

Introduction

The new Report, prepared thanks to the cooperation between Federchimica-Assobiotech (National Association for the development of biotechnology – part of Federchimica) and ENEA (National Agency for new technologies, energy and sustainable economic development), provides an update on the Italian biotech industry's overall situation during the crucial period of the Covid-19 pandemic, which had a significant impact on the country's economy.

The report is based on the information provided by companies operating in the biotech field at the end of 2021, data gathered from their 2020 financial statements, the National Statistical System and other public sources, and provides an overall picture of the national biotech industry which is unique in terms of richness and information details. Starting from the figures which characterize the productive structure of the companies operating in Italy and focusing on R&D activities, as well as on the development of the bioeconomy, the main features and trends of the industry in the last two years have been outlined.

The Italian biotech industry, keeping a stable or slightly growing population of active firms, ranks among the main research-intensive sectors of the economy with several success stories in all the biotech fields of application.

In the first months of 2020 especially, the industry has shown all its potential in responding to the needs of the society and to the health emergency caused by SARS-CoV-2 pandemic.

The still ongoing pandemic has highlighted the importance of investing in research and trusting in an industry such as the biotech one, which has proven to be critical in providing the necessary tools to tackle the dramatic health crisis due to the outbreak of the Covid-19: from genome sequencing to molecular diagnostic, from vaccines to monoclonal antibodies. This should be a strong signal to the Italian Biotech Industry, whose development is hampered from an industrial ecosystem which is not yet sufficiently competitive on the international level stage.

It is therefore hoped that the lesson learned leads to a renewal of the medium-long term strategic vision and commitment by the national institutions focused on research and innovation. And focusing on innovation means to deal not only with the lab stage and the basic research, but also with the entire process from the technology transfer to the production and the commercialization of research results. A committed effort to support R&D investment and to simplify the regulatory framework, made through policy measures stable over time and managed with an efficient and centralized governance. These are measures which would enable companies to overcome the limit of their business size, which often is too small, and to contribute to the country's growth and competitiveness.

Riccardo Palmisano
Federchimica Assobiotech President

Gilberto Dialuce
ENEA President



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1 Summary

The data analyzed shows that the Italian biotech industry not only has withstood the health crisis due to the Covid-19 pandemic, recording as a whole only a 5% drop in the overall 2020 turnover, equal to less than half of the decrease of the overall Italian Industrial sector, but the nationally controlled biotech R&D dedicated firms have even increased by 30% their biotech turnover during the pandemic year.

With reference to the previous years, the biotech R&D investments of all the firms operating in this field have accelerated sharply with a 7% increase over 2019, an annual growth rate that rises to 15% considering only the biotech R&D dedicated firms, i.e. the firms which invest at least 75% of their total intra-mural R&D to biotechnology R&D.

The biotech sector has thereby been confirmed as one of the main driver for innovation, contributing to more than 5% of the overall manufacturing R&D.

After a slight decrease in 2020, lower than 1%, the number of biotech companies in Italy picked up reaching 790 units at the end of 2021. The temporary reduction in the number of biotech active firms recorded in 2020 is mainly due to the negative trend of the small and micro firms, especially those belonging in the class of firms with less than 10 employees, which have suffered most severely from the consequences of the health crisis.

The vibrant biotech small and micro firms ecosystem, which complements the stable core of big companies and focuses on the development of new technologies and products, represents a 82% share of the total. The biotech sector is, therefore, characterized for an average business size larger than the one in the manufacturing sector.

However, small and micro new firms are pivotal in creating new jobs: up to 65% of total gross job creation in 2020 can be attributed to the "Innovative Start-Ups", as defined by the Italian policy framework for innovative start-ups, also known as the "Start-up Act" (2012), although their share in total biotech employment in the same year has been only 6%.

With reference to the distribution per field of predominant application, even if the firms operating in the human healthcare sector – "red biotech" – represent still the majority share of the Italian biotech companies (48,5%), between 2014 and 2021 continued to grow the share of firms active mainly on the industrial biotech – "white biotech" – (+29%) and, particularly in the most recent part of the period considered, on agriculture and veterinary – "green biotech" – (+34.5%).

The growing share of firms predominantly active on industrial biotech on the overall biotech industry is related to the spreading of the industry throughout the national territory, especially in the North-Eastern regions. In terms of numbers, one third of the total industrial biotech firms is established in this area, and has grown more than 68% between 2014 and 2020, pushing the North-Eastern biotech turnover share from 8.6% to 13.5% over the same period of time.

In 2020, nearly 85% of the intra-muros biotech R&D investments have been stemming from the first 4 Italian regions (Lombardy, Latium, Tuscany & Piedmont). This concentration ratio is inevitably affected by the importance of R&D investments for the health field. Even the Italian Southern regions see an increase in their share on the national's total, above all in terms of number of biotech active companies and of biotech R&D investments, both in the Industrial biotech and in agriculture and veterinary.

In 2020, together, the share of the Italian Southern and North-Eastern regions on the overall total national biotech R&D investments accounts for 23% and more than 58% in the industrial biotech and in the green biotech sectors, respectively.

The capitals needed to fund the activities of the Italian companies active in the biotech industry, both in terms of research and production, mainly derive from resources made available by the ownership: in the form of capital contributions by shareholders, retained earnings or depreciation and provisions according to the structure and size of the company.

From the data gathered between 2017 and 2020 it can be seen a constant growth of the share of companies funded by Business Angels and Venture Capitals' contribution (about 4% and 6% of the total in 2020, respectively).

The role of grants remain central and even more companies have claimed to benefit from them (over 30% in 2020), mainly large size companies which are active in the human health field.

2 Glossary

The current report has been prepared thanks to the cooperation between Federchimica Assobiotech's Study Center and ENEA's Innovation and Development Directorate (National Agency for New Technologies, Energy and Sustainable Economic Development).

The data on the companies analyzed has been collected from the replies received to questionnaires sent to approximately 700 firms, their 2020 financial statements, the National Statistical System and other public sources.

The data from the previous years has been re-elaborated on the basis of the growth in the number of companies and on new information made available.

Among the public sources used: OECD's statistical publications, the EU Clinical Trials Register, AIFI and CDP Venture Capital data referring to innovative SMEs and start-ups financing. The definitions used in the Report follow the guidelines developed by the OECD ¹².

- **Biotech firms:** companies which utilize at least one biotech technique in order to produce goods or services and/or to perform R&D in the biotech field. Some of these firms can be large in size and dedicate only a small share of their economic activities to biotech.
- **Biotech R&D dedicated firms:** companies which invest at least 75% of their total intra-mural R&D to biotechnology R&D.
- **Nationally controlled biotech R&D dedicated firms:** nationally owned companies which are dedicated to biotech R&D research.

- **Total intra-mural R&D investments:** total expenses for R&D activities incurred by a company, carried out with its own personnel and equipment, involving non-biotech R&D activities as well.

- **Biotech intra-mural R&D investments:** overall budget share which a company dedicates to R&D, for biotech R&D activities.

- **Biotech Employees:** employees which are involved in biotech activities

- **Biotech R&D employees:** employees which are involved in biotech R&D activities.

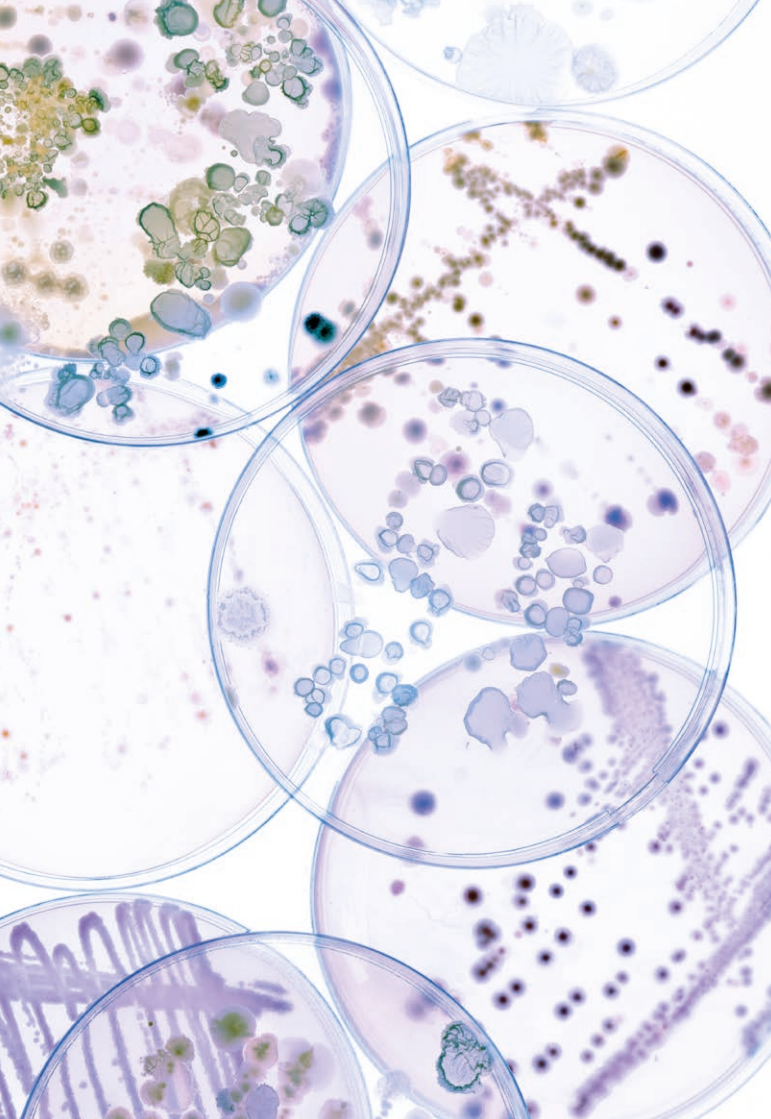
With reference to the fields within which biotech activities are predominantly carried out, in the current report firms are classified as follows:

- **Healthcare:** firms whose predominant activity is in the human healthcare industry, utilizing modern biotech methods for research, development and production of diagnostic products, treatment and disease prevention (drugs, new therapies, vaccines, diagnostic systems, molecular pharming);

- **GPET (Genomics, Proteomics and Enabling Technologies):** firms which use modern biotech methods primarily in the field of «omic» disciplines (genomics, proteomics, transcriptomics etc.); bioinformatic technologies, systems biology, biochips, biosensors; basic

1. OECD (2005), "A Framework for Biotechnology Statistics", OECD Publishing, <http://www.oecd.org/sti/sci-tech/34935605.pdf>

2. Friedrichs, S. and B. van Beuzekom (2018), "Revised proposal for the revision of the statistical definitions of biotechnology and nanotechnology", OECD Science, Technology and Industry Working Papers, 2018/01, OECD Publishing, Paris



research. Taking into account that such technologies, which could be applied to any biotech field, are mainly used in the healthcare sector, the GPET have been allocated within the life science field, in the healthcare sector.

- **Industrial biotech:** firms which utilize modern biotech methods mainly in the industrial field, for the redevelopment of conventional productive processes, for the transformation of renewable biomasses into energy bioproducts, for the application in the food industry, nutraceuticals and cosmeceutics, for the fine-tuning of diagnostic systems and environmental decontamination, or for products used in the restoration and conservation of the artistic heritage;

- **Agriculture and Veterinary:** firms whose predominant activity is in the agricultural and zootechnical industries, using modern biotech methods to improve the animal and vegetal production, increasing production and quality, improving the environmental adaptability characteristics and resistance to pathogens, or to develop biological and environmentally friendly products for the safeguard of plants and animals (including veterinary).

As these last two fields are highly representative for the bioeconomy, they will be taken as reference for this sector.

3

The Italian biotech industry in figures

3.1 Number of biotech firms

Table summarizing the main indicators, per type of firm

Year 2020	Total biotech firms	Biotech R&D dedicated firms	Nationally controlled biotech R&D dedicated firms
Number of firms	777	422	400
Biotech Turnover	10.242.843	3.984.715	1.644.427
Intra-mural R&D investments	1.810.989	531.328	279.003
Biotech intra-mural R&D investments	602.177	507.566	267.231
Biotech employees	13.277	6.522	4.434
Biotech R&D employees	4.876	3.260	2.182

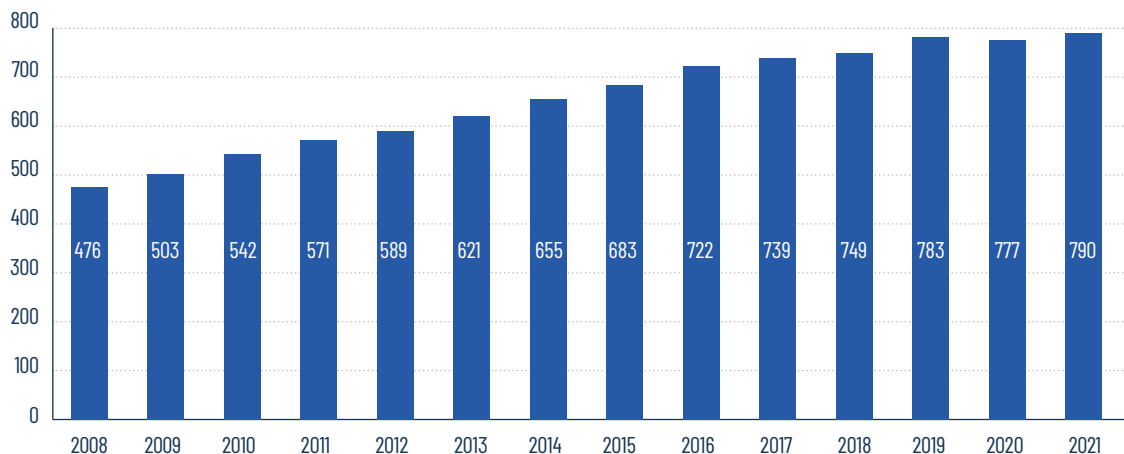
Values in thousands of euros

The data collected and analyzed for this report allows to study the impact on the Italian biotech industry of the health crisis which overwhelmed our social and economic systems in 2020, and its resilience. By the end of 2020, there were 777 biotech companies in Italy while by 2021, there were a total of 790. The main economic data of the firms operating in this sector, provide a clear picture of an industry which has withstood the crisis

in all its fields of application, and not only in the traditionally counter-cyclical ones linked to the human health sector even increasing its biotech intra-mural R&D investments, by over 7% between 2019 and 2020.

With regards to the biotech activities of the nationally controlled biotech R&D dedicated firms, the intra-mural R&D investments is equal to 16% on the overall turnover.

Evolution of the number of biotech firms in Italy

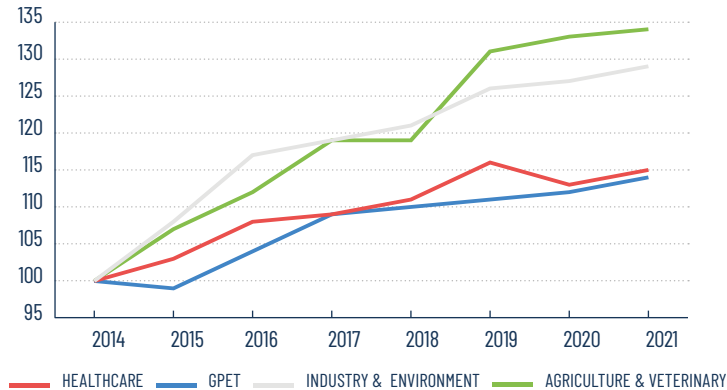


The number of companies active in the biotech industry in Italy, after a slight decrease in 2020, lower than 1%, (on a national level, the industrial reduction has been more than double¹), returned to growth in 2021, achieving 790 registered companies, more than the number of firm registered in 2019.

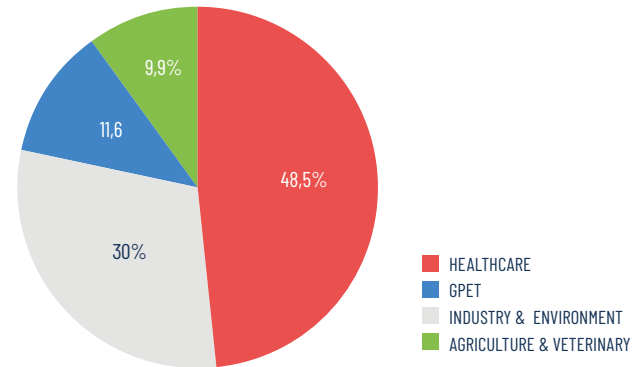
The growing number of companies has involved all biotech area and particularly, the nationally controlled biotech R&D dedicated firms, driven by those companies active in the industrial biotech with an increase of +9% between 2019 and 2020.

¹(INPS, « Private non agriculture firms», November 2021)

**Number of firms' trend,
per prevailing field of application (index number 2014=100)**



**Number of firms distribution,
per prevailing field of application**

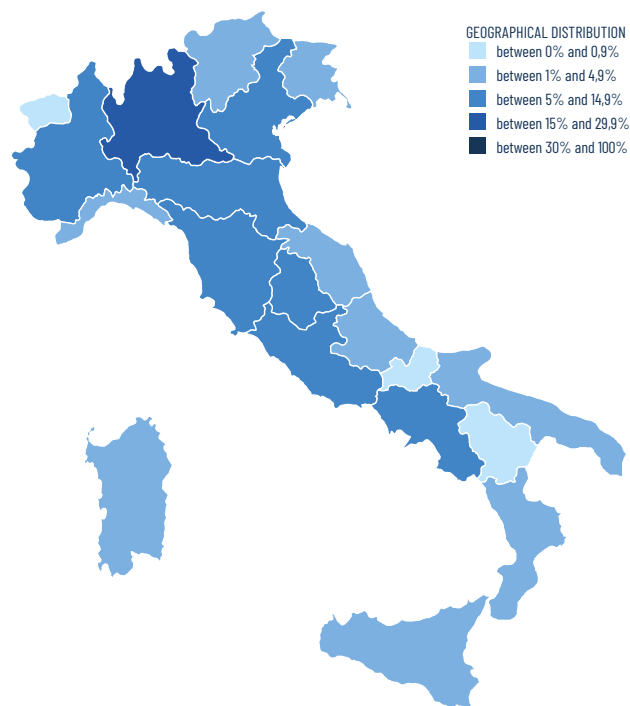


The firms mainly active in the field of human healthcare keep on representing the largest share of Italian biotech companies, but there is a continuous growth in the number of firms active in the field of industry & environment (industrial biotech) (+29% between 2014 and 2021) and especially in the last period, there is a growth among the firms operating in the agriculture and veterinary fields (+35% during the same period of time).

As a result, their share has grown respectively from 28% to 30% (Industrial biotech) and from 8,9% to almost 10% (agriculture and veterinary biotech). This same structural dynamic change in the field's composition, can be appreciated, despite to a lower degree, also for the economic variables referring to the R&D investments and the turnover.

Number of firms - geographical distribution, per legal head offices

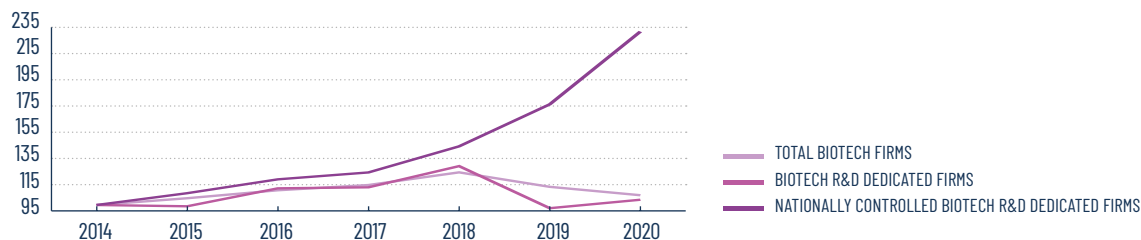
Region	Share
Abruzzo	1,1%
Calabria	2,0%
Campania	7,5%
Emilia-Romagna	4,6%
Friuli-Venezia Giulia	8,7%
Latium	9,2%
Liguria	1,4%
Lombardy	27,1%
Marche	2,4%
Piemonte	7,8%
Puglia	4,6%
Sardinia	1,6%
Sicily	3,5%
Tuscany	6,2%
Trentino Alto Adige	2,8%
Umbria	1,0%
Veneto	7,6%
Other Regions	0,9%



Despite the industry maintaining a strong territorial concentration, the share of firms on the overall total for the first 4 regions (Lombardy, Latium, Emilia Romagna & Piedmont) has dropped from 57% in 2014 to 53% in 2021. This confirms a growing distribution of the

Biotech productive industry, all over the national territory, especially towards the southern and north-eastern regions, with the latter mainly active in the industrial biotech.

Biotech turnover's trend per type of firm (index number 2014=100)



The turnover for the biotech companies in 2020, in which the Covid-19 crisis had the maximum impact, shows a substantial stability, recording decrease of 5% compared to 2019, less than half the loss recorded for the turnover of the overall Italian industry (-12%).

As previously highlighted, the decrease recorded in 2019 with respect to 2018, was due to accounting operations linked to a change in the business model within several multi-nationals, without a significant impact on the amounts of products or on the profitability of the companies involved. The continuous turnover growth of the nationally controlled biotech companies, on the other hand, is particularly significant.

1. «Industry's orders and turnover» Press Release, February 23rd 2021, ISTAT

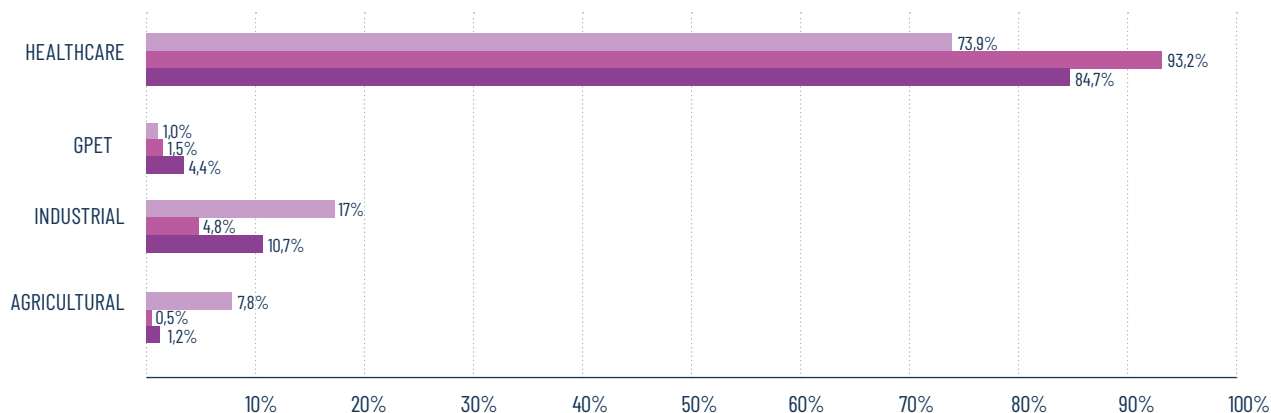
Biotech turnover's trend per type of firm, from 2014 to 2020

	2014	2015	2016	2017	2018	2019	2020
Total biotech firms	9.537.024	10.012.807	10.588.299	10.887.439	11.891.054	10.830.280	10.242.843
Biotech R&D dedicated firms	3.831.775	3.781.666	4.304.188	4.337.779	4.957.876	3.739.150	3.984.715
Nationally controlled biotech R&D dedicated firms	710.975	761.601	838.268	879.195	1.025.268	1.252.805	1.644.427

Values in thousands of euros

Biotech turnover distribution per field of prevailing application and type of company

- TOTAL BIOTECH FIRMS
- BIOTECH R&D DEDICATED FIRMS
- NATIONALLY CONTROLLED BIOTECH R&D DEDICATED FIRMS



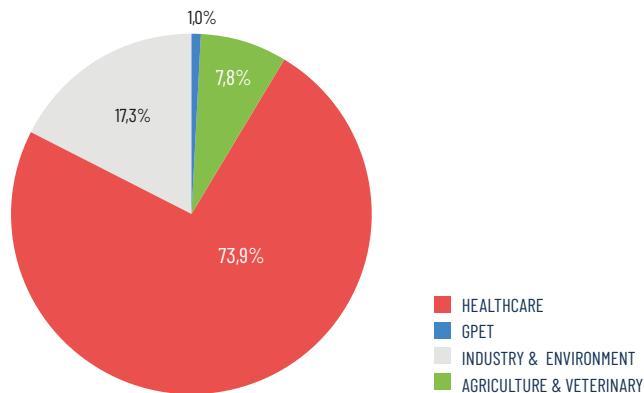
Taking into account the total number of companies, almost three-quarters of the overall biotech turnover is generated by the healthcare field, while a considerable 17% is generated by the Industry and Environment sector.

The percentage contribution of the firms using biotechnologies predominantly for industrial and environmental applications to the total biotech turnover decreases if we

consider only the biotech R&D dedicated firms, both nationally and foreign controlled (10% and 5% respectively).

Even in the case of biotechnology application to agriculture and veterinary, the largest percentage contribution is observed for the whole of the firms mainly active in such a field, while the share is reduced considering only the biotech R&D dedicated firms.

Total biotech turnover distribution, per prevailing field of application



Compared to the human healthcare sector, which has historically driven the development of the biotech industry, the applications of biotechnology to the bioeconomy are more recent, but they are gaining more and more consideration. This is related to the emerging interest in the environmental sustainability, in the reduction of the impact of human activities, and in the supply of strategic resources, starting from energy. The share of the biotech turnover achieved by the firms which apply biotechnology predominantly to the industry & environmental and agriculture & veterinary fields has grown in the last 3 years (from 2018 to 2020) from 16% to 17% and from 7% to 8% respectively.

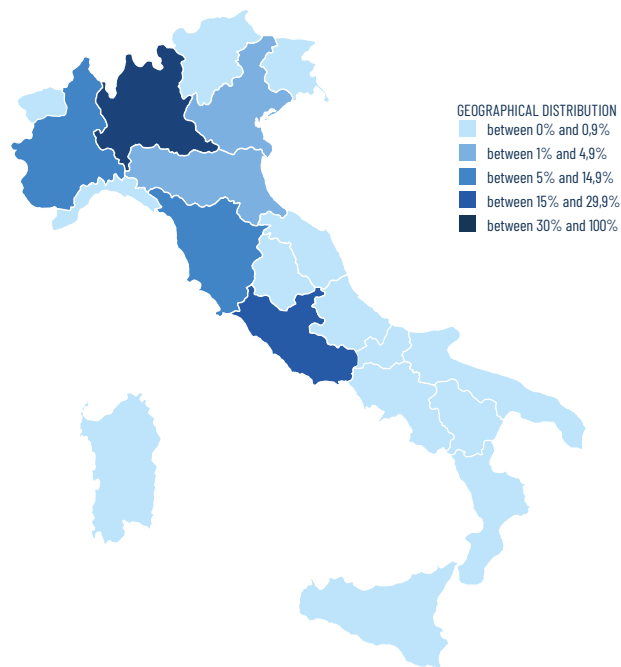


Biotech turnover - geographical share distribution, per legal head offices

The total biotech turnover share of the biotech firms concentrated in the first 4 regions (Lombardy, Latium, Tuscany, Piedmont) exceeds 90% of the total, in 2020 as well, with Lombardy leading with a share above 51%, slightly increasing between 2014 and 2020.

The industry & environment is the only field of application where Lombardy's leading position is downsized while there has been a significant growth in the share of the north-eastern regions: with a rise of over 68% between 2014 and 2020, that led the share from 9% to 14%. Nearly all the total turnover for the biotech industry (over 97%) is concentrated in the north.

With reference to the human healthcare field, Latium and Tuscany, together with the north-western regions, concentrate 93% of the total turnover generated. The center part of the country mainly focuses in the human health sector, recording turnover shares on the bioeconomy field lower than those of southern Italy.

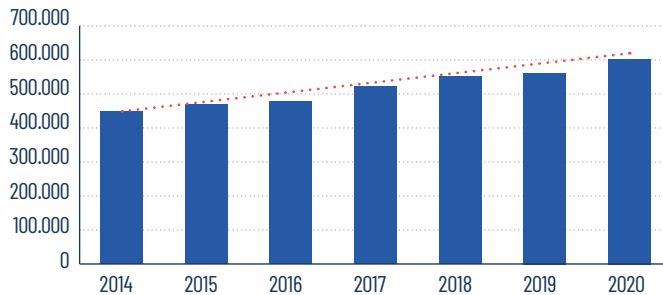


3.3 Intra-mural R&D investments

Biotech intra-mural R&D investments' trend, from 2014 to 2020

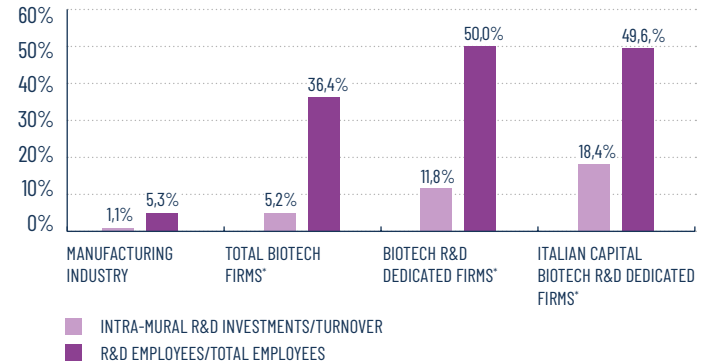
	R&D intra-muros investments	Biotech R&D intra-muros investments
Total biotech firms	1.810.989	602.177
Biotech R&D dedicated firms	531.328	507.566
Italian capital biotech dedicated firms	279.003	267.231

Biotech Intra-mural R&D investments (2014 - 2020)



Unlike the turnover, the biotech R&D investment has grown at a rate of +7,3%, higher than the previous two years.

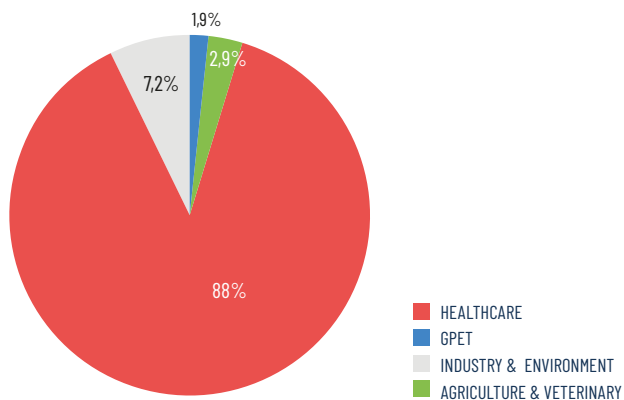
Intra-mural R&D investments, compared to the manufacturing industry (2019)



The biotech sector has thereby been confirmed as one of the main driver for innovation, contributing to more than 5% of the overall manufacturing R&D.

*Only for biotech activities (2019)
Source: for manufacturing selected data 28 March 2022, 15h41 UTC (GMT) da I.Stat - last available data 2019

Intra-mural R&D investments' distribution, per prevailing field of application (2020)



The human healthcare field remains the driving force of the biotech industry, but after several years in which the investments of some large industrial groups have been lacking, due to financial crisis, the R&D investment by firms operating in the industrial biotech field picked up, and in 2020 its share was close to 12%.



Intra-mural R&D investments allocation per field of prevailing application and per type of company

Field of prevailing activity	Type of firm	Total Intra-mural R&D investments	Biotech Intra-mural R&D investments
Healthcare	Total biotech firms	1.512.541	530.054
	Biotech R&D dedicated firms	496.124	473.937
	Nationally controlled biotech R&D dedicated firms	2.492.856	238.644
GPET	Total biotech firms	32.177	11.193
	Biotech R&D dedicated firms	7.596	7.456
	Nationally controlled biotech R&D dedicated firms	7.258	7.117
Industry & Environment	Total biotech firms	214.850	43.608
	Biotech R&D dedicated firms	17.290	15.907
	Nationally controlled biotech R&D dedicated firms	13.934	12.997
Agriculture & Veterinary	Total biotech firms	51.421	17.322
	Biotech R&D dedicated firms	10.318	10.266
	Nationally controlled biotech R&D dedicated firms	8.525	8.473

value in thousand of euros

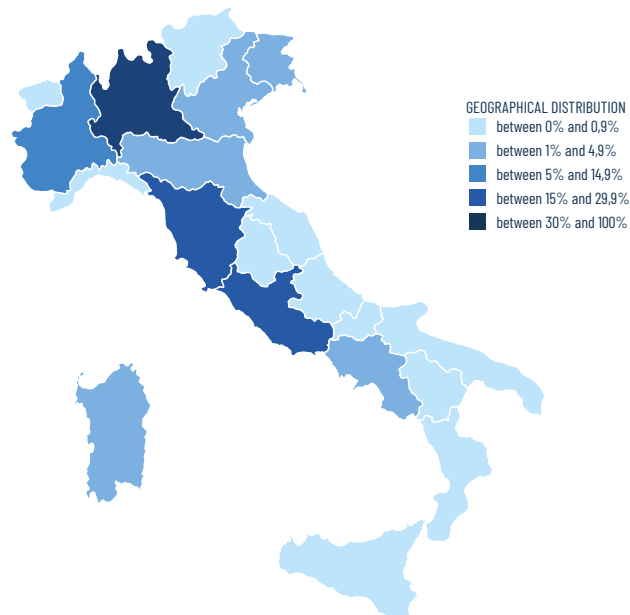
With reference to the total intra-mural R&D investments, 85% comes from the life sciences sector (healthcare and GPET), and the percentage increases up to 90% in reference to the investments from both, the biotech R&D dedicated firms as a whole and the nationally controlled ones.

The percentage of intra-mural R&D investments for the bioeconomy sector (industry & environment, Agriculture & Veterinary) is roughly 15% of the total, with a slight increase (+1%) when compared to the data recorded in 2015.

Biotech intra-mural R&D investments – geographical distribution, per legal head offices

Similarly, to biotech turnover, biotechnology for health is dominant also for R&D investments. The concentration of such investments in the first 4 regions (Lombardy, Latium, Tuscany and Piedmont) is close to 85% on the overall total in 2020, with Lombardy (36%), followed by Latium (24%) and Tuscany (almost 19%).

The territorial areas where the productive fabric is spreading, the southern and north-eastern regions, are characterized by a strong specialization on the bioeconomy field, which is also apparent in biotech R&D investments. Taken together, their share on the overall total R&D investments is nearly 23% for industrial biotechnologies and even exceeds 58% for the “green” biotech in 2020.





4

Developing knowledge

4.1 Scientific publications

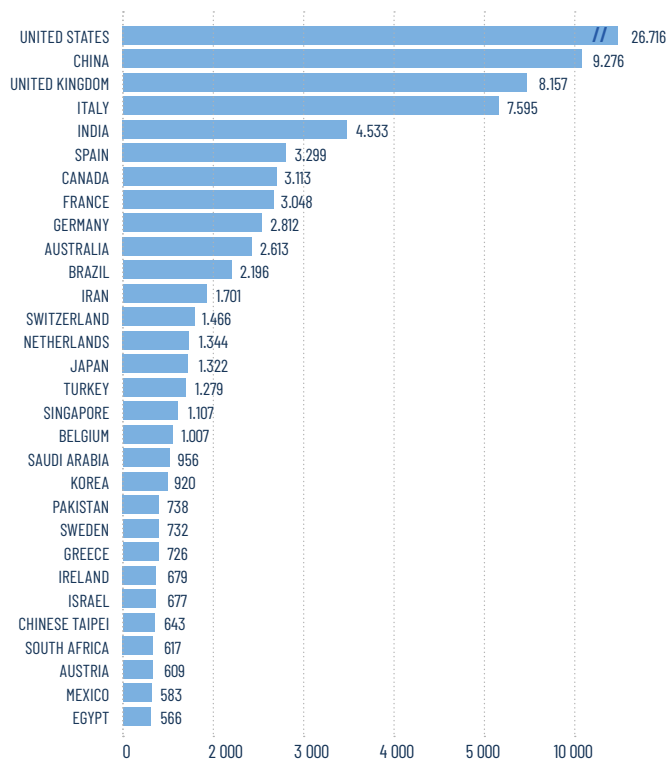
A recent OECD¹ statistical publication has compared data on scientific publications and on citations of the main countries.

In the last decade, as a result of the progress made by China as a scientific superpower, some nations such as USA, UK, Germany and France have fallen behind not only in terms of worldwide scientific articles, but in terms of percentage contribution to the 10% most cited articles.

Our country's scientific structure occupies an important place at international level, although its under sizing problems.

In the next figure, are listed the top contributors to COVID-19 research publications, all with a greater research capacity.

Number of scientific publications on Covid-19, per country (year 2020)



1. OECD Science, Technology and Innovation Outlook 2021 - © OECD 2021

Scientific publications by some OECD countries. Elsevier-OECD database (fractional numbers)

Country	Country's share on the overall total publications			Country's publications share among the 10% most cited publications		
	Year 2010	Year 2020	% change between 2010 and 2020	Year 2010	Year 2020	% change between 2010 and 2020
Italy	3,0	2,9	-3,3	11,2	13,5	20,5
Germany	5,0	3,7	-26,0	12,2	11,8	-3,3
France	3,5	2,2	-37,1	11,2	10,7	-4,5
USA	21,4	15,6	-27,1	15,5	13,1	-15,5
UK	5,1	3,8	-25,5	13,7	13,6	-0,7
China	15,3	21,2	38,6	-	-	-

Source: OECD, <https://stip.oecd.org/stats/SB-StatTrends.html?i=TOP10>

The share of publications by some member states from the Elsevier-OECD database is shown in the above table. Italy's contribution to the worldwide publications, is roughly 3%.

It should be noted that in the 2010-2020 period, our country held substantially its position, whereas its main competitors, registered a one-fourth reduction of their share, to the advantage of China which has grown almost 39%.

Examining the data referring to the 10% most cited articles, it can be observed that the share of Italian publications has grown 21% over the last decade, while that of the US, UK, Germany and France decreased.

The data suggests that the country's skills are eligible for fundings and support over time. It is reasonable to think that the experience acquired during the pandemic, will also lead to a change in the perception of the value of science.

Number of most cited scientific publications per country of origin

Country	Infectious Diseases					Environment			Energy		
	Year 2010	Year 2019	Year 2020	Variation between 2019 and 2020	% Variation between 2010 and 2020	Year 2010	Year 2020	% Variation between 2010 and 2020	Year 2010	Year 2020	% Variation between 2010 and 2020
Italy	6,3	10,8	14,9	38,0	136,5	10,5	13,0	23,8	13,9	10,4	-25,2
Germany	10,2	14,9	13,1	-12,1	28,4	9,1	9,7	6,6	10,4	10,5	1,0
France	9,6	10,8	10	-7,4	4,2	9,8	8,7	-11,2	11,3	9,3	-17,7
USA	16	14,5	11,5	-20,7	-28,1	11,5	8,7	-24,3	12,9	12,3	-4,7
UK	15,3	15,7	13,9	-11,7	-9,2	12,9	11,4	-11,6	15,0	12,4	-17,3
China	7,3	7,4	14,8	100,0	102,7	10,5	13,0	23,8	5,6	9,7	73,2

Elsevier-OCED database (fractional numbers)

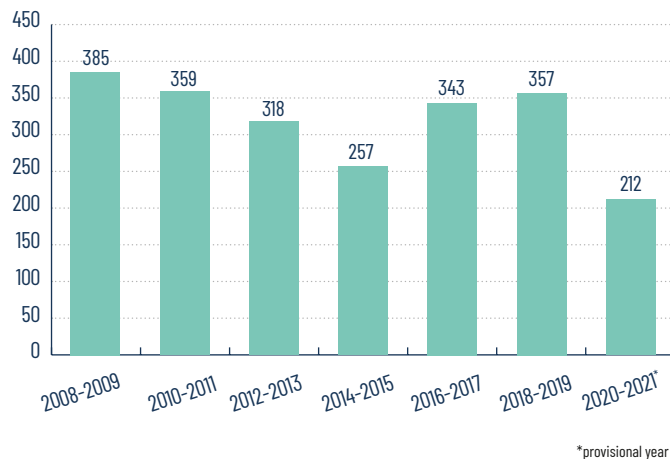
In the case of infectious diseases, the most relevant increase concerns Italy and China, the two mostly affected countries at the beginning of the pandemic. The most significant leap was recorded between 2019 and 2020 (38% and 100%, respectively), which was matched by a decrease for the other countries.

The scientific infrastructure of the infectious diseases, has shown a quick responsiveness as soon as it underwent the Covid ordeal; and same goes for the environmental field.

Our country has a scientific structure available which holds a relevant position on a worldwide stage. During the 2010-2020 decade, such structure has been able to maintain and consolidate, both comparatively and in absolute terms, in terms of citation index.

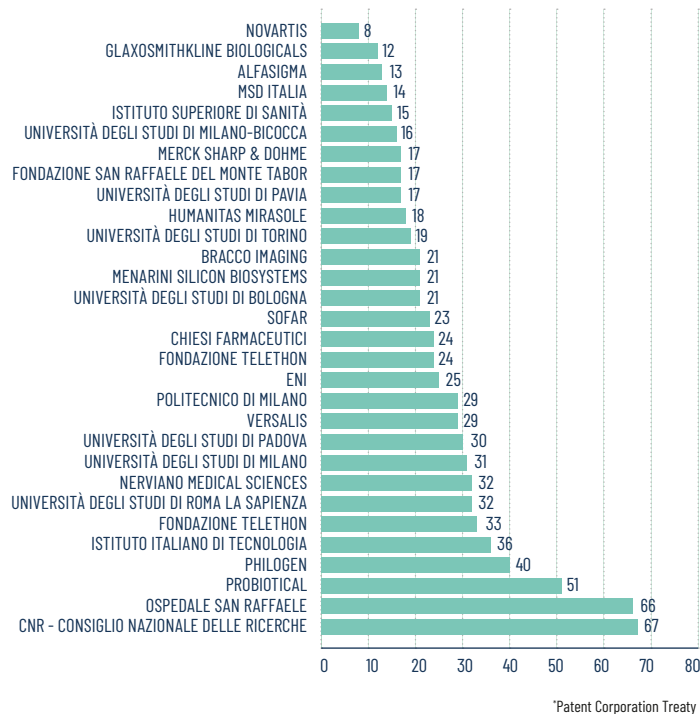
4.2 Patents

Number of biotech PCT* patents applications, filed by Italian assignee, by priority date, between 2008 and 2021



*The PCT (Patent Cooperation Treaty) is a multilateral treaty managed by WIPO (World Intellectual Property Organization), joint by 156 Contracting States, which aims to facilitate the request of protection for an invention simultaneously in several countries, depositing a single international patent application at the Receiving Office (RO) of one of the States Members, instead of several national/regional applications at the competent offices.

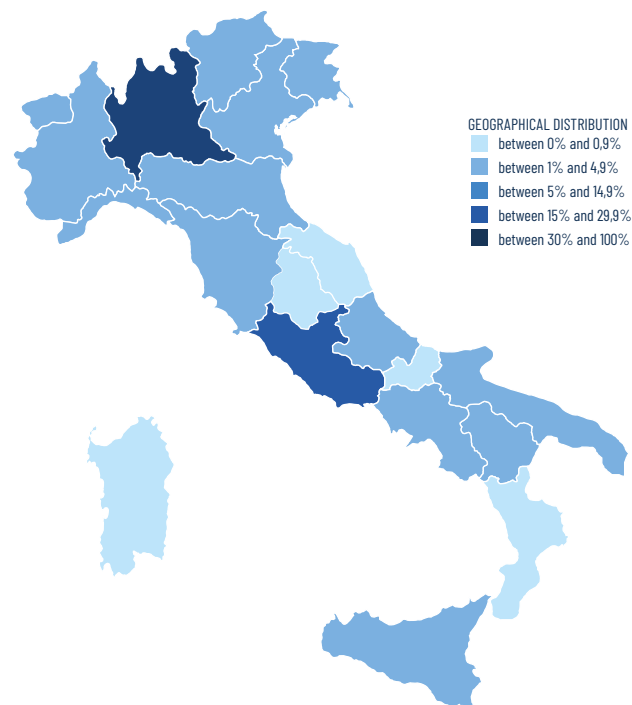
Top Italian assignee of biotech PCT* patent applications by priority date, between 2008 and 2021



Among the main national assignee of biotech PCT patent applications, the relevant contribution of universities, research institutions and hospitals, confirms supporting the competitiveness of the national system of innovation.

National distribution of biotech PCT patents application by assignee and priority date, between 2018 and 2020

Region	Share
Abruzzo	1,5%
Basilicata	0,0%
Calabria	0,5%
Campania	3,8%
Emilia-Romagna	8,6%
Friuli-Venezia Giulia	3,7%
Lazio	15,5%
Liguria	2,6%
Lombardy	34,0%
Marche	0,9%
Molise	0,9%
Piedmont	6,9%
Apulia	1,6%
Sardinia	0,6%
Sicily	1,4%
Tuscany	5,1%
Trentino-Alto Adige	4,2%
Umbria	0,0%
Valle d'Aosta	0,0%
Veneto	8,1%



More than 68% of the biotech PCT patents applications, have been filed by companies or local institutions located in the northern part of the country. It has to be pointed out how the contribution of the north-eastern regions (roughly 25%) and of the southern region (roughly 10%), tends to have a higher percentage compared to what has been recorded in terms of firm's biotech R&D shares, thanks to the significant contribution of public research from universities, research institutions and hospitals

4.3 Technology transfer

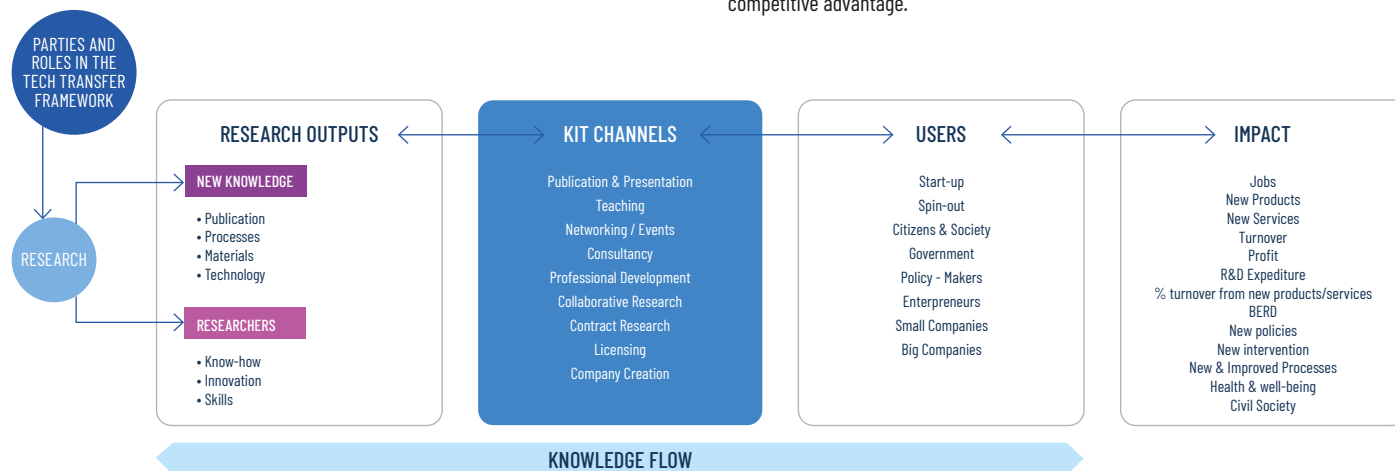
The sectors's strong focus on R&D activities is strictly linked to the nature of its knowledge base.

Biotech is one of the Key Enabling Technologies (KETs) and is therefore characterized by high intensity of knowledge and R&D, rapid innovation cycles and highly qualified personnel.

Biotech also is a "science-based" sector and the nature of knowledge on which is based on has a strong impact on the way and ability to successfully innovate.

The "science based" sectors such as biotech:

- Are highly dependent on developments in the scientific reference base and tend therefore to have close links with public research organizations (Universities and research institutions);
- Should have in-house expertise, nurtured by continuous internal research, which allows to «absorb» knowledge from external sources and manage innovative «open innovation» models;
- Compared to other productive sectors, they tend more to use formal property rights, such as patents for industrial inventions, to appropriate innovations and defend their competitive advantage.



Campbell, A., Cavalade, C., Haunold, C., Karanikic, P., Piccaluga, A., Knowledge Transfer Metrics. Towards a European-wide set of harmonised indicators, Karlsson Dinnetz, M. (Ed.) (2020)

The introduction of changes in the Industrial Property Regulation, first in the US with the Bayh-Dole Act (1980) and later in Europe, has led to a significant increase of the patenting and licensing activity of universities and public research organizations, and to the establishment of Technology Transfer Offices (TTOs). The first TTOs were established in Europe starting from 2000, while in Italy, they were established starting from 2004/2005 with the introduction in the legal system of the Industrial Property Code (DL n. 30 dated 10th February 2005) and nowadays, they are present within all universities and Public Research Institutions. As pointed out by NetVal, the network which gathers the Italian TTOs, some highly recommended actions are outlined here below:

- Modify Art.65 of the Industrial Property Code (Professor Privilege) – which will allow to recognize the institutions' ownership of the innovations stemming from public research
- Reinforce the TTOs which are usually undersized and lack the necessary technical and legal competences
- Increase the “proof of concept” funding – in order to fund those phases which preceding the industrialization of the researches' outcome
- Clarify the existing legal framework related to the State-controlled companies, which hamper the development of academic spin-offs

Supporting actions

- In April 2022, the Italian Council of Ministers has approved the Draft Law for the reform of the Industrial Property Code overturning the current relationship between researchers and universities or public research organizations on the ownership of public research inventions (Professor Privilege).
- So far, 3 tenders have been issued by the MiSE (Minister of Economic Development), to enhance the TTOs, with the last being in 2019
- In 2019, the MiSE has also issued the first experimental tender in order to set-up patents enhancement programs, through proof of concept (poc) projects' funding. This initiative joins the existing experimental initiatives already activated by some universities and public research organizations using their own funds.
- In 2016, the Credit and Deposit Treasury and the European Investment Fund (EIF) have launched the ITAtech investment platform, with 200 million euro available and the aim of filling the gap between the high quality of the Italian scientific production and the investments in the public research results by venture capital funds

The activities related to technology transfer have assumed considerable importance for the top five institutions. «These institutions represent one fifth of the Italian TT employees but their importance, in terms of patents, licensing contracts and income, is much higher»². On the other hand, this data is consistent with what was also found, at a european level, by ASTP (Association of European Science and Technology Transfer Professionals) which in its Report on 2018³ refers in 2018³ that 31% of the TTOs do not declare licensing income, 30% declare less then 50.000 euro and only 13% declare income for more than 1 mln euro. A distortion in the income distribution which has also a sector-bias, with the biomedical technologies contributing with the largest share⁴.

2020 TTs data

TTOs (ETP) employees	473,9
New patents applications	550
Portfolio patents	7815
IP protection investments	5,5 mln euro
Number of license/options	158
Licenses income	3,8 mln euro
New spin-off companies	113

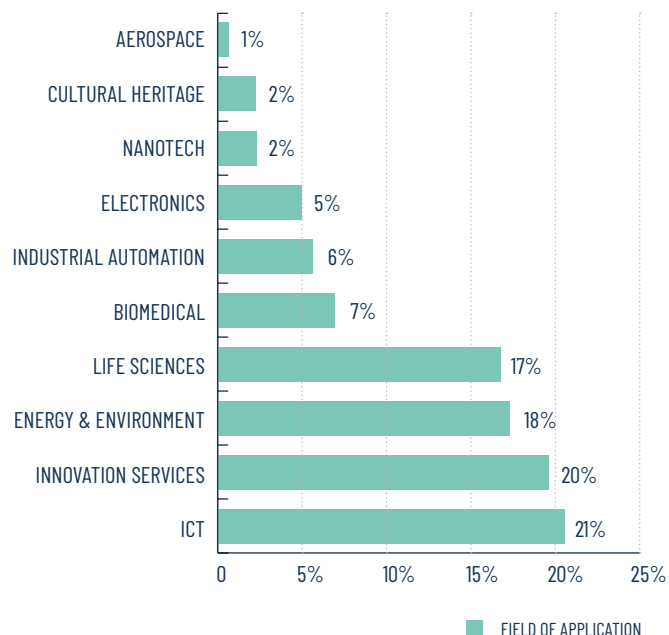
Source: 2021 NetVal Report

2. NETVAL (2021), 17th Report 'investing in research enhancement for regenerative resilience'»

3. ASTP 2020 Survey Report on knowledge transfer activities in Europe

4. Science and Technology Options Assessment, DG Impact Assessment and European Added Value (2012): Knowledge Transfer from Public Research Organisations

Public research spin-offs share distribution, per field (2009 - 2019)



With regards to inventions stemming from universities and public research organizations, the legal framework on the inventions' ownership and allocation of the income deriving from it, can represent a tough challenge in the relationship between each single party who have taken part in the research, and/or for the activity of the company, which is based on the results of each research and eventually becomes a business.

As observed in the table, the Life Sciences and the Biomedical sectors represent roughly 24% of the spin-offs founded between 2009 al 2019, with 335 Spin-offs for Life Sciences and 140 Spin-offs in the Biomedical field. The overall highest number is related to the ICT field (411), followed by the Innovation field (392) and the Energy & Environment field (346).

5

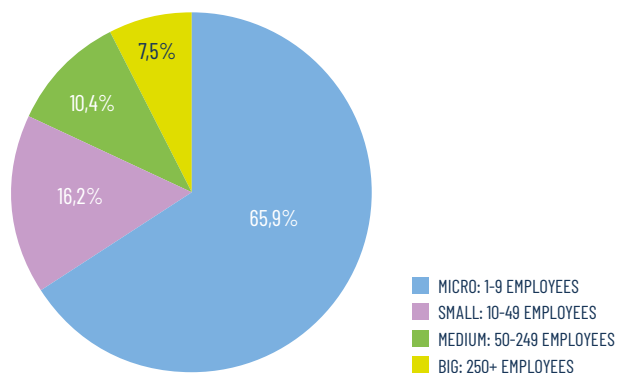
Business categories

5.1 Business size

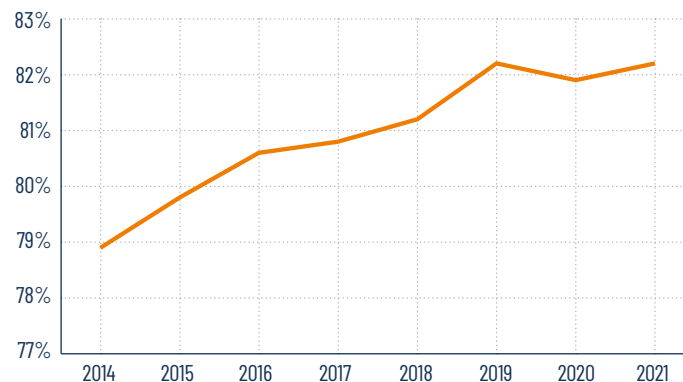
The micro firms (1-9 employees) represent the major proportion of the national biotech firms which added to the small firms (10-49 employees) account for 82% of the biotech firms as a whole. The temporary reduction of the number of companies registered in 2020 is mainly due to the trend followed by this dynamic system of small and micro enterprises focused on the development of new technologies and products, that has grown around

the stable core of large companies. These companies have been most affected by the health crisis, especially in the lower class, up to 10 employees. In any case, as can be seen from the trend line, the slight slowdown recorded in 2020 (-1% compared to 2019) seems to have been recovered in 2021, with the resumption of the expansion trend.

2021 biotech firms distribution, by business size



Number of small and micro biotech firms, between 2014-2021

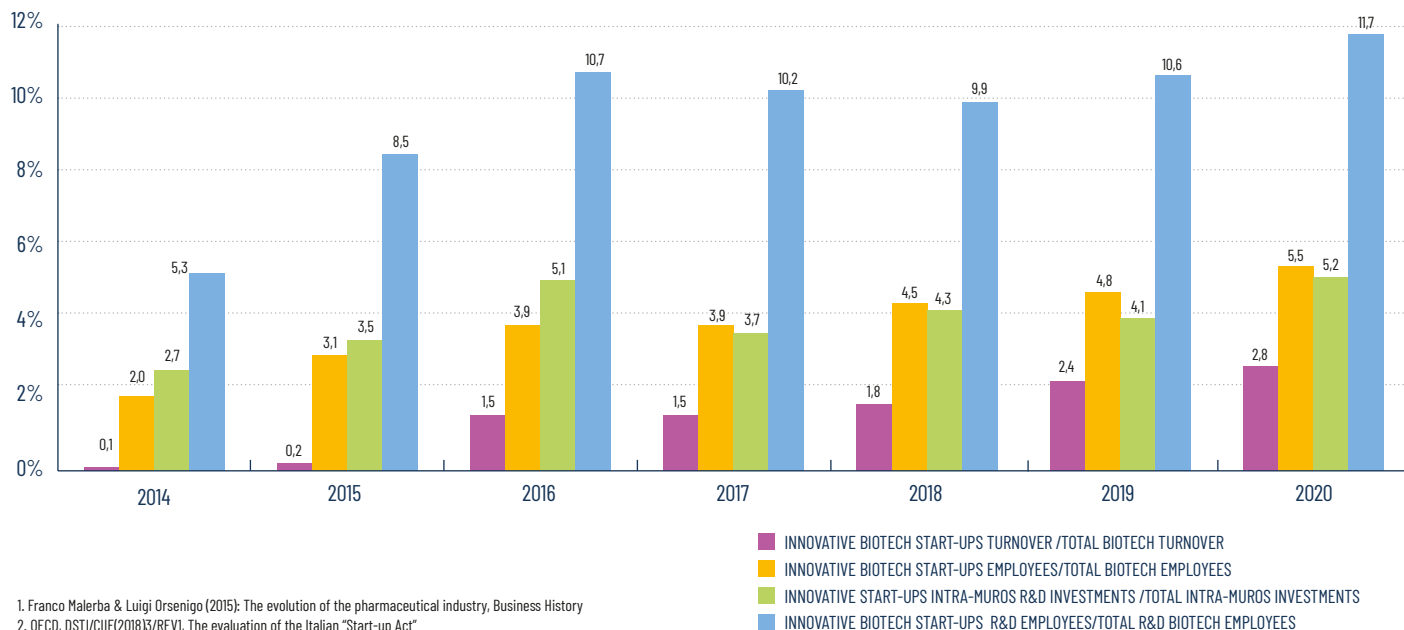


5.2 Innovative Start-Ups

Most start-ups are essentially qualified as supplier of specific skills, to “traditional” companies which have the necessary complementary assets to reach the market and enhance innovations¹ (as for example, the clinical trials required to develop drugs, rather than the regulation procedures to be followed in order to launch, produce and promote a new product on the market).

This creates alliances and strategic cooperation networks, which determine a working distribution in the production chain.

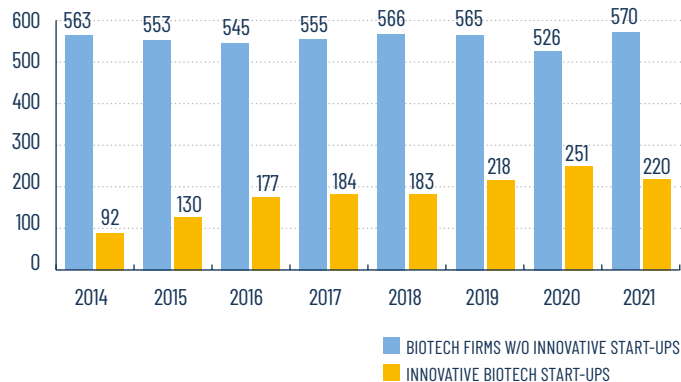
Moreover, empirical evidence, demonstrates a big contribution by these firms in the creation of new jobs, which goes beyond their importance on the overall employment². In 2020, 65% of the new biotech jobs are ascribable to the innovative start-ups, despite these representing only 6% of the total biotech employment.



1. Franco Malerba & Luigi Orsenigo (2015): The evolution of the pharmaceutical industry, Business History
 2. OECD, DSTI/CIE(2018)3/REV1, The evaluation of the Italian “Start-up Act”

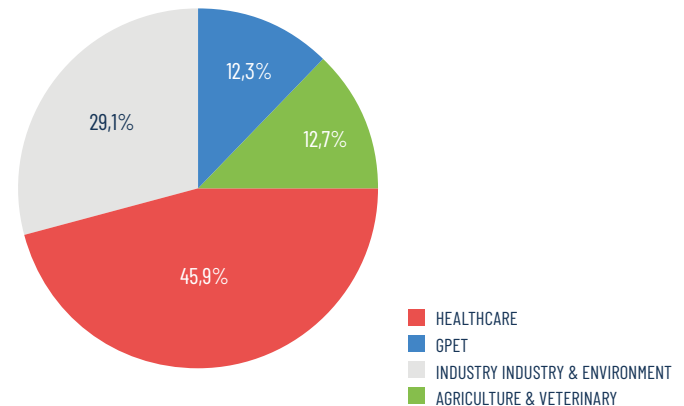
By observing the histogram here below, which shows the innovative start-ups compared to the overall total biotech firms in details, the number of innovative start-ups has progressively grown, between 2014 and 2021, and represents roughly one third of biotech firms.

Number of Innovative start-ups and biotech firms, between 2014 and 2021



Evaluating the industry's composition per field of application, the firms operating in the human health sector are prevailing (46%), followed by the firms operating in the bio-industry sector (30%), with firms operating in the agriculture and GPET fields having a similar percentage, 13% and 12% respectively.

Innovative Start-Ups distribution, by predominant field of application



6

Financing sources

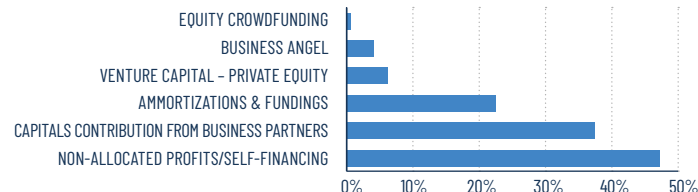
6.1 Funds raising

The capitals needed to fund the activities of the Italian companies active in the biotech industry, both in terms of research and production, mainly derive from resources made available by the ownership: in the form of capital contributions by shareholders, retained earnings or depreciation and provisions according to the structure and size of the company.

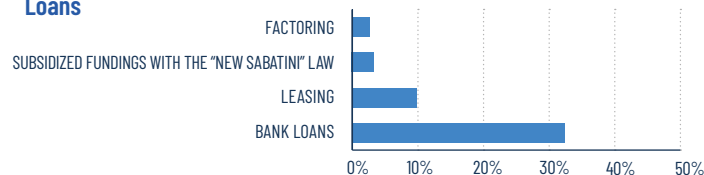
From the data gathered between 2017 and 2020 it can be seen a constant growth of the share of companies funded by Business Angels and Venture Capitals' contribution (about 4% and 6% of the total in 2020, respectively).

The role of grants remain central, and even more companies have claimed to benefit from them (over 30% in 2020), mainly large size companies which are active in the human health field.

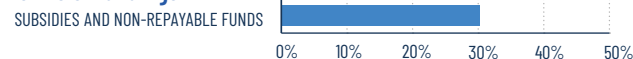
Capital fundings



Loans



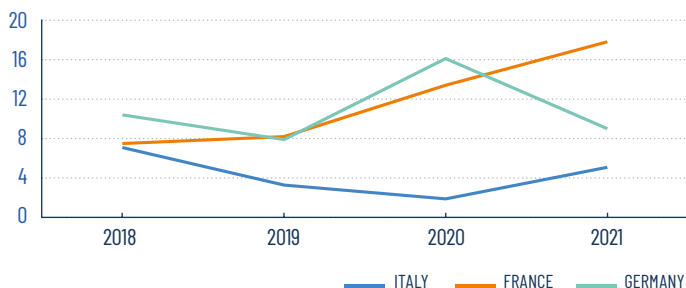
Other forms of fundings



6.2 Biotech Venture Capital

Starting from the Italian Private Equity, Venture Capital e Private Debt Association (AIFI) data, we've been able to compare the number of financing operations made by France and Germany, European reference countries, with Italy in relation to biotech SMEs and Star-ups' financing.

Average size investments for Italy, France and Germany, in mln of €



As per the below table, Italy sadly ranks last with an average investment of 5 million euros in 2021. Despite this figure doubling since 2020, it is still half compared to Germany and less than a third when compared to France.

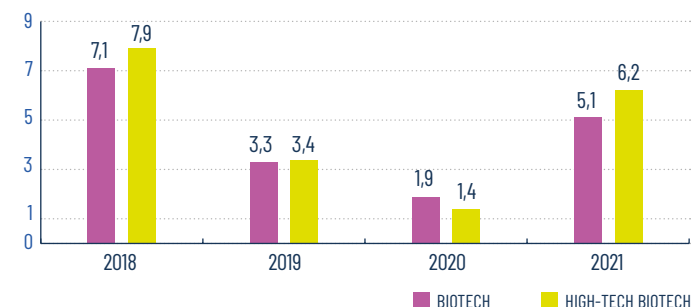
Average investment sum for Italy, France and Germany

	2018	2019	2020	2021
Italy	7,1	3,3	1,9	5,1
France	7,5	8,2	13,4	17,8
Germany	10,4	7,9	16,1	9,0

Source: AIFI – PwC for Italy, France Invest for France, BvK for Germany, values in million of euros

With reference to the financing operations in the biotech field in Italy for 2021, there have been 22 financial operations for a total of 112 million euros. Most of these operations, 16 out of 22 for a 73%, have been in favor of high-tech biotech firms

Average size investments in the biotech and high-tech biotech fields



The average investment in the biotech field, which is roughly 5 million euros, is lower than the average investment in the high-tech biotech, which exceeded 6 million euros in 2021.

Biotech and high-tech biotech average investment sum

	2018	2019	2020	2021
Biotech	7,1	3,3	1,9	5,1
High-tech biotech	7,9	3,4	1,4	6,2

6.3 Public schemes

With the aim of developing the growth of specialized start-ups within potential markets, Terra Next has been launched. It's an acceleration program for Innovative SMEs and start-ups operating in the bioeconomy field. Promoted by CDP Venture Capital, the program is part of the CDP National Accelerator network, a network operating on national level. Terra Next also involves Intesa Sanpaolo Bank's Innovation Center, as promoter and the support of Cariplo Factory, which will manage the operations.

In September 2021, a new partnership agreement has been signed between CDP Venture Capital SGR and the European Investments Fund (EIF), in order to perform 260 million euros investments aimed at launching new funds, to develop deep-tech start-ups. These are entrepreneurial entities which develop frontier technologies, conceived within universities' labs and research institutions.

In the month of January 2022, the new "ENEA Tech & Biomedical" has started operations and it will manage, on behalf of MiSE, both the "Tech Transfer Fund" and the new "Research & Industrial Development Fund", set up with the new budget law. The foundation, will initially have 500 million euros available, for both funds mentioned here above, in order to sustain tech transfer and research activities investments, facilitating the cooperation between SMEs, innovative start-ups and universities and in general, between the research field and firms, in all strategic sectors for the country's competitiveness.

7

**Life
sciences**

The scientific development is an unstoppable process. Every single evolutionary leap comes with revolutionary repercussion in the medical assistance field. In less than 40 years, the biotech healthcare has gone from the 'simple' replication of the natural cellular mechanisms, for the production of therapeutic proteins, to tissue engineering, surgical correction of DNA pathologies and the development of fast diagnostics which uses artificial intelligence. From the mix of know-how which weave together and influence one another, new promising applications are born and will eventually be developed in the coming years: big-data, artificial intelligence, machine learning, 3D printers, tools which will be available in several personalized, precision and general healthcare fields.

The firms in Italy that mainly deal with applications linked to the human healthcare field are 48% of the total, and increases to 58% for biotech R&D firms which dedicate 75% or more of their total costs in biotech activities, and which happen to be, for the most part, Italian owned firms.

The overall turnover of the firms operating in the healthcare field exceeds 7,5 billion euros. The health sector has generated in 2020 a preponderant share of the overall turnover (75%), as a result of bigger investments (88%) and a bigger share of biotech R&D employees (74%), compared to firms operating within other prevailing fields of application. With reference to the biotech turnover trend, the most significant data is the 158% increase from 2014 to 2020, which refers the nationally controlled biotech R&D dedicated firms.

Year 2020	Total firms	Biotech R&D dedicates firms	Nationally controlled biotech R&D dedicated firms
Number of firms	376	246	231
Turnover	7.569.343	3.713.378	1.392.685
Intra-mural R&D investments	1.512.541	496.124	249.286
Biotech Intra-mural R&D investments	530.054	473.937	238.644
Biotech employees	8.757	5.478	3.465
Biotech R&D employees	3.596	2.673	1.624

Values in thousands of euros

7.2 GPET

Since the 50s, molecular biology has made enormous progress. With the discovery of DNA as messenger molecule of genetic information, by Watson and Crick, there have been a series of scientific progress which now have an omic extension and reflect the so-called central dogma of molecular biology: from DNA to proteins through RNA.

The omic sciences enables to go from a “general” approach to an “individual” approach which medical science has always been looking for and meets the patients’ and its pathology’s needs, in a very specific way. The uniqueness of a patient, and the necessity to calibrate the therapy, finds within the omic sciences, the necessary tools for an appropriate clinical management of the disease¹.

Year 2020	Total biotech firms	Biotech R&D dedicates firms	Nationally controlled biotech R&D dedicated firms
Number of firms	91	48	46
Turnover	106.730	60.648	56.388
Intra-mural R&D investments	32.177	7.596	7.258
Biotech Intra-mural R&D investments	11.193	7.456	7.117
Biotech employees	521	216	205
Biotech R&D employees	279	135	130

Values in thousands of euros

The total number of firms within this field has been unchanged in the last years, representing roughly 11% of the total biotech firms recorded. However, there is a promising

trend in terms of both, the total and the nationally controlled biotech R&D dedicated firms, with an increase of 62% and 52% respectively.

1. https://www.simg.it/Riviste/rivista_simg/2018/01_2018/1.pdf

7.3 Strategic therapeutics fields

The biotech contribution in the collective fight against the coronavirus SARS CoV-2 has been crucial, to sequence the virus, to identify the entry receptor, to develop diagnostics and, let's not forget it, research an efficient therapy through antiviral drugs and the testing of new monoclonal antibodies for therapeutic and prophylactic purposes. The Italian biotech companies have been on the frontline in this fight against the pandemic, having committed and invested heavily in the infective diseases field, throughout 2021 as well.

From the data gathered and recorded by ISTAT, there have been 49 thousands more deaths throughout March and April 2020, when compared to the same months of the previous five years.

In addition to Covid-19, which happens to be the second cause of death right after tumors, the national biotech research interests are focused on developing a therapeutic solution for oncology. There has also been a strong commitment in developing products, which are currently undergoing testing, for the infective diseases field. This field has attracted a lot of interest in the last few years and has recorded an increase in the investments from many companies.

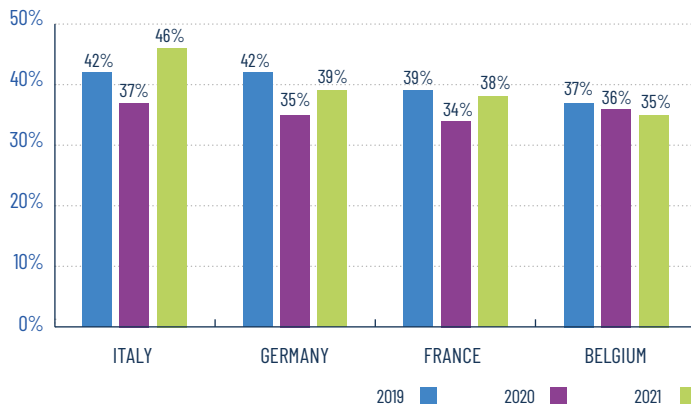
In the above-mentioned therapeutic fields, there are firms which are committed in treating rare diseases and develop advanced therapies focusing on the necessities and characteristics of each patient.



7.4 Rare diseases

Here below there is a comparison between some of the most active European countries in the clinical research field. We are looking in particular at the percentage of rare diseases dedicated projects on the overall total.

Rare Diseases trials percentage on the total active trials

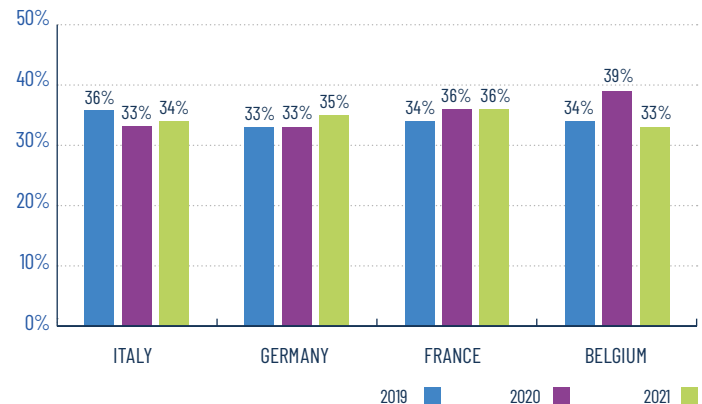


Data source: <https://www.clinicaltrialsregister.eu/>

With reference to the commitment towards these pathologies, Italy ranks first with a 46% in 2021, followed by Germany (39%), France (38%) and Belgium (36%). It is interesting to note a decrease in 2020, for all countries.

In the following histogram we can observe the trend, regarding the percentage of completed projects on rare diseases against the overall total, for the last three years 2019-2021.

Rare Diseases trials percentage on the total completed trials



Despite France having completed the biggest percentage of RD dedicated projects in 2021 with 36% (150/422), Italy remains first in terms of absolute numbers (305/890), followed by Germany (225/642). Belgium's number is equal to France (150 studies) but with a lower percentage of studies due to the higher number of overall projects (454).

As observed with the projects' tendency, the major commitments in the RD dedicated studies are concentrated on phase III, due to the market's demand of therapies undergoing studies. More than 50% of the active or completed studies in Italy for 2021, were in phase III.

7.5 Advanced Therapies

For advanced therapies, technically known as ATMPs (Advanced Therapy Medicinal Products), we mean those therapies or innovative drugs which differentiate from "classic" drugs as they are based on DNA or RNA, cells and tissues. The advanced therapies, which are the result of the progress made in the last twenty years within biotech, are an emerging field within biomedicine and offer new opportunities for diagnosis, prevention or the treatment of severe diseases which have limited or no therapeutic options such as: genetic diseases, chronic diseases and tumors. These innovative therapies are also being used to treat severe burns and injuries.

The advanced therapies can be split within the following categories:

- Gene therapy products, which treat diseases caused by faulty genes. The active mechanism is being carried out by DNA or RNA, with the aim of correcting the genetic defect within the patient's cells. This also includes the genomic editing techniques, with the well known CRISPR- Cas9 first and foremost.
- Cell therapy products, which use a formula containing life cells in order to obtain a therapeutic, diagnostic or preventing effect. This type of therapy could involve the use of adult stem cells, which are present within our body and are able to differentiate themselves in order to create several different tissues.
- Tissue engineering products, which are based on cells and tissue developed within a lab, in order to regenerate, repair or replace human tissues. Through the use of this technique, skin, bones and cartilage have been regenerated.

- The regenerative medicine projects are dedicated to musculoskeletal diseases while those referring to the gene and cell therapies, involve the cardiovascular, oncological and dermatological therapeutic fields, followed by the neurological or of metabolic or musculoskeletal interests, with a greater variable for those projects referring to cell therapies, where we can find projects dedicated to inflammatory and autoimmune diseases.

Based on the results of the survey carried out in 2021, 35 projects, split as per type of advanced therapy and phase's stage, have been identified and recorded in the below table.

	Cell Therapy	Gene Therapy	Regenerative Medicine	Total
Discovery	2	1	1	4
Preclinical	3	0	2	5
Phase I	1	8	0	9
Phase II	1	11	0	12
Phase III	3	2	0	5
Total	10	22	3	35

Source: 2021 survey's results

8

Bioeconomy



The pandemic has unveiled the weaknesses of the current consumption and production model, which is based on the dissipation of natural resources, production delocalization and territorial disconnection, having a strong impact on the environment. It is time to leave this development approach based on reaching our goals in the short time, and the idea of an unlimited growth, to the detriment of a better life quality and the natural and social wealth of the community.

At the heart of the bioeconomy is the smart commitment to renewable resources of biological origin, which in a circular logic, gives value to the recyclable opportunity through the use of technological innovation.

Within the bioeconomy the following fields: agriculture, fishing, silviculture, wood & paper industry and bio-based industry are included. This is an articulate concept including multiple fields, which as a common ground have the biological and renewable origin of the inputs, that could follow different developing dynamics, influenced by the various peculiarities of each field.

The reuse of wastes and secondary prime materials, is vital for those industrial fields which traditionally use biological resources as main refueling source (forestry, starch, sugar, biofuels/bioenergy, biotech) and for others for which biomass is among the prime materials being used (chemical field, plastic and consumer goods).

Despite the impact of the health emergency caused by Covid-19, the circular bioeconomy model has proven a strong resilience, thanks to its intrinsic ability to adapt and rethink its production logic, without compromising the productive stability, health and the community's safeguard.

8.1 Industrial biotech

The industrial biotech uses cells – yeasts, molds, bacterium, plants – and enzymes, in order to develop bios-based products such as bio-plastic, biological materials for construction, cosmetic products and bio-fuels, just to mention a few.

The conscious and consolidated use of the richness offered by nature, by an industry which is capable of converting natural products and processes into market solutions, is not something new. The first enzyme developed for the detergent industry has been launched in the late 1988.

Thanks to the industrial biotech, we now have high value products, with more efficiency in terms of costs and environmental sustainability but also biodegradable solutions, which require less water and fossil fuels, producing less wastes during the production cycle.

The industrial biotech's fields of application are numerous: from biotransformation for redeveloping the traditional industrial processes through enzymatic catalysis, to the preparation of chemical composite by fermentation, from bioplastic production to bioremediation and environmental diagnostics, from bioenergy production to the restoration and conservation of the cultural heritage, up to the development of new tissues for the clothing industry.

Applying these techniques will allow to innovate developed fields such as: prime materials, energy production and intermediates, sticking to the environmental sustainability, economic and social principles, which belong to the bioeconomy.



Year 2020	Total biotech firms	Biotech R&D dedicated firms	Nationally controlled biotech R&D dedicated firms
Number of firms	233	101	97
Turnover	1.768.807	189.945	175.248
Intra-mural R&D investments	214.850	17.290	13.934
Biotech Intra-mural R&D investments	43.608	15.907	12.997
Biotech employees	2.871	664	609
Biotech R&D employees	784	346	323

Values in thousands of euros

The sector's turnover has exceeded 1,7 billion euros, a slight decrease when compared to the previous year. A trend in the same direction is also observed for the biotech R&D dedicated firms. The biotech intra-mural R&D investments for the overall total number of firms has grown 9% in the same period.

With reference to the total number of employees, there has been an increase for all three companies' categories, when compared to the previous year, with a 4% for the overall total number of companies and 7% for the biotech R&D dedicated firms (both nationally and foreign controlled).

8.2 Agriculture & Veterinary

The bio-agromedicines, biostimulatives and biofertilizers production, the genetic improvement activities (breeding) of various plants are all sectors which will provide biotech solutions to various agro-zootechnical productive fields, which is always on the look out for new innovative and sustainable systems.

The Italian public research had widely demonstrated an excellent profile with regards to the applied biotechnologies, aimed at the plant genetic improvement (Plant Breeding Innovation). The information availability on the cultivations' genome represents the basis upon which enhancing the local biodiversity, in response to the needs of the specialized and diversified Italian agriculture. The frontier of plant genetic improvement is represented by the most sophisticated genetic editing techniques.

The plants' genetic profile know-how and the availability of fast and precise techniques which can act within a single specie, without any use of external genetic material, allows to challenge a series of problems which are typical of the Italian cultivations.

In a wider framework, the development of genetic improvement programs based on biotech will allow to carry out research aimed at capitalizing the results of genomic sequencing of various species which are important for the country, build new genotypes which fulfill the needs of the country's agriculture (to safeguard local production as well), and overcome the genetic material supply dependence from abroad, through the exploitation of the biodiversity (local genotype).



Year 2020	Total biotech firms	Biotech R&D dedicated firms	Nationally controlled biotech R&D dedicated firms
Number of firms	77	27	26
Turnover	797.963	20.744	20.106
Intra-mural R&D investments	51.421	10.318	8.525
Biotech intra-mural R&D investments	17.322	10.266	8.473
Biotech employees	1.128	164	155
R&D biotech employees	218	106	105

Values in thousands of euros

The industry's turnover for 2020 was nearly 800 million euros, recording a 23% increase since 2015. On the other hand, the turnover of the biotech dedicated firms, including the nationally owned firms, has decreased 15% compared to 2015.

The biotech R&D intra-muros investments represent half the turnover of the biotech dedicated firms, and more than 40% for the nationally owned biotech firms, recording an increase of 30% and 17% respectively for 2015.

With regards to the employees, there has been a 10% decrease for the total overall firms operating in this industry while for the biotech dedicated firms, including the nationally owned firms, the decrease has been 5% when compared to the previous year.

8 Credits

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