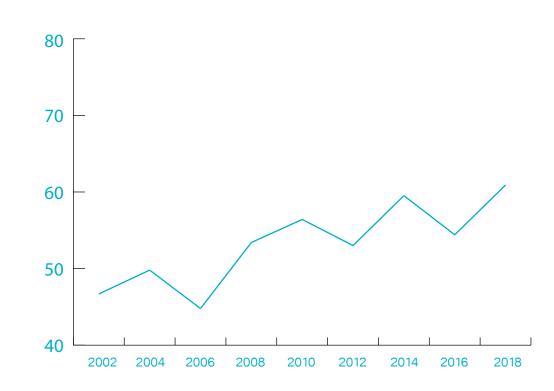
We're living in a time when technological and scientific advances happen at breakneck speed. This has caused some people to fear, and even reject, certain scientific and technological developments, from GMOs to vaccines or artificial intelligence.

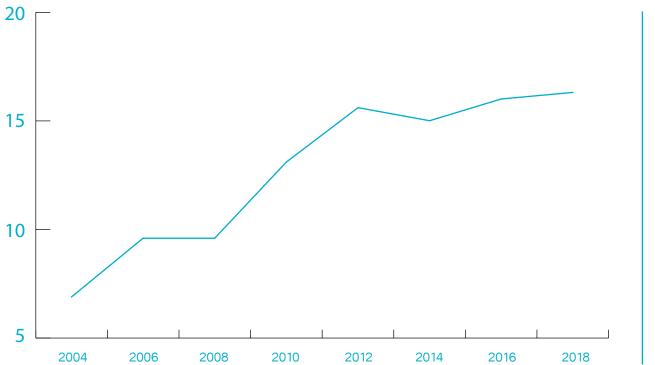
Science, and biotechnology in particular, plays a key role in addressing the social and environmental challenges we are facing. So, we need people to be aware of the social benefits of our work, which include innovative drugs, bioproducts, vaccines and drought-resistant crops.

Spanish society values and is increasingly interested in science and technology.

Every two years, the Spanish Foundation for Science and Technology (FECYT) conducts its Social Perception of Science and Technology in Spain survey, the results of which have shown a substantial improvement in the relationship between science and society over the past two decades.

People's image of science has improved steadily over the past twenty years. In the latest survey, from 2018, more than 60% of those asked said science and technology have more benefits than drawbacks, compared to 46% in 2002. If we look at the evolution in recent years, we can see that the situation improved notably between 2016 and 2018, up 12.2% (graph 7.1).





THAT'S WHY WE'RE SCIENCE



A growing and ageing global population and constant pressure to ensure quality food supply while using natural resources more efficiently and responsibly are some of the challenges we are now facing as a society.

At Bayer, we share one vision: health and food for all. And, grounded by our purpose, Science for a better life, we are helping build a world where diseases are not only treated, but prevented or cured; where people can protect their health more effectively; where we produce enough food for everyone, while respecting our planet's natural resources; where business growth and sustainability go hand in hand.

"Shaping agriculture to benefit farmers, consumers and our planet."

Never before has innovation in agriculture been so important. Our world is facing huge challenges, including climate change, limited natural resources and a growing population. And we believe agriculture is part of the solution.

At Bayer, we are working to shape agriculture through scientific innovation, setting new standards in sustainability and leading the digital transformation to benefit farmers, consumers and our planet.

We combine modern science with the genius of farmers to put innovation within their reach, to help feed the population and preserve our natural resources. And, although we don't have all the answers, our passion, pioneering spirit, collaborative nature and curiosity mean we will never stop working to find them.

"Biotechnology: a key element in our commitment to transparency and sustainability."

To create new varieties, at Bayer we use both traditional and novel techniques to develop hearty, high-quality plants with high vield even in difficult conditions. New plant breeding techniques allow us to create plant varieties that adapt to production systems, and to increase the use of existing genetic diversity so farmers can better adapt to quickly changing climate conditions. Even more important, these new varieties could help considerably improve efficiency in terms of use of resources in crop production, resulting in a more limited impact of fertilizers and plant protection products, as well as giving plants new properties quickly and specifically.

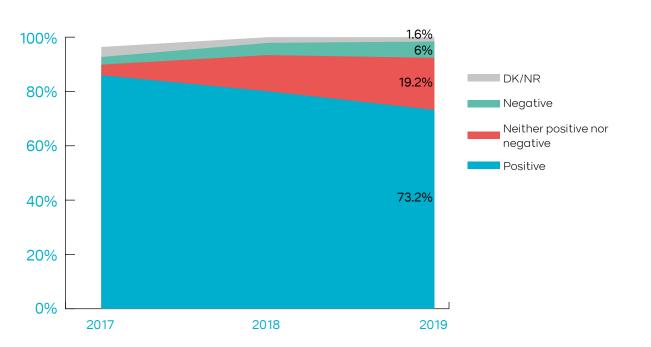
At Bayer, we recognize the power of innovation and apply it in everything we do. In line with our purpose of Science for a better life, we are committed to continuing to work closely with consumers and patients to help build better products, solutions and services for everyone.

Bayer CropScience

Spanish society has a positive opinion of innovation; however, this confidence has dropped in the past two years.

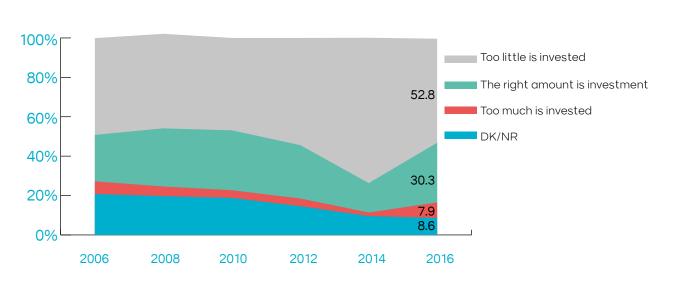
Since 2017, the COTEC Foundation has conducted its survey on Social Perception of Innovation in Spanish society, which shows 73% of those

surveyed (graph 7.3) have a positive opinion of innovation. Three in four Spaniards have a positive view of innovation, however their confidence is unstable and dropped sixteen percent in just two years (89% in 2017, 80% in 2018, 73% in 2019).



Spanish society considers investment in science and innovation in Spain to be insufficient.

In terms of the resources we earmark for science and innovation, as a country, 53% of Spanish society considers it is not enough. This figure was nearly 74% in 2014.



Graph 7.4. Evolution of Perception of resources devoted to Science and Technology.

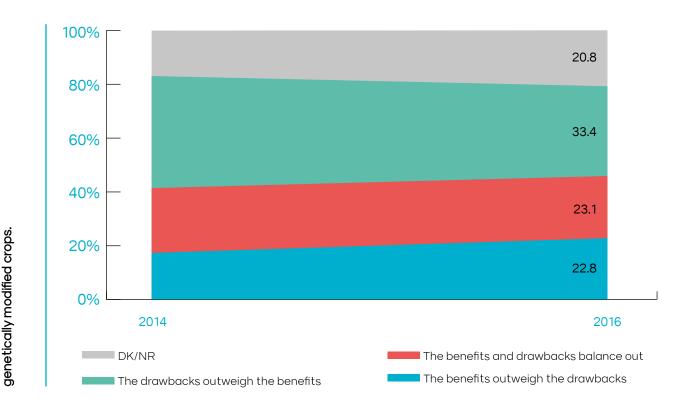
Graph 7.3. Evolution of opinion of

innovation 2017-2019.

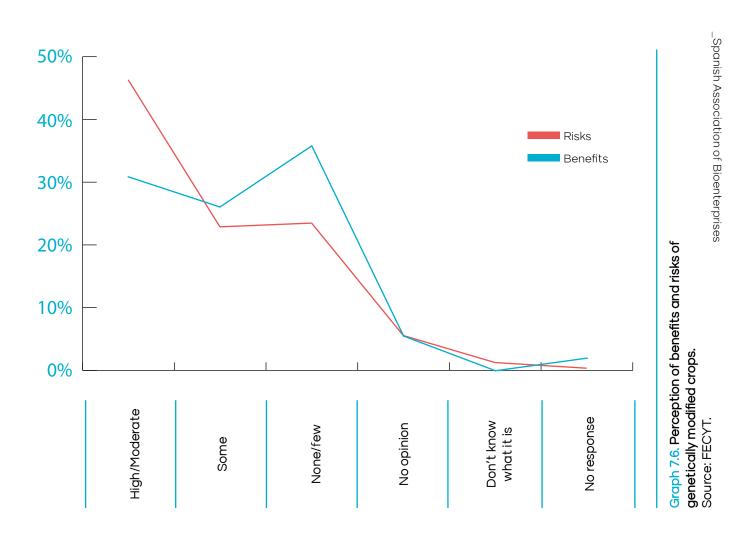
Spanish society's view on genetically modified plants has improved 32% in recent years.

Genetically modified plants and crops are one of the biggest opportunities for science and technology to combat climate change and help meet the food needs of the growing population. The FECYT survey includes a

question on Spanish society's view of this technology, which is key in biotechnology. Although the way the question is asked has changed over time, society's view of this type of innovation has improved notably in recent years. While in 2014, 17.3% of those surveyed felt that the benefits outweighed the drawbacks, in 2016 the same figure was 22.8%, up 32% in just two years.



In 2018, this question was re-formulated and revealed that nearly 31% of those surveyed see this innovation as highly beneficial and 26% believe it has some benefits. This means nearly 57% of Spanish society sees many or some benefits to genetically modified crops, compared to 35.7% who see few or no benefits. When asked about the risks, however, 49% feel GMOs have high or moderate risk and nearly 23% say there are some risks involved. These results show that, despite positive progress and wide-reaching scientific consensus on the safety of genetically modified crops, society still feels there is risk involved in this sort of innovation.

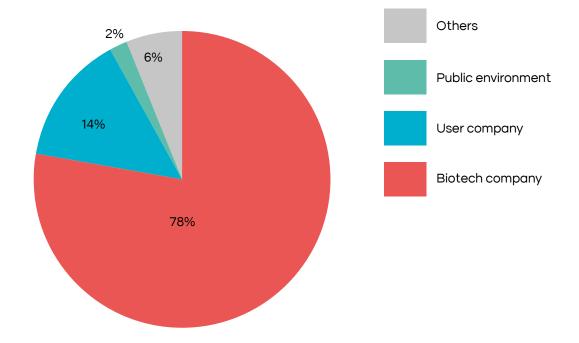


7.2. How the biotechnology sector sees its environment

Through the 2018 AseBio Report, AseBio used the AseBio Index to take the temperature of the biotechnology sector in Spain, with the survey we send out each year to all our members. In this survey, members assessed how a series of factors had helped or hindered development of biotechnology in our country.

For this edition, AseBio has simplified the questionnaire and reworked data from past editions, asking members to rate a series of factors positively or negatively.

This year's survey had 51 participants, the vast majority purely biotechnology companies, followed by companies associated with or that use biotechnology, as can be seen in graph 7.7.



Graph 7.7. Breakdown of participants in the AseBio survey by type of organization. Source: AseBio.

The sector rates employee training and availability very highly, while the cost of innovation continues to be a roadblock.

Table 7.1 shows the results of the survey rating 21 factors. A rating of 1 or 2 is very negative or negative and a 3 or 4 is positive or very positive.

The first 12 on the list are factors that participants rated positively. These include: employee training level, number of bioentrepreneurs, internationalization process, qualified personnel, creation of new companies in Spain, public opinion of biotechnology, attracting international companies, availability of specialized facilities,

increase in average size of biocompanies, cooperation with other organizations, availability of specialized suppliers and demand for more sophisticated products.

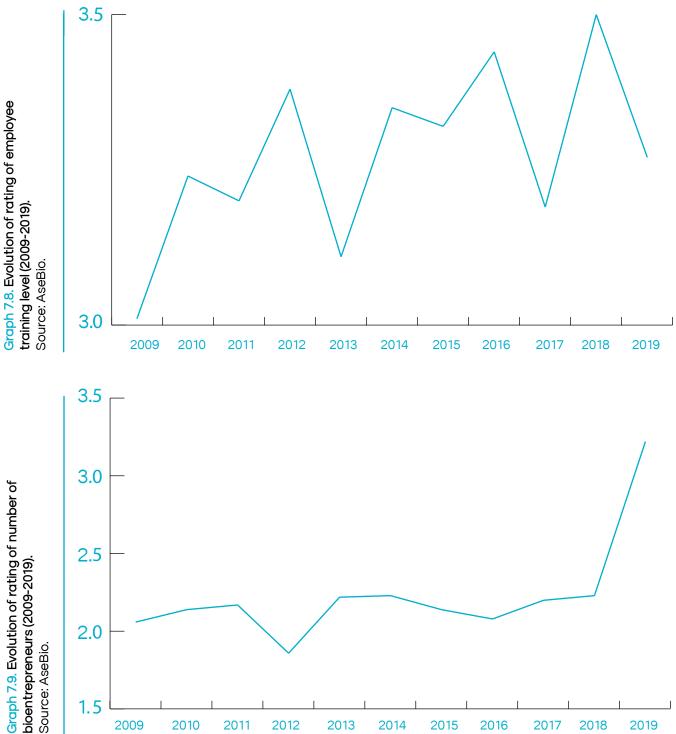
The other side of the coin, however, shows the nine factors companies rated negatively (lower than a 3): mergers and acquisitions or strategic alliances, information on the biotechnology market, market-oriented nature of the public technology offering, the regulatory framework, access to funding, the public administration, time to profitability, the economic situation and, the lowest of all, the cost of innovation.

Factors	2019	2018	Average 2000-2019	% change from 2018 y 2019
Employee training level	3.275	3.500	3.9473	-33.9%
Number of bioentrepreneurs	3.202	2.234	2.1978	44.1%
Internalization process	3.216	1.977	1.2031	62.6%
Qualified personnel	3.216	2.421	1.9913	32.8%
Creation of new companies in Spain	3.200	3.127	2.7426	2.3%
Public opinion of biotechnology	3.157	2.123	2.1040	48.7%
Atraccting international companies	3.120	3.286	2.7682	-5.1%
Specialized facillities (technology centers, auxiliary services centers, etc.)	3.060	2.123	2.0998	44.1%
Increase in average size of biotechnology companies	3.040	3.021	2.6708	0.6%
Cooperation with universities/IPOs and technology centers	3.040	2.462	2.1273	23.5%
Specialized suppliers (consultnts, lawyers, etc.)	3.040	2.165	2.1120	40.4%
Demand for more sophisticated products with higher value added	3.021	3.091	3.3197	-26.7%
Mergers/acquisitions/strategic alliances	2.922	3.339	2.8620	-12.5%
Information on the biotechnology market	2.900	2.123	2.1675	36.6%
Market-oriented nature of the public technology offering	2.804	2.310	2.3037	21.4%
Regulatory framework	2.375	0.749	0.2796	217.0%
Access to funding	2.327	1.356	1.0354	71.6%
Public administration	2.326	0.916	0.7540	154.0%
Time to profitability	2.277	2.041	2.1613	11.6%
Economic situation	2.146	2.968	2.2366	-27.7%
Cost of innovation	2.085	2.180	2.1771	-4.3%

Table 7.1. Rating for factors, average and % change.
Source: AseBio

The rating for talent in the sector (graph 7.8) has fluctuated over the past decade and dropped over the past year. The level of employee training, however, has always been rated above a 3 and, as we saw above, is the highest-rated factor on the 2019 survey.

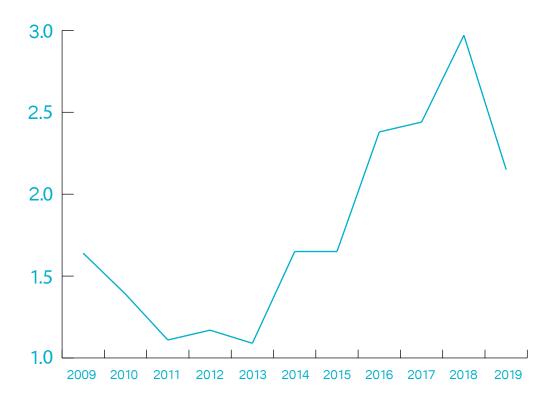
AseBio companies rated the number of bioentrepreneurs (graph 7.9) positively for the past ten years. In 2019, this rating improved substantially.

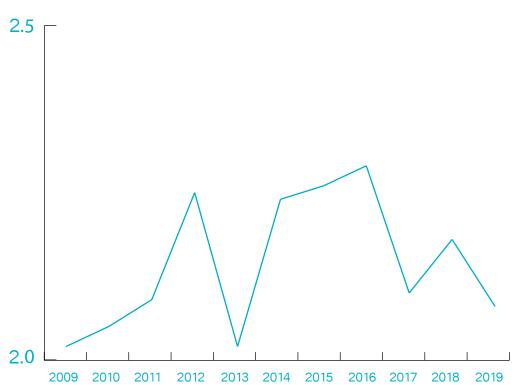


Graph 7.10. Evolution of economic situation and cost of innovation factors 2009-2019.

At the other end of the spectrum, we have the economic situation and the cost of innovation (graph 7.10). In both of these cases, the rating dropped from 2018, but the difference was more pronounced for the economic situation factor. Nevertheless, this rating isn't as low as it was in 2012, 2013 and 2014, when the economic crisis

that reached the sector somewhat later than the rest of the economy pushed it to its lowest levels. The rating for the cost of innovation has been negative over the past ten years and was also at its worst in 2013, probably for the same reasons.





Source: AseBio.

7.3. Regultory environment

The biotechnology sector has very high potential as a key tool for coming up with solutions to challenges like ageing, rare diseases, sustainable food and climate change. However, it is a highly regulated sector, which has a significant impact on costs and the time it takes to develop innovations. This is why it is essential to have an efficient, predictable regulatory environment that provides legal security for putting new technology and products into practice and, above all, is based on scientific criteria.

One of the changes in our regulatory environment in 2019 was the request from the Council of the European Union to the European Commission for a study to analyze the impact of the Court of Justice of the European Union ruling on new gene-editing techniques. This ruling was handed down in 2018, establishing that organisms obtained using new mutagenesis techniques (including CRISPR) are to be regarded as genetically modified organisms (GMOs) within the meaning of Directive 2001/18/EC. This decision endangered the work of researchers and innovators in the European biotechnology sector and threatened to stymie R&D with these promising techniques in Europe, as well as the positive impact they could have on European competitiveness and technological development. The new term of the Council has opened the door to reviewing this ruling and AseBio is already working on it.

To better understand how this ruling has impacted work in the Spanish biotechnology sector, AseBio surveyed its members in 2019 on the subject. The results of the survey show the negative impact it is having on lines of work that are offering solutions to wide-reaching challenges like sustainable food, plant breeding, climate change and health research.

Impact of Court of Justice of the European Union ruling on new gene-editing techniques on AseBio members

- 73% said it will have an impact on setting up new collaborations or contracts with companies. This ruling also makes Spanish companies uncertain and unsure about embarking on new projects outside of Europe, as the results may not be transferable to potential clients in Europe. Furthermore, they are afraid there will be a negative impact on investors' confidence in European companies.
- 88% say this ruling disincentivizes research and will have an impact on company development, forcing them to move their activity outside of the European Union.
- 97% believe that companies and research centers from other countries with regulations more favorable to these techniques will push forward in innovation compared to European companies and centers. This ruling would increase the technology gap, as countries in the European Union would have a technology lag that would put a damper on their international competitiveness and disincentivize research due to the unfair conditions on use of this type of technology.

_Spanish Association of Bioenterprises

BIOTECHNOLOGY, A DRIVING FORCE FOR THE POST-CORONAVIRUS ECONOMY

AMGEN®

Amgen, in 1980, was one of the first companies to recognize biotechnology's potential for developing treatments that would address the needs of patients with serious illnesses.

Four decades later, what began as a small start-up in California, has become one of the world's leading independent biotechnology companies. Part of our success lies in our values: applying the scientific method in our work, tenacity, ensuring quality, gaining the empathy of our socio-economic environment and making it our priority to make biotechnology advances available to society, are some of them.

The Covid-19 crisis has shined a spotlight on biotechnology, showing the crucial role it plays in saving lives. At the same time, we've witnessed how hard it is to find solutions to a crisis of this magnitude and how anticipation and applying genetics can be key in finding those solutions as quickly and effectively as possible.

The current situation is also an opportunity for biotechnology's other contributions to society and the economy to shine through. It is a source of economic stability, essential in these uncertain times; it provides quality employment based on meritocracy; it feeds and boosts a country's general research capacity; it is an essential partner for the national health system, as a driving force for innovation and clinical and translational research;

it facilitates new projects of value in health; and, now, it has proven to be an essential ally in Covid-19 research.

Despite the difficult times we are going through as a country, no one doubts the importance of strengthening our national health system, ensuring it remains based on equal access to healthcare and therapeutic innovation; consolidating its ability to adapt, which was tested and proven during this crisis, during which innovations like the digitalization of many processes have been implemented much more quickly and easily than we could have anticipated. So, strengthening the healthcare system requires several actions. There is no question, we firmly believe that one of the most necessary is the commitment to innovation, which is essential for ensuring the best treatments possible and, therefore, people's health, which is the most important, but also as an essential driving force for rebuilding the country.

To do so, we have to develop and support a holistic innovation strategy that covers all areas and levels of the system. This way, we will not only improve the quality of care, but also help create a critical mass of knowledge, attract talent and investment capital, encourage entrepreneurship and research capacity, the impact of which will go well beyond the national health system.

Improving healthcare is another point we have to strengthen with a multi-pronged approach. It is clearly a priority to support healthcare professionals and technology in the broadest sense to improve quality and equal access to healthcare. The progress of medicine, diagnostics (incorporating biomarkers), digital technology and data analysis is making it possible to take a personalized, targeted approach to healthcare. By making it faster and easier to incorporate this type of innovation into the system and through public-private partnerships, we will gain therapeutic and diagnostic capacity, get better health results, be more efficient and competitive compared to external benchmarks, and create a feedback loop between the R&D component of our national health system and the economy as a whole. Only through this commitment will we be able to make biotechnology develop in all its splendor and guide us, successfully, as the driving force for the economy, towards the "new reality".

> Fina Lladós, General Manager of Amgen for Spain and Portugal





Graph 8.1. Bibliometric overview of Spanish research in biotechnology, 2008-2018 Source: FECYT, from data using the SciVal-SCOPUS tool in

8.1. Production of scientific knowledge

Spanish biotechnology makes up 2.8% of global production in this area and is cited 31% more than the global average.

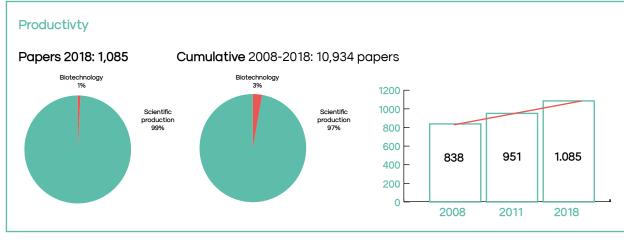
In 2018, scientific production in biotechnology made up 1.2% of all scientific production in Spain, with 1,085 papers, and 2.8% of global scientific production in this area (graph 8.1).

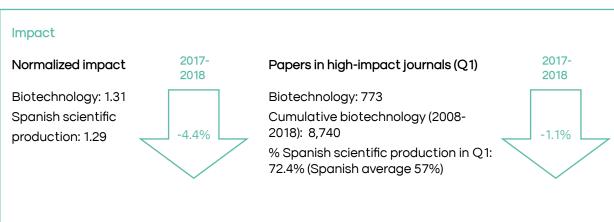
This same graph also shows the normalized impact of biotechnology scientific production in Spain, which was 1.31 in 2018. This means that Spanish scientific production in biotechnology is cited 31% more than the global average in this area.

In 2018, of the 1,085 scientific papers produced by Spanish institutions in biotechnology, 72% (773) were published in high-impact journals. This proportion has been notably higher than the Spanish average for the past decade.

Spanish biotechnology produces science of excellence, with 23% of

papers among the mostcited 10%. This percentage puts biotechnology clearly above the Spanish average for science in general.





May 2020

Excellence

Articles of scientific excellence (10%)

Biotechnology: 249

Cumulative biotechnology (2008-2018): 2,385

% Spanish scientific production in 22.9% (Spanish average 14.1%)



Spain has the highest percentage of scientific papers in biotechnology published in high-impact journals of any country, above countries like the United States and the United Kingdom.

Table 8.1 shows the main bibliometric indicators for the 10 countries that publish the most documents on biotechnology for the 2008-2018 period. China and the United States have the highest production in terms of number of documents in this area. The proportion of scientific production in biotechnology to general scientific production is the highest in India and South Korea. Spain, in addition to being ranked 9th in number of documents in biotechnology, is the country with the highest percentage of scientific papers in biotechnology in high-impact journals: 83.3%.

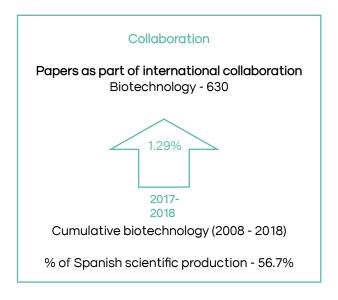
Ranking	anking Country Numbe docume		Number of documents in biotechno- logy	Scientific production in biotechnolo- gy as a per- centage of total scientific production	Normalized impact of biotechno- logy	Scientific production in biotechnolo- gy in high-im- pact journals (Q1) (%)	Scientific production in biotechnolo- gy of exce- llence (%)	Scientific production in biotechnolo- gy as part of international collaboration (%)
1	China	4,685,413	67,900	1.45%	1.09	56.2%	17.5%	22.2%
2	United States	6,006,558	66,206	1.10%	1.54	81.5%	24.3%	38.9%
3	India	1,195,076	32,349	2.71%	0.6	23.2%	8.3%	12.7%
4	Japan	1,364,395	22,232	1.63%	0.84	47.0%	9.5%	26.7%
5	Germany	1,614,431	20,704	1.28%	1.38	75.4%	22.1%	49.2%
6	South Korea	767,031	19,924	2.60%	0.9	40.5%	12.3%	24.3%
7	United Kingdom	1,706,362	16,178	0.95%	1.48	80.7%	24.1%	59.4%
8	France	1,135,087	11,083	0.98%	1.37	80.8%	21.2%	59.2%
9	Spain	834,238	10,935	1.31%	1.34	83.3%	21.8%	48.1%
10	Canada	961,654	10,248	1.07%	1.37	79.7%	21.0%	49.6%

Table 8.1. Top 10 countries in scientific production in biotechnology. 2008-2018.

International collaboration in Spanish scientific production in biotechnology has grown steadily in recent years.

The internationalization of Spanish science can be measured by looking at co-authorship of documents published jointly by Spanish institutions and institutions in another country. International collaboration in Spanish scientific production in biotechnology has grown steadily in recent years. The

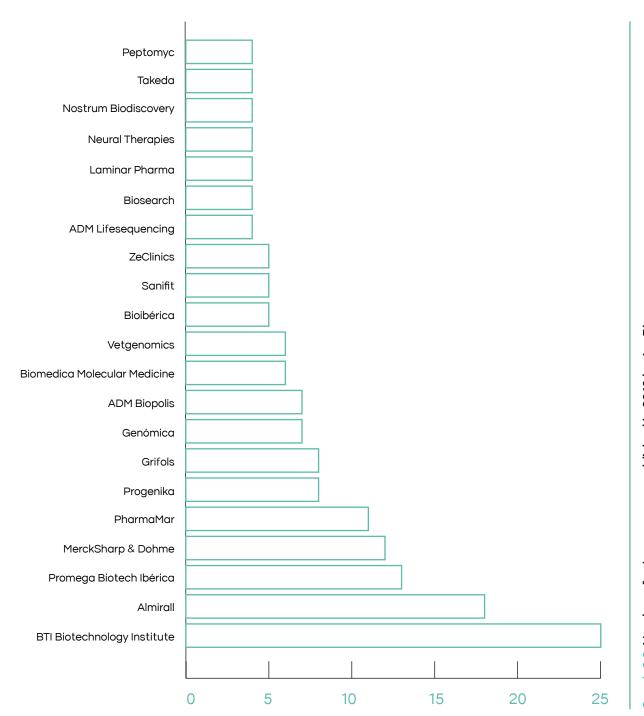
percentage of documents on biotechnology authored by Spanish and foreign institutions went from 38% in 2008 to 58% in 2018, with 630 documents. Over these ten years, the percentage of Spanish scientific production in biotechnology published as an international collaboration is above the Spanish average (graph 8.2).



Biotechnology companies increased scientific production efforts by 38%.

Every year, AseBio studies the publications in high-impact science journals authored by Spanish biotechnology companies and multinational corporations with offices in Spain that are AseBio members.

In 2019, biotechnology companies published 185 papers, which was 51 more than in 2018, up 38%. Among the companies with the most publications (graph 8.3), we find BTI Biotechnology Institute first with 25, followed by Almirall with 18, Promega Biotech with 13, MSD with 12 and PharmaMar with 11.



Graph 8.3. Number of science papers published in 2019 by AseBio member companies.
Source: AseBio.

SCIENCE FOR A BETTER FUTURE



BTI Biotechnology Institute, five years leading scientific production in biotechnology in Spain.

We are experiencing one of the most complex healthcare and socioeconomic situations of our time. Like in any crisis, new problems arise, but there are also new opportunities and I believe now is the right time to start designing a better future.

The first lesson we have to learn to design that future is that there is no better investment for a society than science and education. It's true that the return on investment in science isn't immediate, in fact it normally takes years to see the fruit of research. This leads many leaders, stuck in their short-term vision, to not make science a priority.

It is clear, however, that it will be science (and biotechnology and biomedicine in particular) that will show us the path and bring us solutions to this pandemic and many other issues we will have to face in the future. Once this crisis is over, then, society should demand that its leaders encourage investment in science and consideration for scientists, including them in decision-making.

Business investment in science is called R&D. R&D is a company's commitment to the future, its way of anticipating the present and preparing for market changes to come. So, R&D investment can be decisive in the survival of many companies when there are abrupt changes in the markets because it is a tool for improving production processes and adapting to offer new services or manufacture new products.

A species' key to survival is its ability to adapt to its environment. Likewise, in the business ecosystem we know that adapting to the market is key to survival. R&D is the driving force for that evolution, that ability to adapt, so a lesson for the future (meaning the present) is that companies should concentrate more on it and governments should pay more attention to companies and innovative projects. When we founded BTI more than 20 years ago, we knew that the company's main goal had to be generating scientific knowledge and developing new treatments to improve patients' quality of life. So, from the beginning, we have been committed to R&D.

The fact that a company with the size and nature of BTI has

been leading scientific production in biotechnology in Spain for the past five years shows that our commitment to R&D is as valid as ever, renewed year after year. The fact that these efforts are reflected in the Report that AseBio puts together wastrum each year is a huge incentive eduards for us to continue researching and the and developing new advances in biomedicine. We know this commitment to science is the way to find solutions to existing and forthcoming problems, and that this way we will help improve quality of life for many, many people. This will undoubtedly be our greatest reward.

> Dr. Eduardo Anitua, Scientific Director of BTI Biotechnology Institute

8.2. Technological innovation

The biotechnology sector is patenting more and more in international arenas.

We have counted 513 patent applications and 241 patents granted in Spain in 2019. Patents with a Spanish priority claim or stakeholder in the biotechnology sector were identified through the

various patent offices (OPEM, EPO, USPTO, JPO and WIPO).

As has happened since 2013, the 2019 data again shows that the sector continues choosing to protect its innovation mainly through the European Patent Office and with international PCT patents (table 8.2).

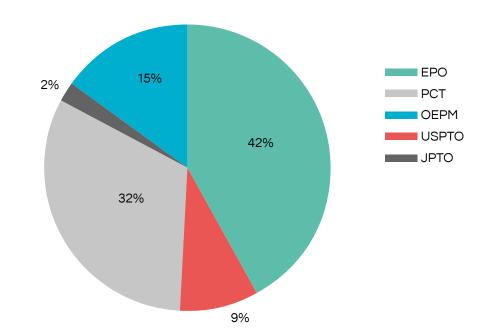
Patents issued 2019*	OEPM	EPO	USPTO	JPTO	PCT	TOTAL
Applications	79	214	45	11	164	513
Granted	63	131	36	11	(NA)	241
TOTAL	142	345	81	22	164	754

Table 8.2. Number of patent applications and patents granted to Spanish biotechnology organizations (2019).

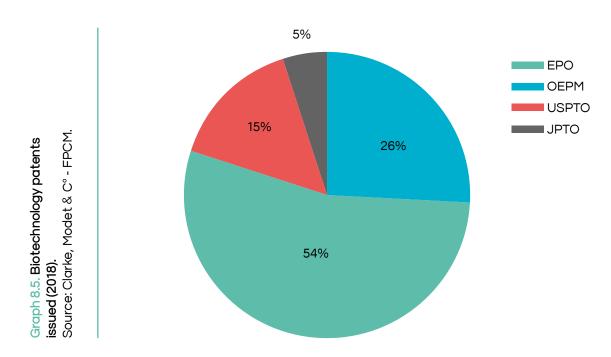
The majority of the sector has chosen to protect innovations on a European level, with 214 patents, while only 79 patents were issued through the Spanish Patent and Trademark Office.

Graph 8.4 shows that the highest percentage of patent applications in the biotechnology sector were filed with the European Patent Office, 42%, followed by 32% through international PCT patents and 15% through the Spanish Patent and Trademark Office.



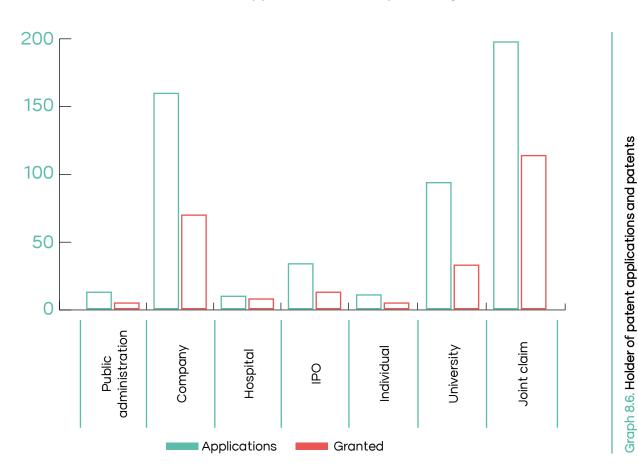


The patents granted (graph 8.5) follow the same trend as the applications. 54% of patents were issued by the European Patent Office, 26% by the Spanish Patent and Trademark Office, 15% by the United States Patent and Trademark Office and 5% by the Japan Patent Office.



The biotechnology sector continues to patent in collaboration, with nearly 200 joint patent applications.

Joint ownership (with 197 applications and 113 patents issued) continues to be the main pathway to protecting innovation, highlighting the relevance of collaboration on R&D development involving several types of organizations (graph 8.6). Companies are ranked second as the main claimants, with 159 applications and 69 patents granted.



The evolution of industrial property since 2009 shows an increase in European and international patents alongside a decrease in patents through the Spanish Patent and Trademark Office.

Over the past decade, applications to the Spanish Patent and Trademark Office have dropped drastically. This is due not only to a general preference for patenting on an international level, but also regulatory changes brought in through the Spanish Patent Law of 2017,

which could have had a direct impact on the biotech sector as it introduced a compulsory examination of novelty and inventive activity that made it more difficult to get patents that do not meet those requirements.

Comparing European patents registered in 2009 with those 10 years later, there has been a considerable increase, with six times more patents registered with the European Patent Office.
This increase has also been seen in international patent

applications under the Patent Cooperation Treaty (PCT). While only 65 were registered 10 years ago, in 2019 there were 154.

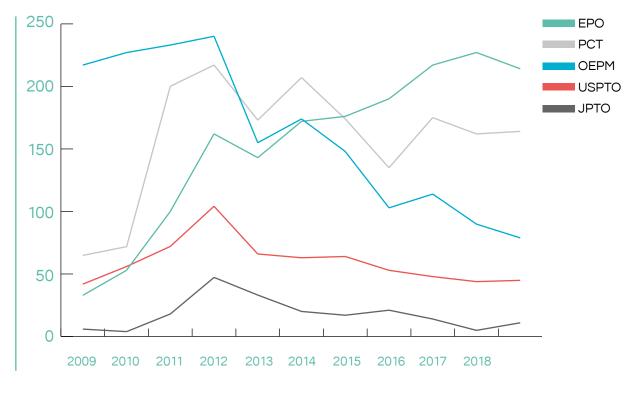
Protection through the Spanish Patent and Trademark Office dropped again, from 217 applications in 2009 to just 79 in 2019, down 64%.

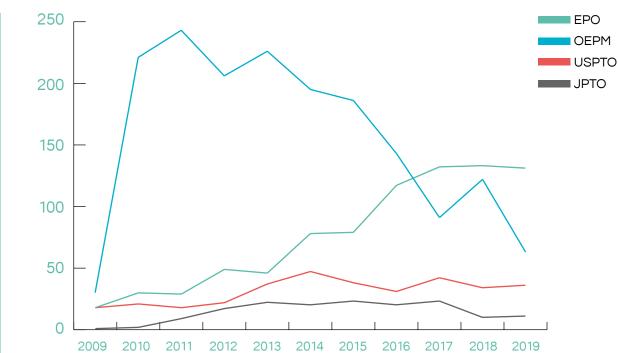


Graph 8.8. Trend of patents granted

Source: Clarke, Modet & C° – FPCM.

(2009-2019).





In collaboration with





THE TRANSFORMATIVE CAPACITY OF BIOTECHNOLOGY



Ingenasa

For over two decades, the biotechnology sector has developed innovative solutions that have helped protect us from healthcare crises like the one we are currently experiencing, but also to tackle challenges like the ageing population and infectious diseases in humans and animals, sustainable food and the climate emergency. Now, however, is when all the cumulative knowledge and hard work of these past years are bearing fruit.

The SARS-CoV-2 healthcare emergency has highlighted the value of the biotech sector's great agility and versatility, as it has been able to refocus its capacities quickly to address this crisis with solutions that cover the whole cycle of the virus, ranging from vaccines to antiviral treatments and diagnostic methods.

Eurofins Ingenasa is a Spanish company that has spent over 35 years developing diagnostic tests for infectious diseases in animals. Today, however, it is not only working in animal health but has pivoted the majority of its resources and knowledge to benefit public health, offering diagnostic solutions for SARS-CoV-2, like PCR tests, ELISA assays and the first quick

antibody test developed wholly by a Spanish company.

Its prior experience in detecting diseases caused by viruses, which affect a high percentage of the animal population, has been key in Eurofins Ingenasa's reaction, adapting its technology quickly to the emerging situation. This is why the company has been able to apply biotechnology techniques like genetic engineering to develop one of the most specific, accurate antibody tests on the market and will be able to ensure there are tests available if there is a new outbreak.

Public health has become the focus of many biotech companies, which faced with the Covid-19 healthcare emergency, have pivoted their efforts to find a quick, effective solution, understanding that only having as much information as possible now will we be able to offer the best response in the future. It is precisely this transversal nature that gives our sector its great ability to transform.

This cannot be explained, however, without years of research and innovation to understand the molecular foundations of genetic

engineering and recombinant proteins, or without years of investment in R&D to come up with effective biotechnology drugs to treat Covid-19 and other conditions like Ebola, cancer, arthritis, hepatitis C and HIV. The knowledge and experience of the biotechnology sector and the hard work put in over decades of research are the foundation that has allowed us to respond to this pandemic. It is time to give our science and innovation system a new push and align it with the challenges we are now facing in order to build a better future.

_Spanish Association of Bioenterprises

8.3. Product launches

In 2019, we identified 60 new products or services launched to market by AseBio members. Here is a list of the products and services launched to market and some of the most noteworthy deals to license or distribute these products and services.

Licensing and distribution deals

Algenex signed a deal with Argentinian company Bioinnovo for the rights to use the Algenex APCH molecule for animal health.

The Foundation for Biomedical Research of the Ramón y Cajal University Hospital and Aptus Biotech reached a licensing deal for an aptamer to treat breast cancer.

For its part, Palobiofarma closed a licensing deal with royalties for six products from the US Xoma Corporation.

PharmaMar reached an exclusive licensing deal for lurbinectedin in the US.

A with Irish company Jazz Pharmaceuticals and with Chinese company Luye Pharma in China.

Genomica signed a deal with Chinese firm HuaSin to commercialize its HPV diagnostic kit.

Histocell continued distributing its product Reoxcare in Europe through ALLWECARE (Netherlands), APOFIT (Germany), BTC Health (Australia) and P3Medical (United Kingdom).

Merck reached a deal with Elypta to commercialize liquid biopsy tests in Sweden.

OWL with Laboratorios Rubió agreed to commercialize the OWLiver test in Spain and Latin America.

PharmaMar continued closing deals to commercialize Yondelis in various countries, with Megapharm (Israel), Specialised Therapeutics Asia (Singapore), Janssen and J&J (USA), regaining the rights to Yondelis everywhere in the world except the United States.

Plant Response Biotech reached an exclusive licensing deal with the University of Tübingen in Germany for technology that boosts plants' innate immunity to fungicidal infections.

For its part, AlgaEnergy reached a deal with Krishi Rasayan Group to manufacture and sell agriculture products in India, among others.

ArtinVet Innovative Therapies closed deals with Dutch company Phytotreat and Irish company Novavet for distribution of its Vexoderm line of products in those two countries.

In 2019, we identified 60 new products or services launched to market by AseBio members, down 26 from 2018.

Table 8.3 shows the full list of all the products and services, along with the indication for each one, and 8.9 shows the breakdown by areas of activity.

Organization	Name of product/ service	Indication of product/service
Abbvie	ToucHS	Digital platform for clinical assessment of patients with hidradenitis suppurativa.
ABT Agarose Bead Technologies	Protein G Affinity Car- tridges (ready-to-use 5ml format)	Isolation and purification of antibodies from cell culture media and biological fluids.
ADM Biopolis	Microbiot Fit	Nutritional supplement containing B. lactis BPL1.
ADM Biopolis	Probiolog	Nutritional supplement containing Atopic Dermatitis blend.
ADM Biopolis	Skinesa	Nutritional supplement containing Atopic Dermatitis and Psoriasis blend.
ADM Biopolis	Bi1 Bificare	Medical nutrition product containing B. lactis BPL1.
ADM Biopolis	Central Lechera Asturiana con Bifidus	Fresh milk containing B. lactis BPL1.
Agrocode Bioscience	Technology Priming	Formulations to improve plants' resistance to adverse conditions.
AlgaEnergy	PLANKTON7®	Active ingredient for the cosmetic industry, based on 7 different species of microalgae.
Almirall	Digital Garden	Digital platform to promote innovation in dermatology.
Almirall	Seysara	Seysara™ (sarecycline): new oral antibiotic to treat acne in USA.
Amslab	Organic cotton verification test	Test that detects genetically modified cotton in final products labelled as organic cotton.
Bayer Cropscience	Pure biologicals	Plant protection products that combat pests without affecting other fauna.
Best Medical Deit	Zero Allergen	Allergy-free line of foods.
Biochemize	D-panose from micro- bial fermentation	Non-carcinogenic trisaccharide sweetener with probiotic properties to encourage growth of intestinal flora and inhibit growth of E coli and Salmonella.
Biochemize	Cis-hexenol obtained through biocatalysis from linseed.	Molecule highly in demand in the aromas, cosmetics and food sector.

Biochemize	Chymosins from cows and camels expressed in fungal and bacterial strains.	Enzymes from cows and camels to produce dairy products.
Biochemize	Microbial extracts from sea water.	Extracts with high hygroscopicity and UV filtration, chelating agents and healing properties.
Bioibérica	Klorexivet®	Spray formula to help pet wounds heal.
Bioibérica	Prolivet®	Promoting proper liver function in dogs and cats.
Bioibérica	Active ingredient thyroids.	Active ingredient from natural sources to treat hypothyroidism.
BIOLAN	BIOFOOD SUL	Biosensor to measure sulfites in dried fruit.
Biomedal	GlutenDetect App	App for a gluten-free diet.
Bionos Biotech	Bio3D Structures-Light Scanner	High-resolution assessment of skin surface.
Bionos Biotech	Bio Blue Light Scanner	In vivo assessment of efficacy of cosmetics using blue light.
Biorizon Biotech	Photopower	Formulation to boost photosynthesis.
Biorizon Biotech	Absolut-T	New bioprotector.
	Hereditum® IMMUN-	Probiotic supplement that improves immune response, protects against future infections and
BiosearcH	ACTIV K8	reduces the symptoms associated with respiratory infections in seniors.
BiosearcH Biosearch	ACTIV K8 Hereditum® BfM26	, ,
		infections in seniors.
Biosearch	Hereditum® BfM26	infections in seniors. Probiotic supplement for colic in infants. Natural source of omega-3 with high DHA content,
Biosearch	Hereditum® BfM26 Eupoly-3® Algae	infections in seniors. Probiotic supplement for colic in infants. Natural source of omega-3 with high DHA content, not from animal sources, vegan. Combination of extracts to support healthy production of breast milk in cases with perceived
Biosearch Biosearch	Hereditum® BfM26 Eupoly-3® Algae Voluntas®	infections in seniors. Probiotic supplement for colic in infants. Natural source of omega-3 with high DHA content, not from animal sources, vegan. Combination of extracts to support healthy production of breast milk in cases with perceived insufficiency. Uncaria tomentosa extract optimally standardized with scientific support to be used as an
Biosearch Biosearch Biosearch Biosearch	Hereditum® BfM26 Eupoly-3® Algae Voluntas® Optum®	infections in seniors. Probiotic supplement for colic in infants. Natural source of omega-3 with high DHA content, not from animal sources, vegan. Combination of extracts to support healthy production of breast milk in cases with perceived insufficiency. Uncaria tomentosa extract optimally standardized with scientific support to be used as an immunostimulant.
Biosearch Biosearch Biosearch Biosearch	Hereditum® BfM26 Eupoly-3® Algae Voluntas® Optum® Exxentia® Kids	infections in seniors. Probiotic supplement for colic in infants. Natural source of omega-3 with high DHA content, not from animal sources, vegan. Combination of extracts to support healthy production of breast milk in cases with perceived insufficiency. Uncaria tomentosa extract optimally standardized with scientific support to be used as an immunostimulant. Standardized extracts without ethanol for kids. Damiana extract standardized to 0.05% acacetin for female sexual dysfunction associated with
Biosearch Biosearch Biosearch Biosearch Biosearch Biosearch	Hereditum® BfM26 Eupoly-3® Algae Voluntas® Optum® Exxentia® Kids Damilib®	Infections in seniors. Probiotic supplement for colic in infants. Natural source of omega-3 with high DHA content, not from animal sources, vegan. Combination of extracts to support healthy production of breast milk in cases with perceived insufficiency. Uncaria tomentosa extract optimally standardized with scientific support to be used as an immunostimulant. Standardized extracts without ethanol for kids. Damiana extract standardized to 0.05% acacetin for female sexual dysfunction associated with diminished sexual desire. Blend of natural inositols, indicated to improve

Grifols	AlphaID™	Oral test to detect alpha-1 antitrypsin deficiency.
Grifols	QNext® y DG®-PT	Automatic coagulometer with hemostasis reagent.
Grifols	Procleix® Babesia	Blood test to detect the Babesia parasite.
GSK	Pediatric Nucala	Biologic treatment for serious asthma in pediatric patients.
GSK	Zejula	PARP1 and PARP2 polymerase inhibitor (poly ADP-ribose polymerase) for women with recurring platinum-responsive ovarian cancer.
Immunostep	Exosomes	Detecting specific, unequivocal exosomes.
Immunostep	Immunobead assay for fusion proteins	The kit is a simple flow cytometric immunobead assay to detect BCR-AB fusion proteins in cell lysates.
Ingenasa	Ingezim TB CROM	Quick tuberculosis diagnosis using immunochromatography in various animal species (wild fauna).
Ingenasa	IngeCHIP Alergias Ca- ninas FOOD	Diagnostic technique based on protein arrays to determine sensitivity to multiple food-allergen extracts in dogs.
NorayBio	AniBio Web Based	Launch of web-based AniBio platform (software to manage animal facilities).
Pevesa	OryzaPro V80	Rice protein concentrate 80% for extrusion applications.
Promega Biotech Ibérica	Glycerol-Glo™ Assay	Bioluminescent assay to measure glycerol in a variety of biological samples, including cells grown in monolayer or 3D structures, cell culture medium, tissues and serum samples.
Promega Biotech Ibérica	Triglyceride-Glo™ Assay	Bioluminescent assay to measure triglycerides in cell lysates and other biological samples, such as cell culture medium, serum and tissue homogenates.
Promega Biotech Ibérica	Cholesterol/Cholesterol Ester-Glo™ Assay	Bioluminescent assay to measure cholesterol and cholesterol esters in cell lysates and other biological samples, such as lipoprotein fractions, cell culture medium, serum and tissue homogenates.
Promega Biotech Ibérica	Water-Glo™ Microbial Water Testing Kit	Assay to detect microbial contamination by measuring ATP produced by live microbes in real time.
Reig Jofre	Hialsorb® Intraarticular	Hyaluronic acid injection to treat degenerative or mechanical arthritis.
Reig Jofre	Articolageno® Nativo Plus	Dietary supplement based on native type II collagen, hyaluronic acid, turmeric and vitamin C to protect joints.
VIVEbiotech	GMP-grade lentiviral vectors manufactured with PEIpro® as the transfection reagent.	Lentiviral vectors for clinical trials on gene therapy in humans.

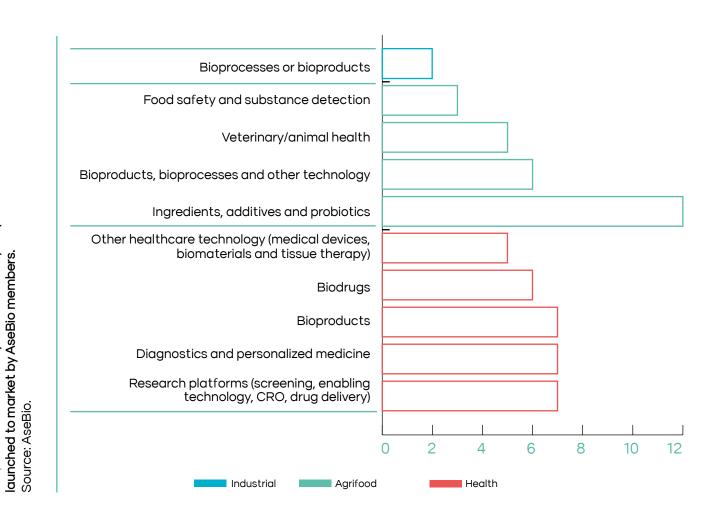
Grifols

XEMBIFY®.

Immune globulin with subcutaneous administration

to treat immunodeficiencies.

ZeClinics	ZeOncoTest	Xenograft model in zebrafish larvae to identify new tumor drugs.
ZeClinics	Macular degeneration trial	AMD model in adult zebrafish to test therapeutic drugs.
ZeClinics	Advance TeraTOX	Teratogen screening trial using zebrafish larvae.
ZeClinics	ZeEDC	Trial to assess the endocrine disruption potential of chemicals.
Zendal	B19 CZV Ocular	Vaccine to treat brucellosis.



8.4. Attracting international companies

Europe and Latin America make up 70% of all international presence of AseBio member companies.

35 AseBio members, four fewer than in 2018, are present in 43 markets on all continents. The total number of subsidiaries is 136 (12 fewer than the previous year). The list is led by the United States, with 22 member subsidiaries, followed by Italy with 9 and Portugal and Germany with 8 each.

The geographic breakdown has remained practically the same in the past two years. Europe holds the greatest weight, with 46% of the total, followed by Latin America, with 23%. Furthermore, as we saw the previous year and as a result of Brexit, the number of companies present in the United Kingdom dropped again.

Europe 46% Latin America 23% USA/Canada 18% Asia/Oceania 12% Africa 1%

Table 8.4 shows where our Spanish companies are present by country and the number of subsidiaries in each market, while table 8.5 is a list of AseBio members with the countries where they have a direct presence.

Country	Number of subsidiaries
USA	22
Italy	9
Germany	8
Portugal	8
Mxico	7
Belgium	6
Brazil	6
United Kingdom	6
France	5
Chile	4

China	4
Argentina	3
Austria	3
Colombia	3
Poland	3
Sweden	3
Switzerland	3
Canada	2
Denmark	2
Ecuador	2

Greece 2 Guatemala 1 India 2 Netherlands 1 Japan 2 Indonesia 1 Peru 2 Kazakhstan 1 Singapore 1 Malaysia 1 Saudi Arabia 1 Morocco 1 Australia 1 Monaco 1 Bolivia 1 Nicaragua 1 Costa Rica 1 Norway 1 El Salvador 1 Thailand 1 United Arab Emirates 1 Turkey 1				
Japan2Indonesia1Peru2Kazakhstan1Singapore1Malaysia1Saudi Arabia1Morocco1Australia1Monaco1Bolivia1Nicaragua1Costa Rica1Norway1El Salvador1Thailand1	Greece	2	Guatemala	1
Peru 2 Kazakhstan 1 Singapore 1 Malaysia 1 Saudi Arabia 1 Morocco 1 Australia 1 Monaco 1 Bolivia 1 Nicaragua 1 Costa Rica 1 Norway 1 El Salvador 1 Thailand 1	India	2	Netherlands	1
Singapore1Malaysia1Saudi Arabia1Morocco1Australia1Monaco1Bolivia1Nicaragua1Costa Rica1Norway1El Salvador1Thailand1	Japan	2	Indonesia	1
Saudi Arabia1Morocco1Australia1Monaco1Bolivia1Nicaragua1Costa Rica1Norway1El Salvador1Thailand1	Peru	2	Kazakhstan	1
Australia 1 Monaco 1 Bolivia 1 Nicaragua 1 Costa Rica 1 Norway 1 El Salvador 1 Thailand 1	Singapore	1	Malaysia	1
Bolivia1Nicaragua1Costa Rica1Norway1El Salvador1Thailand1	Saudi Arabia	1	Morocco	1
Costa Rica 1 Norway 1 El Salvador 1 Thailand 1	Australia	1	Monaco	1
El Salvador 1 Thailand 1	Bolivia	1	Nicaragua	1
	Costa Rica	1	Norway	1
United Arab Emirates 1 Turkey 1	El Salvador	1	Thailand	1
	United Arab Emirates	1	Turkey	1
Finland 1	Finland	1		

Company	Countries
Agarose Beads Technologies	USA
Agrocode	Brazil, China, USA, Peru
AlgaEnergy	USA., India, Italy, Japan, Mexico, Turkey
Almirall	Germany, Austria, Belgium, Denmark, USA, Netherlands, Italy, Poland, Portugal, United Kingdom, Switzerland
AMS Lab	Italy, Morocco, Portugal
Antares Consulting	Belgium, Bolivia, Chile, France, Portugal
Asphalion	Germany, United Kingdom
Biobide	USA
Bioibérica	Germany, Brazil, USA, Italy, Poland
Biolan	Chile, Ecuador, Indonesia, Mexico
BTI Biotecnology Institute	Germany, USA, Italy, Mexico, Portugal, United Kingdom

Elzaburu	China
Ferrer	Germany, Argentina, Belgium, Brazil, Colombia, Costa Rica, Chile Ecuador, El Salvador, USA, France, Guatemala, Greece, Italy, Kazakhstan, Mexico, Nicaragua, Peru, Portugal
Genómica	Brazil, China, Sweden
Grifols	Germany, Saudi Arabia, Argentina, Australia, Austria, Brazil, Canada, Chile, China, Colombia, Denmark, USA., United Arab Emirates, Finland, France, India, Italy, Japan, Malaysia, Mexico, Norway, Poland, Portugal, United Kingdom, Singapore, Sweden Switzerland, Thailand
Inveready	USA
Laminar Pharma	USA
Leti	Germany, Portugal
Life Length	USA
Mabxcience	Argentina, Switzerland
Minorys Therapeutics	Belgium
Natac Biotech	USA
Neurofix	USA
Nimgenetics	Brazil, Mexico
Noray Bio	France, Italy
Oncoheroes	USA
One Way Liver	USA
Oryzon	USA
PharmaMar	Germany, Austria, Belgium, USA, France, Italy
Reig Jofré	Belgium, USA, Monaco, Portugal, United Kingdom, Singapore
Sanifit	USA
Sermes CRO	USA
SILO	Colombia
Sistemas Genómicos	Canada, Mexico
Som Biotech	USA



BIONET, as a technology company in the bioprocesses sector, has the skills and motivation to accompany the bioprocess and bioprocessors throughout the project. Providing them with the technology needed to develop bioprocesses from lab to industry, as well as filling in any knowledge and support gaps that may arise along the way.

The path of a bioprocess

What is the first thing a bioprocessor needs once they are sure of the strain or cell line selected? A laboratory bioreactor where they can continue optimizing and analyzing the process. If the right productivity is achieved, the bioprocess continues growing in bioreactor volume until it reaches industrial scale.

At the same time, although it is often left to the end, bioprocessors need to see how to isolate and purify the product they are working on, which they've produced with their bioreactor. They need downstream technology (which is often tangential flow filtration) to get a product that can be processed for storage and use. Before and during the process of selecting technology there are many questions upstream and downstream experts will have to ask during the R&D scale-up phases.

"What process parameters do I need to control in the bioreactor and TFF to optimize productivity and what technology options are available for this?"

"What operating modes or strategies could give me better yield?"

"Which downstream technology is right?"

"What variables do I have to take into account in the scale-up?"

"What additional technology will we need for efficient workflow during production?"

In short, on this path bioprocesses companies not only need suppliers that can design the right technology on several scales, but also collaborators that offer adaptability and support for scientific engineers.

We'll explain how BIONET resolves this below.

Line of bioreactors (lab, pilot and industrial) and bioprocesses software

Bioprocesses are born in the lab and we are there for their first steps, from the

flask shaken in the bioreactor, where we are one of the leading suppliers designing and building laboratory bioreactors in the world. We play this role of supplying bioreactors through to the industrial scale, with bioreactors of up to 20,000 liters. Our line of bioreactors stands out for our commitment to plug&play technology and software development. The plug&play technology allows the bioreactor's set-up to grow as the R&D process advances and so do its functions. This means that many of them can be acquired in the future as modules or external IoT that will be recognized automatically by the software platforms (ROSITA and MARTA).

Plus, given their ease of use and advanced automation, viewing and datacapture tools, ROSITA and MARTA can easily become the bioprocessor's best friend, as they can even be controlled remotely.

Line of tangential flow filtration systems (lab, pilot and industrial)

BIONET also specializes in purification and concentration using tangential flow filtration systems (biomass and/or biomolecules). For labs, our M1 stands out for its flexibility and scalability, as it can be used with cassettes, hollow fiber or ceramic membranes. On an industrial level, we've designed unique systems with, for example, comprehensive sterilization.

Pilot plant services

All the technology options (PATs, actuators, types of membranes, etc.) and process strategies (fed-batch, continuous, perfusion, etc.) can be overwhelming. BIONET has a pilot plant managed by PhDs who specialize in upstream and downstream for:

- Proof of concept for processes looking to scale up.
- Testing to select the right technology. Support for process optimization.

Free knowledge

Supporting clients and their bioprocesses is at the heart of our business. One example is our online Knowledge Hub, which has different types of resources, from practical guides and recommendations to demonstrations of the technology, webinars on topics of interest and interactive contests.

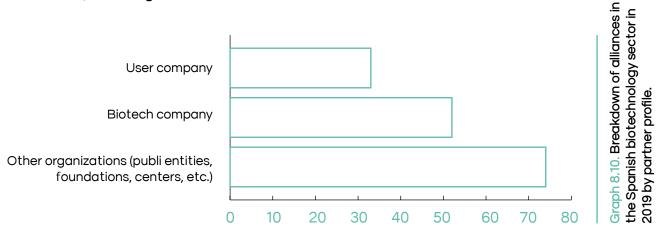
Engineering services

Digging into the process and how it interacts with the engineering at various spots along the path takes collaboration from different profiles with different types of knowledge. BIONET has the multidisciplinary team and tools needed to help, through our engineering consultancy services, establish the right technology and workflows on an industrial level.

8.5. Alliances: 68% of all alliances are forged with international partners

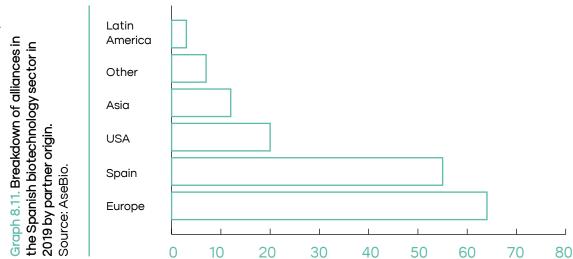
In 2019, a total of 155 alliances were identified (22% fewer than in 2018), just over half of which (74 - graph 8.10) involved an organization from the public sector, a foundation or technology center, 52 were established with another biotechnology company and 33 with a company that uses biotechnology.

These are the business development activities of AseBio members, meaning the alliances and/or collaborations in biotechnology, such as comarketing, co-development and product and market exchanges, started in 2019 with other entities. In addition to the total number of agreements, the analysis includes the type of organization, country of origin for entities the sector forges alliances with and the goal of those alliances.

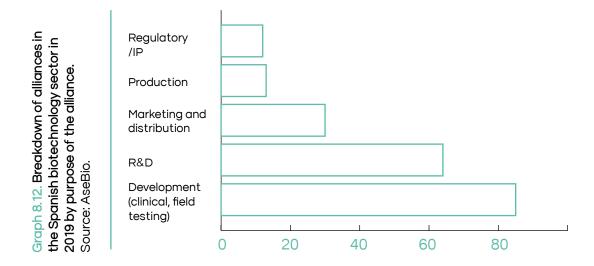


64 of these alliances involved another European body (graph 8.11), 55 with a Spanish organization, 20 with one from the United States and 3 with partners from Asia.

If we only analyze these alliances in the international arena, 68% included at least one non-Spanish organization. This highlights the importance of forging agreements with partners from other countries in the Spanish biotechnology sector.



Graph 8.12 shows that 85 of the alliances were aimed at clinical development or field trials, 64 on the preliminary phase, R&D; and 30 of these alliances were for marketing or distribution purposes. 13 of the deals were about production and 12 were concerning regulatory or industrial protection issues.



MSD: COLLABORATION AND KEY ALLIANCES TO ADVANCE IN RESEARCH



2020 hasn't been just another year. We've experienced the worst healthcare crisis in generations and, in this context, it is important to make a few reflections.

First of all, all of the countries affected by Covid-19 are inevitably facing a difficult recovery. To advance in this journey, both in terms of economic recovery and response to future health threats like this one. the biopharmaceutical industry is an important ally. The European Federation of Pharmaceutical Industries and Associations (Efpia), which MSD belongs to through Farmaindustria, has offered the European Union its full support from the very beginning in order to pull through this pandemic together. Because this healthcare crisis has highlighted, more than ever, the importance of getting all the stakeholders involved, and specifically of public-private partnerships, to tackle challenges of this magnitude. If we are able to learn this lesson, we'll come out of this even stronger.

Both healthcare professionals, on the front lines in fighting the novel coronavirus, and the biopharmaceutical industry have made huge efforts in record time. Having these sectors join forces, and work with healthcare authorities, is key to advancing. Clinical trials are one of the clearest examples of the significance of collaborations among laboratories, professionals, administrations and patients themselves. All eyes are on these trials now, given the importance of coming up with therapeutic tools to fight the pandemic.

Clinical trials not only generate highquality knowledge and are the first step towards new treatments and vaccines, the scientific advances they bring about benefit society as a whole, as has been seen with Covid-19. At MSD, we are firmly committed to this line of research. Our company spent \$9.9 billion on R&D projects last year, making us leaders in number of clinical trials. In Spain, we participated in 118 trials in phases I, II and III.

Another of the reflections this crisis has led us to is that it is equally important to take steps forward in research as it is for them to be solid and firm. We all want to do away with SARS-CoV-2 and other threats that may come along. But prudence and scientific rigor must always guide us in our search for solutions. So, from the beginning of the crisis, MSD has been working discreetly yet tirelessly in this line. We've even been able to announce three important alliances.

These are two agreements to develop SARS-CoV-2 vaccines and one collaboration to develop an antiviral drug. Specifically, MSD acquired Themis Bioscience, a company that focuses on vaccines and immunomodulatory therapies for infectious diseases,

including Covid-19. Additionally, IAVI (International AIDS Vaccine Initiative) and MSD will be collaborating to develop a vaccine for SARS-CoV-2. And, finally, MSD and Ridgeback Bio will be working together to advance development of an oral antiviral candidate for Covid-19, EIDD-2801.

Through these three clearly promising projects, we hope to help get us closer to the end of this hard road we are all on together.

_Spanish_Association of Bioenterprises

8.6. Advances in development

The Spanish biotechnology sector has made advances over the past year in biohealth, agrifood and industrial fields. Many of these advances have been thanks to deals with other organizations to continue research, which is why we would like to highlight some of these agreements.

BIOHEALTH

Research agreements

Algenex signed a deal with FATRO to develop a second vaccine based on CrisBio.

Bioncotech Therapeutics closed a collaboration deal for a phase II clinical trial with MSD.

Genetracer Biotech, through an R&D project, kicked off a project with IBM and several universities to develop a new artificial intelligence tool for early detection of breast and pancreatic cancer.

GSK, with the University of Granada, kicked off development of research projects on isolating circulating pulmonary cells in patients with chronic obstructive pulmonary disease (COPD), which will allow for diagnosis using a blood test.

Nostrum Biodiscovery established collaborations with IRB Barcelona, University of Santiago de Compostela and Vall d'Hebron to develop new drugs for ischemia, to treat diseases of the central nervous system and to alleviate the progression of Parkinson's and dermatological disorders.

QualitecFarma established a collaboration with Prestige Biopharma of Singapore to carry out a phase III clinical trial for the Asian pharmaceutical corporation to treat breast cancer.

VIVEbiotech established an agreement with Germany firm PAN-Biotech to set up the production process for lentivirus without serum from animals.

ZeClinics signed an agreement with Taros Chemicals GmbH (Germany) to develop new therapies to treat cardiac ischemia.

Algenex agreed with Global DX Ltd. to develop and commercialize diagnostic products to detect African swine fever virus.

Regulatory authorizations

Ability Pharmaceuticals gained approval in China for a clinical study on ABTL0812 for pancreatic cancer.

Aurora Medicine was granted initial approval for a medicinal cannabis product in Ireland.

Oryzon Genomics received FDA approval for an IND (Investigational New Drug Application) for ETHERAL, a phase IIa clinical trial with epigenetic drug vafidemstat in patients with mild or moderate cases of Alzheimer's.

Osasen was granted a preliminary operating license for medical devices and disinfectant establishments by the AEMPS.

Reig Jofre and Ojer Pharma were granted the first European authorization to commercialize their Impetine Gel antibiotic.

VCN Bioscience gained regulatory approval for a phase I trial with its product VCN-01 with Durvalumab (MEDI4736).

Derma Innovate patented a new device to promote cutaneous and capillary regeneration and VIVEbiotech for its LENTISOMA technology.

Advances in studies

Biohope announced it has completed its TRANSBIO clinical trial showing that IMMUNOBIOGRAM® allows doctors to personalize immunosuppressive therapy in kidney-transplant patients.

Bionure concluded the phase I clinical trial on BN201 for neurodegenerative diseases like multiple sclerosis.

Sanifit announced that the CaLIPSO phase IIb trial on SNF472 met its main goal of delaying progression of cardiovascular calcification in hemodialysis patients.

Minoryx Therapeutics completed enrollment in the FRAMES phase II trial on leriglitazone for Friedreich's ataxia.

PharmaMar announced it has reached the goal of its phase I study with the lurbinectedin monotherapy for small-cell lung cancer.

Takeda announced that the Ministry of Health will fund Alofisel, the first allogeneic cell therapy developed and manufactured wholly in Spain.

Aptatargets began its ApTOLL-FIH-01 clinical trial in humans to assess tolerance to and pharmacokinetics of ApTOLL for acute treatment of strokes.

Bioiberica began a clinical trial to verify the effect of Impromune® in dogs with leishmaniasis that receive standard treatment.

Palobiofarma began clinical development of PBF-1650, a novel treatment for autoimmune diseases like NASH and psoriasis.

AGRIFOOD

Research agreements

Agrocode Bioscience and the CSIC began developing priming technology to improve plants' resistance to adverse conditions.

Ingenasa, through the VACDIVA project, is developing a DIVA vaccine and diagnostic tool for infections caused by the African swine fever virus.

VLP Bio and Bayer Animal Health reached a deal to research and develop veterinary immunotherapies.

Zendal and Irish firm Marinnovac set up the Aquatreck joint venture to manufacture vaccines for aquaculture.

Expanded capacities

In 2019, AlgaEnergy opened up subsidiaries in the USA, India and Mexico; Grupo Agrotecnología Biotech, in Colombia; and Natac Biotech began construction of a new plant in Hervás, Extremadura.

INDUSTRIAL

3P Biopharmaceuticals closed a production deal with Swedish company Intervace and was granted FDA approval for its facilities to manufacture the target molecule to be commercialized in the USA.

ZYMVOL signed a research agreement with the Massachusetts Institute of Technology (MIT) in the USA to develop enzymes to break down plastics.

Bionet kicked off the AD-VISOR project to use animal byproducts to produce bioplastics and biomethane.







Graph 9.1. Impact of biotech companies on the GDP (€ millions of 2018 GDP).

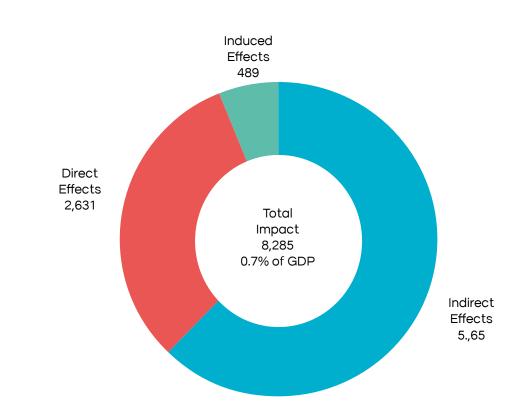
Source: Compiled from the information on

companies collected by AseBio.

9.1. Economic impact

Impact on GDP: Biotech companies account for 0.7% of the GDP.

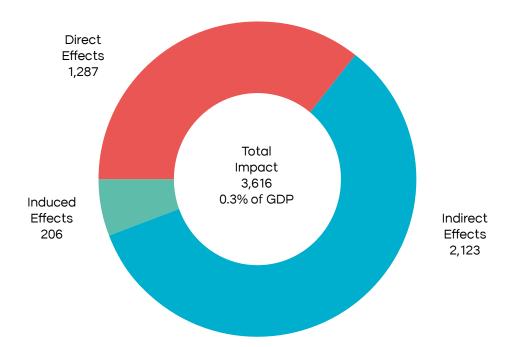
We've determined the total impact of biotech firms on the gross domestic product (GDP), both through their direct contribution and from their indirect and induced effects on the whole production chain. The activities of these biotech firms have generated more than €8.2 billion in income, roughly 0.7% of the national total, mainly through indirect effects (graph 9.1).



Impact of tax revenue: Biotech firms contribute 0.3% of the GDP in taxes.

Investments in science and innovation generate a significant flow of income for the State, which helps protect our social welfare model.

We've estimated the various flows of income generated as a result of the activity of biotechnology companies, with average tax rates for each type of income to calculate the tax revenue the public administrations see from these biotech firms. In 2018, the impact of the tax revenue of biotech companies was €3.6 billion, or roughly 0.3% of the GDP (graph 9.2).



Graph 9.2. Impact of total tax revenue from biotech companies (€ millions of 2018 tax revenue).

Source: Compiled from the information on companies collected by AseBio.

Total production of biotech firms: 0.8% of the GDP.

In 2018, total production (turnover) was more than €9.8 billion, up nearly 6% year on year, similar to the growth seen the previous year.

To generate this turnover, biotech firms had to acquire intermediary goods valued at €7.2 billion, which generated just over €2.6 billion in turnover (GDP). This income mainly (68%) went to compensation for the more than 27,000 workers employed directly by biotech companies.

	2018	2017	2016	2015	2014	2013	2012	2011	2010
€ millions	9,861	9,315	8,787	8,777	7,664	6,368	7,045	7,038	6,255
% GWTH	5.9%	6.0%	0.1%	14.5%	20.4%	-9.6%	0.1%	12.5%	0.0%
% GDP	0.8%	0.8%	0.8%	0.8%	0.7%	0.6%	0.7%	0.7%	0.6%
	7,230	6,433	6,592	6,907	5,952	5,040	5,523	5,455	4,781
	2,631	2,882	2,195	1,870	1,712	1,328	1,522	1,582	1,474
€ millions	1,759	1,515	1,330	1,244	1,096	875	947	976	844
	872	1,368	866	626	616	453	575	606	630
Number of people % GWTH Total %	27,085 8.2% 0.14%	25,029 10.6% 0.13%	22,637 5.3% 0.13%	21,504 12.5% 0.13%	19,120 26.4% 0.12%	15,129 -8.1% 0.09%	16,470 -1.5% 0.10%	16,723 10.2% 0.09%	15,180 0.0% 0.08%
	% GWTH % GDP € millions Number of people % GWTH	€ millions 9,861 % GWTH 5.9% % GDP 0.8% 7,230 2,631 € millions 1,759 872 Number of people 27,085 % GWTH 2,881	€ millions 9,861 9,315 % GWTH 5.9% 6.0% % GDP 0.8% 0.8% 7,230 6,433 2,631 2,882 € millions 1,759 1,515 872 1,368 Number of people % GWTH 27,085 25,029 10.6%	€ millions 9,861 9,315 8,787 % GWTH 5.9% 6.0% 0.1% % GDP 0.8% 0.8% 0.8% 7,230 6,433 6,592 2,631 2,882 2,195 € millions 1,759 1,515 1,330 872 1,368 866 Number of people 27,085 25,029 22,637 % GWTH 8.2% 10.6% 5.3%	€ millions 9,861 9,315 8,787 8,777 % GWTH 5.9% 6.0% 0.1% 14.5% % GDP 0.8% 0.8% 0.8% 0.8% 7,230 6,433 6,592 6,907 2,631 2,882 2,195 1,870 € millions 1,759 1,515 1,330 1,244 872 1,368 866 626 Number of people 27,085 25,029 22,637 21,504 % GWTH 8.2% 10.6% 5.3% 12.5%	€ millions 9,861 9,315 8,787 8,777 7,664 % GWTH 5.9% 6.0% 0.1% 14.5% 20.4% % GDP 0.8% 0.8% 0.8% 0.8% 0.8% 0.7% 7,230 6,433 6,592 6,907 5,952 2,631 2,882 2,195 1,870 1,712 € millions 1,759 1,515 1,330 1,244 1,096 872 1,368 866 626 616 Number of people % GWTH 27,085 25,029 22,637 21,504 19,120 8,2% 10.6% 5.3% 12.5% 26.4%	€ millions 9,861 9,315 8,787 8,777 7,664 6,368 % GWTH 5.9% 6.0% 0.1% 14.5% 20.4% -9.6% % GDP 0.8% 0.8% 0.8% 0.8% 0.7% 0.6% 7,230 6,433 6,592 6,907 5,952 5,040 2,631 2,882 2,195 1,870 1,712 1,328 € millions 1,759 1,515 1,330 1,244 1,096 875 872 1,368 866 626 616 453 Number of people % GWTH 27,085 25,029 22,637 21,504 19,120 15,129 % GWTH 8.2% 10.6% 5.3% 12.5% 26.4% -8.1%	€ millions 9,861 9,315 8,787 8,777 7,664 6,368 7,045 % GWTH 5.9% 6.0% 0.1% 14.5% 20.4% -9.6% 0.1% % GDP 0.8% 0.8% 0.8% 0.8% 0.7% 0.6% 0.7% 7,230 6,433 6,592 6,907 5,952 5,040 5,523 2,631 2,882 2,195 1,870 1,712 1,328 1,522 € millions 1,759 1,515 1,330 1,244 1,096 875 947 872 1,368 866 626 616 453 575 Number of people % GWTH 27,085 25,029 22,637 21,504 19,120 15,129 16,470 % GWTH 8.2% 10.6% 5.3% 12.5% 26.4% -8.1% -1.5%	€ millions 9,861 9,315 8,787 8,777 7,664 6,368 7,045 7,038 % GWTH 5.9% 6.0% 0.1% 14.5% 20.4% -9.6% 0.1% 12.5% % GDP 0.8% 0.8% 0.8% 0.8% 0.8% 0.7% 0.6% 0.7% 0.7% 4 7,230 6,433 6,592 6,907 5,952 5,040 5,523 5,455 2,631 2,882 2,195 1,870 1,712 1,328 1,522 1,582 € millions 1,759 1,515 1,330 1,244 1,096 875 947 976 872 1,368 866 626 616 453 575 606 Number of people 27,085 25,029 22,637 21,504 19,120 15,129 16,470 16,723 % GWTH 8.2% 10.6% 5.3% 21,504 19,120 15,129 16,470 16,723 10.2% 10.6% 5.3% 12.5% 26.4% -8.1% -1.5% 10.2%

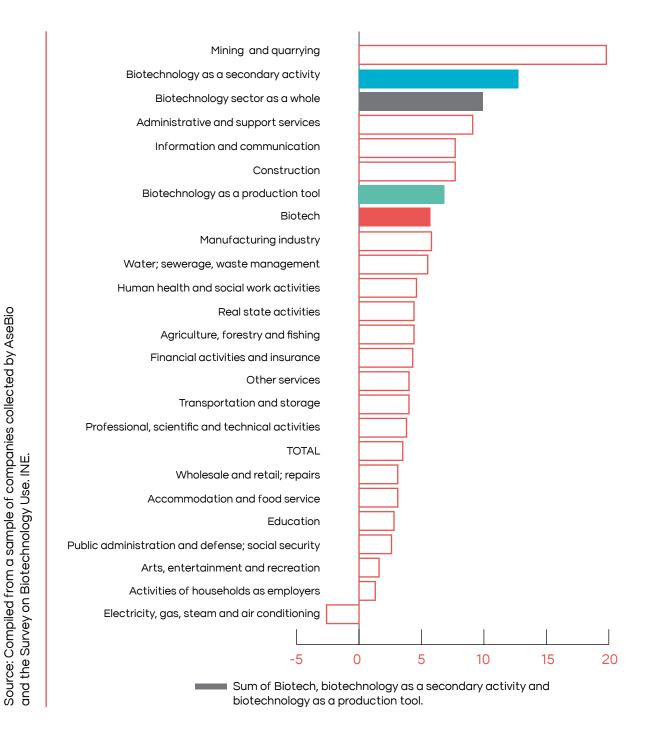
Table 9.1. Estimated economic activity of biotech firms.

Source: Compiled from the information on companies collected by AseBio.

The biotechnology sector led production growth in 2018.

Biotechnology activities are at the top of rankings on production growth of economic activities for 2018. To calculate this, we used our estimates of the evolution of biotech companies' turnover and data from the INE for companies with biotechnology as a secondary activity and those that use biotechnology as a production tool.

The increase in production in the biotechnology sector is only surpassed by mining industries. Companies with biotechnology as a secondary activity were the most dynamic.

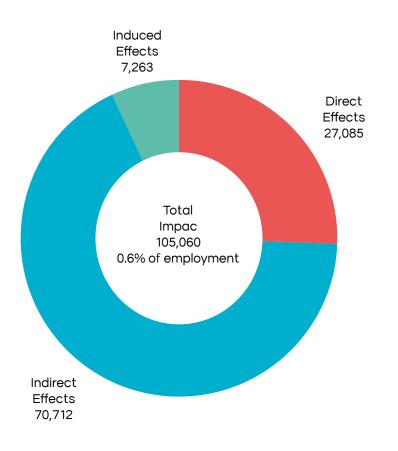


9.2. Impact on employment

Spanish biotech companies create 105,000 jobs, 0.6% of total employment nationwide.

As in the case of income, the impact on employment from activities carried out by biotech firms is amplified throughout the production chain. So, for each direct job created, almost three indirect or induced jobs are also generated. These companies are responsible for maintaining just over 105,000 jobs, which is 0.6% of total employment nationwide.

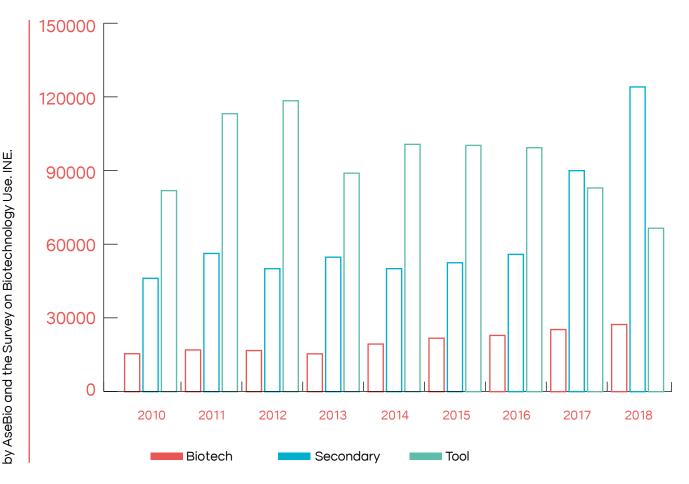
If we broaden our analysis to look at all companies doing biotechnology activities, the total employment that directly or indirectly depends on the activities carried out by these companies is more than 1,195,000 jobs, or 6.7% of the national total.



Graph 9.4. Impact on total employment of biotech firms (Total jobs in 2018). Source: Compiled from a sample of companies collected

The direct impact in terms of employment of companies doing biotechnology activity has been growing steadily since 2014, to over 217,000 jobs in 2018. Of these, 12% are at strictly biotechnology companies (biotech firms), 57% at companies with biotechnology as a secondary activity, and the other 31% at companies that use it as a production tool.

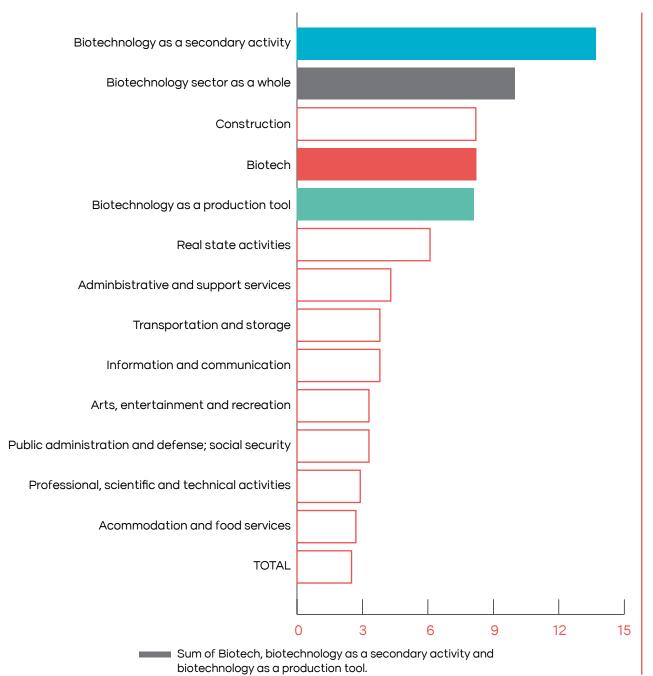
Over the past year, the total volume of employment posted strong growth, around 10%, and companies with biotechnology as a secondary activity were the most dynamic, posting 38% growth, followed by biotech firms with 8.2%. This strong growth also led to the relative increase in people employed in biotechnology relative to the national total, which is more than 1.2% of all employment.



The biotechnology sector as a whole led all other productive activities in employment growth in 2018, ahead of construction and real estate activities, which also showed strong growth in line with the recovery seen in these two sectors that were the hardest hit by the Spanish real estate crisis of 2008-14.

The strong employment growth rates for companies with biotechnology as a secondary activity put them ahead of all other productive activities.

For their part, exclusively biotechnology companies (biotech firms) had one of the highest rates of growth in employment, on par with construction, which led the ranking, and very close to the numbers posted by companies with biotechnology as production tool.



Graph 9.6. Comparative employment growth dynamics of companies with biotechnology activity (Employment growth rates 2018).

Source: Compiled from a sample of companies collected by AseBio and the

9.3. Macroeconomic indicators

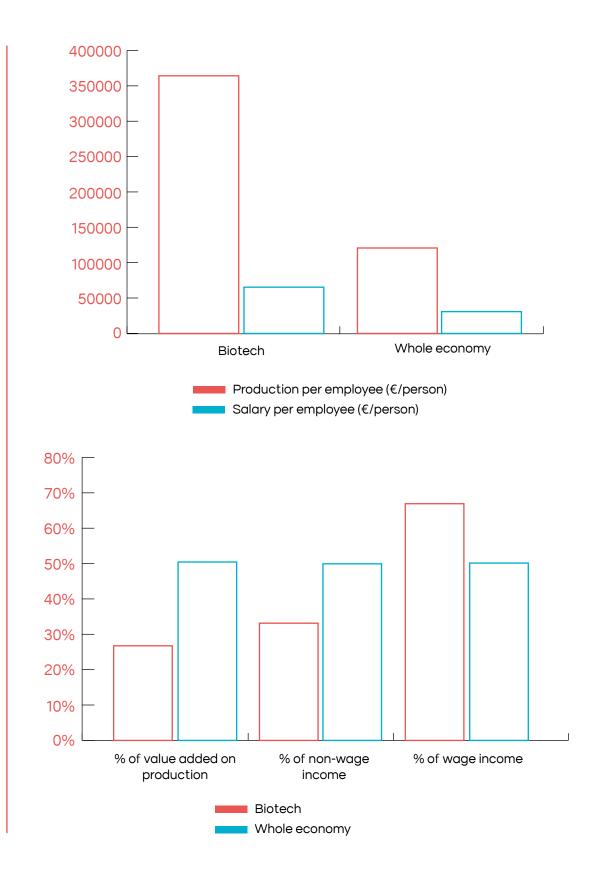
Productivity and salary per employee at biotech firms is three times higher than for the economy as a whole.

Biotech firms show average productivity and salary per employee three times higher than for the economy as a whole (graph 9.6).

On the other hand, if we compare biotech firms to the economy as a whole, we see that they generate less value added per unit produced due to the greater need for intermediate goods. A good proportion of this income goes to employees' salaries.

Source: Compiled from the information on companies Graph 9.7. Basic productivity and salary ratios for employees at biotech firms.

collected by AseBio.



THE LEADING EUROPEAN STOCK EXCHANGE FOR LIFE SCIENCES



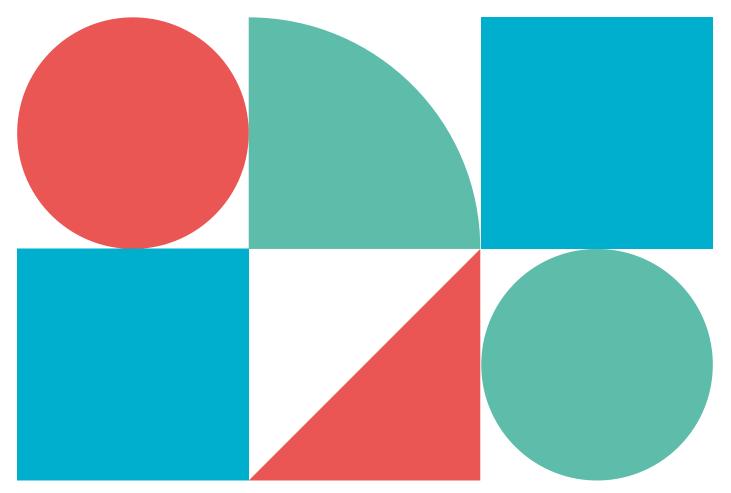
With some 480 listed Tech companies representing circa €700 billion in market capitalisation, Euronext is the primary venue for innovative companies in Europe. Since 2015, €26 billion have been raised in equity by Tech companies, including 110 IPOs and multiple secondary offerings. Our strong Tech franchise includes companies from the Life Sciences (Biotech & Medtech), TMT, and Cleantech sectors.

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Biotechnology for a healthier, more sustainable and better fed society.

In 2020, when the 2019 AseBio Report was published, the world was shaken by an unprecedented healthcare emergency, the economic impact of which is still unclear. With the 2030 Agenda and the European Green Deal, we have a new roadmap for growth to build a new, sustainable economic model that creates jobs with high value added in strategic, knowledge-intensive sectors.

It is time to once again give our science and innovation system a new push and align it with challenges like ageing, protecting society against emerging illnesses, sustainable eating and the climate emergency. Although the Spanish R&D system hasn't yet returned to pre-crisis investment levels, the biotechnology sector showed its commitment to science and innovation as a driving force for growth and social well-being in 2019.

Spain, as a member of the United Nations, approved the Sustainable Development Goals (SGDs) on the 2030 Agenda in September 2015. These 17 goals are a universal call to action to end to poverty, protect the planet and improve the lives of everyone in the world, and achieving them will require the best tools and policies, among which biotechnology will be key.



Our sector's innovative capacity has allowed biotechnology to offer up ways to protect ourselves against healthcare emergencies, like the one caused by Covid-19, with vaccines, treatments and diagnostic solutions. But beyond that, biotechnology also has innovative solutions to challenges like curing diseases, food safety, curbing greenhouse gases and achieving more sustainable agriculture.

The 2030 Agenda poses new global challenges for the biotech sector that require comprehensive, innovative solutions and biotechnology is an essential tool for 11 of the 17 Sustainable Development Goals.

SDG #2 End hunger, achieve food security and improved nutrition and promote sustainable agriculture.

Biotechnology, thanks to genetic engineering techniques like CRISPR, helps eradicate hunger by improving the nutritional properties of foods like golden rice, developing genetically modified strains that have a higher yield and are more drought resistant, and improving food security by detecting toxins, microorganisms and allergens.

SDG #3 Ensure healthy lives and promote well-being for all at all ages.

69% of medicines being developed worldwide are biotechnology drugs. Our sector is conducting research to end cancer, Alzheimer's and autoimmune diseases, while also developing vaccines to prevent infectious diseases and diagnosing and treating illnesses in a more effective, personalized manner. Plus, as a country, we are a pioneer in advanced therapies, like allogeneic cell therapy and CAR-T therapy.

SDG #5 Achieve gender equality and empower all women and girls.

The biotech sector has great female researchers, directors and entrepreneurs, and stands out for being 59% women in R&D activities, compared to 30% on average for the economy as a whole.

SDG #6 Ensure availability and sustainable management of water and sanitation for all.

We are working to ensure sustainable water management using microorganisms, microalgae and cyanobacteria to purify and eliminate chemical contamination. We are developing genetic diagnostic platforms to identify contaminants like viruses, bacteria and fungi, and implement processes and crops that reduce water needs.

SDG #7 Ensure access to affordable, reliable, sustainable and modern energy for all.

Our research allows us to replace fossil-derived materials with clean,

renewable, reliable alternative energy sources, like biofuel, which has a significant impact on reducing greenhouse gases.

SDG #9 Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation.

Innovation flows in the veins of biotech companies, which are ranked in the top three for investment relative to production: 5.5%.

SDG #12 Ensure sustainable consumption and production patterns.

Biotechnology is one of the key cogs in the circular bioeconomy, playing an essential role in reusing urban, forestry and industrial waste, optimizing resource efficiency and promoting responsible consumption through projects like Biovoices and Biobridges.

SDG #13 Take urgent action to combat climate change and its impacts.

European strategies like the Green Deal and the Biodiversity Strategy depend on science and technology to provide solutions for member States that mitigate the effects of climate change, such as bioplastics and biofuels.

SDG #14 Conserve and sustainably use the oceans, sea and marine resources for sustainable development.

Cleaning water with microorganisms and monitoring marine habitats are highly effective biotechnology approaches to preserving these ecosystems.

SDG #15 Sustainably manage forests, combat desertification, halt and reverse land degradation and halt biodiversity loss.

Technology like transgenic crops and bioproducts like biostimulants make crops more efficient, preventing deforestation, land degradation and loss of biodiversity.

SDG #17 Strengthen the means of implementation and revitalize the global partnership for sustainable development.

The Sustainable Development Goals require complex solutions, which makes it essential to forge alliances with other stakeholders in the system. Public-private partnership and international aspirations have allowed biotechnology to have a huge social, environmental and economic impact for decades now.

Today more than ever, with the 2030 Agenda and the Green Deal on the roadmap for rebuilding the country, we can say that biotechnology is helping improve the lives of millions and offering up solutions to our sustainability challenges on this planet. To do so, many of our members have been working to achieve these goals for years now. Biotechnology and chemicals corporation Merck uses innovation and technology to achieve its commitment to human health and well-being, while other companies like Bioiberica are helping us bring about an agricultural system that can improve the quality of our food. Plus, some of our members are working to reuse waste, ensuring a transition towards a sustainable circular economy. AseBio's commitment to the circular economy has led us to take part in two international consortia, Biovoices and Biobridges, to promote the bioeconomy and use of bioproducts in European society.

SUSTAINABLE GALS DEVELOPMENT





































MERCK AND ITS CONTRIBUTION TO A HEALTHIER SOCIETY

MERCK

More than 350 years ago, Merck laid the groundwork for what has become its commitment to society. Since 1668, the year it was founded, the company has had a clear connection with the spirit of SDG 3 on the 2030 Agenda, to ensure healthy lives and promote well-being for all at all ages. As the company has grown (it is now present in 66 countries and employs 57,000 people) and diversified, Merck has increasingly taken responsibility for tackling some of the great challenges facing all of us as a society, promoting sustainable innovation to have a real impact on society and contribute to human progress. Merck helps improve our general well-being through cutting-edge drugs (Healthcare division), tools for science and research (Life Science division) and technology for daily life (Performance Materials division).

The company's commitment to healthier living and greater wellbeing is realized, among other factors, by promoting talent and science, and developing innovation and technology, which are two of the company's strategic areas of activity. Currently, the company has 7,800 employees working in R&D and invested €2.3 billion in 2019. Its R&D investment focused mainly on three areas, immunology, immuno-oncology and oncology, to find treatments to diseases that are a serious threat to the lives of millions of patents (like cancer) and conditions that can significantly limit quality of life and autonomy of patients and caregivers (like multiple sclerosis). As one disease can affect different people in different ways, the company is currently focusing its strategy on personalized solutions and advancing in knowledge of new biomarkers and therapeutic targets. Precision medicine is part of Merck's commitment to healthier living and greater well-being. This has translated into support for research

in individualized molecular medicine, significant advances in liquid biopsy and studying new molecules or indications for existing molecules as a result of biotechnology innovation for conditions like kidney cancer, non-small-cell lung cancer, urothelial carcinoma, head and neck cancer, multiple sclerosis and rheumatoid arthritis, among others.

At the same time it looks to the future, Merck remains committed to people affected by other conditions where it has consolidated experience. One of these is infertility. The company has been working in this field since 1906, helping more than 3.2 million children be born around the world. Merck has a portfolio of innovative devices and drugs for all stages of the assisted reproduction cycle, incorporating new technology to standardize laboratory processes at fertility centers to improve success rates. Merck's biotechnology plant, located in the town of Tres Cantos outside Madrid, has been key in achieving this. The plant is a global benchmark in biotechnology at Merck, with production capacity to supply the global market with both recombinant human follicle stimulatina hormone (r-hFSH) and recombinant human growth hormone (r-hGH) to treat growth hormone deficiency in children. As part of its commitment to industrialization, economic growth and employment, the Tres Cantos plant is carrying out a significant project to expand its production capacity, investing €22 million in recent years and €23 million more through 2022 to expand new production areas, acquire new equipment and incorporate new technology.

Merck is focused on promoting innovation and technology, accelerating scientific discovery by incorporating highly powerful biotechnology tools in laboratories,

including gene editing (the company holds 23 CRISPR patents around the world, including CRISPR/CAS9 and Proxy CRISPR). The Merck Life Science division also supplies products and solutions for academic (in chemistry and biology) and pharmaceutical research, develops diagnostic solutions and contributes techniques for environmental, food safety and industrial quality analyses. All of this is essential to facilitate research and innovation to improve society's health and well-being.

In Spain, Merck promotes talent and science by collaborating with academia to foster and support talent among future professionals, which has led to the creation of three university chairs: the Merck Biotechnology Chair with Universidad CEU-San Pablo and AseBio to promote Biotechnology, the Francisco de Vitoria University-Merck Immunology Chair to promote translation research in Immunology, and the Autonomous University of Madrid-Merck Chair in Individualized Molecular Medicine to research and promote training in this area.

A healthier society is possible through strategic alliances among all the stakeholders in the healthcare system (in line with SDG 17). Merck has already taken important steps to bring about this change, contributing its knowledge, activity and people.

SCIENCE AND INNOVATION FOR SUSTAINABLE AGRICULTURE

b Bioiberica

The latest Climate Summit held in Madrid in 2019 highlighted the important role of agriculture in the fight against climate change, through more sustainable agricultural practices and more efficient use of water and agricultural materials. In this regard, new strategies like precision agriculture, biostimulants and other complementary tools for pest control and plant pathogens play an important role.

Biostimulants promote plant growth and development by stimulating photosynthesis and improving absorption of nutrients, which is vital and must be efficient as crops and agricultural land are huge carbon sinks, meaning they absorb CO2. Biostimulants and other biological products also increase the efficiency of water and nutrients, crop yield and tolerance to abiotic stress.

To contribute to the advancement of agriculture, providing sustainable solutions to overcome plant stress, boost crop yield and improve quality, Bioiberica Plant Health has developed the Enzyneer® extraction technology, based on enzymatic hydrolysis to obtain amino acids in their biologically active L-form, as well as facilitating release of glycerolipids and sterols that act in synergy to stimulate plants' physiological processes.

These bioactive compounds extracted with Enzyneer® make

plants more resistant to stress, boost the absorption of nutrients and improve the quality of their fruit. Their effectiveness has been proven in photosynthesis-regulation studies, bioassays on hormone-like activity and analysis of gene and proteome expression.

So, these products play an important role in the fight against climate change, allowing for more efficient use of fertilizers and integrated, more organic crop management.



BIOECONOMY FOR INDUSTRIAL TRANSFORMATION: EUROPE'S COMMITMENT TO A GREENER, MORE

SUSTAINABLE ECONOMY

Industrial biotechnology (IB) is one of Europe's strengths. It allows the EU to manufacture over half of all enzymes in the world used to produce a wide range of products in industrial sectors, including chemical and pharmaceutical products, food and animal feed, detergents, paper and pulp, textiles, power, materials and polymers.

Industrial biotechnology ensures companies sustained, sustainable growth, which in addition to helping preserve the environment by using green or eco-friendly industrial machinery also helps conserve resources like water and power. So, it offers solutions to the great challenges we are facing today, including more efficient use of resources, reducing CO2 emissions, producing healthy, nourishing food, and improving our energy security.

One of the most important applications of IB is to develop the bioeconomy, as it makes up 8% of the workforce in the EU and includes sectors and systems that comprise the parts of the economy that use, produce, process and are fueled by renewable biological resources from the land and sea, such as crops, forests, animals and microorganisms.

The European Green Deal, announced by the new European Commission in December 2019, aims to promote the transition towards a just and prosperous society, with a modern, resource-efficient, competitive economy in Europe. In line with this, the circular bioeconomy proposes a comprehensive approach to tackle issues of ecology, the environment, energy, food supply and natural resources that Europe and the world are currently facing.

At AseBio, we believe that biotechnology will be a key element for building a green, sustainable economy. That's why we're working on two projects funded by the **European Commission: Biovoices** and Biobridges, through which we hope to promote the development and promotion of the bioeconomy and help bioproducts reach society. We know that knowledge, education and awareness of production and consumption are important factors in fueling behavior changes towards a more sustainable lifestyle, which is why at AseBio we will continue working together with companies, scientists, administrations and citizens to achieve this transformation.









Co-funded by the Horizon 2020 programme of the European Union



https://www.biovoices.eu/

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 774331

https://www.biobridges-project.eu/

This project has received funding from the Bio Based Industries Joint Undertaking under the European Union's Horizon 2020 research and innovation programme under grant agreement No 792236.

Spanish Association of Bioenterprises





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ENRIQUE CASTELLÓN **CRB INVERBIO**



CHRISTIAN SÁNCHEZ NANOIMMUNOTECH



ENRIQUE SAMPER NIMGENETICS



BELÉN SOPESÉN PHARMAMAR



ANTONIO LÓPEZ SCIENCE INNOVATION LINK OFFICE



GURUTZ LINAZASORO VIVEBIOTECH



ANDRÉS BALLESTEROS VIVIA BIOTECH



Work Comissions

Agrifood Committee



Led by Richard Borreani (Bayer CropsScience)

GOALS

- To promote an appropriate, stable regulatory framework in Spain and Europe that can facilitate the contributions of biotechnology to agrifood production and environmental conservation.
- To continue putting agrifood biotechnology on the agenda of public institutions and governments, encouraging measures to promote and support the sector.
- To boost visibility and recognition of biotechnology for agrifood and the role it plays in ensuring safe, sustainable, quality nutrition.
- To raise awareness of and communicate the positive impact biotechnology has on land use, food security and better nutrition, water management and preserving ecosystems, offering up solutions to our planet's sustainability challenges in line with the 17 sustainable development goals on the 2030 Agenda.

WORKGROUP

• Sustainable agriculture and healthy eating. Coordinator: Richard Borreani (Bayer CropsScience).

Industrial Transformation Committee

Led by Carlos Rodríguez-Villa (AlgaEnergy)

GOALS

- To valorize industrial biotechnology for a green, circular economy.
- To identify barriers to its full development in our country and influence support for R&D and regulations to promote it.
- To make visible the positive impact of industrial biotechnology on the circular bioeconomy, sustainable biomass, employment and innovation, climate change and consumers and society in general.

WORKGROUP

• Bioeconomy, circular economy and industrial sustainability. Coordinator: Carlos Rodríguez-Villa (AlgaEnergy).



Work Comissions

Funding, Internationalization and Technology Transformation Committee





GOALS

- To carry out actions to bring about a framework of incentives that encourages R&D and investment to cover funding needs, especially in SMEs.
- To facilitate internationalization by putting in place measures that facilitate access to complex markets.
- To encourage participation in international R&D projects, and to lead them.
- To facilitate development of the connection between biotechnology and new technology.
- To contribute, alongside other social and institutional stakeholders, to achieving the goals on the 2030 Agenda.
- To promote a regulatory framework based on ethical and bioethical needs to ensure safety.

WORKGROUPS

- Funding R&D and business development. Coordinator: Belén Sopesén (Pharmamar).
- Biotechnology and Digitalization. Coordinator: Elisa Díaz (Merck).
- New markets for Spanish biotechnology. Coordinator: Antonio López (SILO).

Health Committee

Led by Enrique Castellón (CRB Inverbío)

GOALS

- To influence regulatory processes that affect the application of biotechnology in healthcare.
- To help develop and improve the national health system, promoting access to biotechnological innovation that is compatible with sustainability.
- To raise awareness of the contributions biotechnology makes to help and further recognition as a sector that generates a lot of value added.
- To lead collaboration and partnership initiatives with stakeholders in the public and private sectors that foster innovation in healthcare and new technology and public policies that valorize R&D throughout the chain.

WORKGROUPS

- Market Access. Coordinator: Beatriz Perales (ROCHE).
- Personalized Medicine and Advanced Diagnostics. Coordinator: Ana Martín (Amadix).
- Drug Discovery. Coordinator: Arsenio Nueda (Almirall).
- Advanced Therapies. Coordinator: Gurutz Linazasoro (ViveBiotech).



Work Comissions

Association and Talent Committee



Led by Elena Rivas (A4Cell)

GOALS

- To foster synergies among members in order to boost their potential with comprehensive service through collaboration and involvement.
- To facilitate networking, connections among members, and to foster collaboration among public and private institutions.
- To channel members' needs and concerns.
- To generate a framework for actions to encourage young talent.
- To boost partnering with the university arena and dissemination of biotechnology through universities.
- To help valorize diversity and inclusion, particularly gender equality.

WORKGROUPS

- Communication and social impact. Coordinator: Javier Velasco (Bioiberica).
- Talent and Diversity. Coordinator: Tomás Alarcón.







3P BIOPHARMACEUTICALS

ABBVIE

ABILITY PHARMACEUTICALS



ACKERMANN INTERNATIONAL





ADDITUM BLOCKCHAIN

ADL BIONATUR SOLUTIONS







ADMIT THERAPEUTICS



AGAROSE BEAD TECHNOLOGIES



AGRENVEC



AGROCODE BIOSCIENCE



ALCALIBER







ALEXION PHARMA

ALGAENERGY

ALGENEX



ALLINKY BIOPHARMA



ALMIRALL







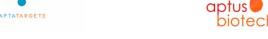


AMGEN

AMS BIOPHARMA LABORATORY

ANTARES CONSULTING







AQUILÓN CYL



APTATARGETS

GRIFOLS



APTUS BIOTECH



ARACLON BIOTECH

ARCHIVEL FARMA

ARRAYS FOR CELL NANODEVICES



ARTHEX BIOTECH



ARTINVET



ASABYS PARTNERS



ASCIL BIOPHARM



ASPHALION



ASTRAZENECA



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AURORA MEDICINE ESPAÑA



ayming

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BAYER CROPSCIENCE

BCN HEALTH







BDI BIOTECH

BEST MEDICAL DIET

BIOBIDE







BIOCHEMIZE

BIOCROSS

BIOHOPE SCIENTIFIC SOLUTIONS FOR HUMAN HEALTH







BIOIBÉRICA

BIOINGENIUM

BIOKIT







BIOLAN

BIOMAR MICROBIAL TECHNOLOGIES

BIOMARIN







BIOMEDAL

BIOMEDICA MOLECULAR MEDICINE

BIONCOTECH



BIONET INGENIERÍA



BIONOS BIOTECH



BIONURE FARMA



BIOREPOS



BIORIZON BIOTECH



BIOSEARCH LIFE



BIOSERENTIA



BIOTECHNOLOGY BUSINESS INSTITUTE



BIOTECHVANA



BIOTOOLS



BRISTOL MYERS SQUIBB



BTI BIOTECHNOLOGY INSTITUTE



CAIXA CAPITAL RISC



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DREAMGENICS



Abogados y Consultores P. Industrial e Intelectual

ELZABURU



ENTRECHEM



ENZYMLOGIC



EUROGENETICS



EURONEXT



EUROPEAN RESEARCH BIOLOGICAL CENTER (ERBC)







FERRER

FERRER INCODE

FITALENT

_Spanish Association of Bioenterprises

GENESIS Biomed





GÉNESIS BIOMED

GENETRACER BIOTECH

GENÓMICA



Gómez-Acebo & Pombo

GRADOCELL

GILEAD

GÓMEZ-ACEBO & POMBO **ABOGADOS**

GRADOCELL





GRIFOLS

GRI-CEL

GRIFOLS ENGINEERING

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GRUPO AGROTECNOLOGÍA **BIOTECH**

GRUPO CELLUS

GSK (GLAXOSMITHKLINE)







HISTOCELL

HOFFMANN EITLE

IDEN BIOTECHNOLOGY







IGEN BIOTECH

IKAN BIOTECH







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INCYTE







INGULADOS RESEARCH



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INNOQUA TOXICOLOGY

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LEUKOS BIOTECH







LIFESEQUENCING



LIM GLOBAL



LONZA



MABXIENCE



MEDMESAFE



MERCK



Small things that matter.





MILTENYI BIOTEC



MINORYX THERAPEUTICS



MSD



MYRIAD



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ONA THERAPEUTICS







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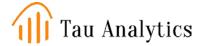
STEMTEK THERAPEUTICS



STRAMMER



SYLENTIS



TAU ANALYTICS



TECBIOCEL, S.L.



TECNIC



TECNIC BIOTECH



THROMBOTARGETS



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TRESCA INGENIERÍA



VALGENETICS



VAXDYN



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Fundación Progreso y Salud CONSEJERÍA DE SALUD





Industria, Innovación y Empleo

FUNDACIÓN PROGRESO Y SALUD







IMIBIC



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INSTITUTO PARA LA COMPETITIVIDAD EMPRESARIAL (ICE)



INSTITUTO DE INVESTIGACIÓN SANITARIA FUNDACIÓN IMÉNEZ DÍAZ



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Instituto de Investigación Sanitaria La Fe





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INSTITUTO DE SALUD CARLOS III



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LEITAT



NEIKER

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PARC CIENTÍFIC DE BARCELONA

PARQUE CIENTÍFICO DE MADRID

PROEXCA



PROYECTO CLAMBER



PTS GRANADA



Sociedad Española de Bioquímica y Biología Molecular

SOCIEDAD ESPAÑOLA DE BIOQUÍMICA Y BIOLOGÍA MOLECULAR (SEBBM)







SOCIEDAD ESPAÑOLA DE NEUROCIENCIA (SENC)



SOCIEDAD ESPAÑOLA DE ONCOLOGÍA MÉDICA



SODENA



UNIVERSIDAD CEU SAN PABLO



UNIVERSIDAD EUROPEA DE MADRID



UNIVERSIDAD DE NAVARRA



VETERINDUSTRIA





METHODOLOGY

CHAPTER 3 - R&D INVESTMENT

For this chapter we compiled the results of the Survey on Biotechnology Use and statistics on R&D activities from the National Statistics Institute. 2018. https://www.ine.es/dyngs/ INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176808&menu=ultiDatos&i-dp=1254735576669

CHAPTER 4 - FUNDING

The data in chapter 4 was compiled from information from the State Research Agency (AEI), the Spanish Venture Capital and Private Equity Association (ASCRI), the National Innovation Company (ENISA), the Center for the Development of Industrial Technology (CDTI), members and the press.

CHAPTER 5 - TALENT AND DIVERSITY

For the data on the evolution of university students enrolled in biotechnology programs, we used data from the Statistics on University Students of the Secretary of State for Universities, Ministry of Science, Innovation and Universities, (https://www.ciencia.gob.es/portal/site/MICINN/menuitem.26172fcf4eb029fa6ec7da6901432ea0/?vgnextoid=9b238e2eb3856610Vg-nVCM1000001d04140aRCRD) and selected data from the past three years for all universities that offer undergraduate studies in biotechnology. To obtain the data on number of researchers, female researchers and female representation, we used the 2018 Survey on Biotechnology Use and INE Statistics about R&D activities. https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176808&menu=ultiDatos&idp=1254735576669

CHAPTER 6 - BUSINESS FABRIC

This section was compiled as follows:

- To reflect the number of biotechnology companies, and their breakdown by the field they apply biotechnology in, size and geographic location, we compiled data from the INE Survey on Biotechnology Use and the list of biotechnology companies identified by AseBio.
- To put together the list of biotechnology companies started in 2019, we requested
 information from various entities in the main Autonomous Communities with biotechnology activity. Plus, to put together the map of biotech-related facilities, we analyzed
 the main Autonomous Communities.

CHAPTER 7 - ENVIRONMENTAL CONDITIONS

For this chapter, we compiled data from the FECYT Social Perception of Science and Technology in Spain survey (https://icono.fecyt.es/informes-y-publicaciones/percepcion-social-de-la-ciencia-y-la-tecnologia-en-espana) and the third COTEC survey on social percep-

tion of innovation (http://informecotec.es/media/IIIEncuestaPercepcionSocialInnovacionEspa%C3%B1a.pdf).

The results of the section on perception of the biotechnology sector were obtained from a survey of AseBio members, who were asked to rate a series of factors. As we simplified this year's survey, we had to adjust the results of surveys from previous years. Previously, there were 14 facilitating factors and 14 hindering factors. The members surveyed gave points for each factor separately and AseBio took the average of the sum of both types of factors, which was used to calculate the AseBio index.

To adapt this data to the new survey, which only has 21 factors, for factors that were only facilitating and didn't have an equivalent hindering factor, or vice versa, a correction factor was applied. And for facilitating factors with an equivalent hindering factor, in addition to adding a correction factor to both, they were subtracted after being corrected. This way, we have been able to maintain the data series from the past 10 years.

CHAPTER 8 - RESULTS OF COLLABORATIONS

To compile this chapter, we obtained information from the following sources:

- In the section of production of scientific knowledge, we included the main indicators for Spanish scientific production in biotechnology, provided by the Spanish Foundation for Science and Technology (FECYT), based on data from the Elsevier SciVal tool, which contains the scientific production from the Scopus database. Normalized impact is an indicator that compares similar publications, in terms of year published, category and document type. A NI of 1.0 means the paper is cited as often as the global average.
 A NI of 2.0 means the paper is cited twice as often as the global average.
- To come up with the number of scientific publications by AseBio members, we requested information from members on their scientific publications in biotechnology, not including communications or posters at congresses or fairs, or publications signed by research centers or universities that don't cite the relationship with studies for business projects.
- The data on patents was obtained for AseBio in a study carried out by the Madrid Science Park based on the ClarkeModet database. The information was obtained using the methodology designed by ClarkeModet and the Madrid Science Park, based on OECD definitions for the biotechnology sector. The Thomson Reuters (now Clarivate Analytics) databases were used. Plus, we checked the public databases of the various offices: Spanish Patent and Trademark Office (OEPM), European Patent Office (EPO), United States Patent and Trademark Office (USPTO), Japan Patent Office (JPO) and the World Intellectual Property Organization (WIPO).
- Both the section on products and services launched and the one on international presence were put together in consultation with AseBio members.

CHAPTER 9 - IMPACT

For chapter 9, we systematically collected and processed registry information for all companies identified as biotech firms, processing their basic financial statements, balance sheets,

and profit and loss statements to get a direct measurement of their business activity.

For each of these companies, we quantified their levels of basic production (turnover), employment, intermediate goods (products and services), value added, salaries (personnel expenditure) and investment over the past 10 years (2008-2018) to get the cumulative levels for all biotech firms, extrapolating the results obtained to the overall totals identified by the INE.

Alongside the detailed analysis of the biotech firms, we also moved forward in quantifying the corresponding levels for companies with biotechnology as a secondary activity and those that use biotechnology as a production tool, which along with biotech firms make up what we call the biotechnology sector.

For these companies, we started with the total employment figures in the INE survey and did an indirect estimation of the other benchmark levels, taking into account both the general ratios in the National Accounting and the specific ones for strictly biotechnology activities calculated previously.

From these figures, we calculated the overall economic impact of the activity carried out by these companies on the Spanish economy as a whole.

This way, using the standard methodology based on input-output tables, we calculated both the direct impact in terms of generating income (GDP), employment and tax revenue, and the induced impact generated by direct and indirect salaries dependent on this activity.

The following figure shows the sequence of calculations for the Impact chapter.



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