LEAP-BIO

Study 1 Europe's life sciences dynamic: a mosaic of challenges and opportunities

LEAP-BIO is a COSME project which aims to develop IP licensing intermediary services for early stage assets in Pharma and BIOtech.

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Introduction & study methodology

Europe is one of the world's main life sciences hubs. Roche, BMS, Sanofi, Bayer, GSK, Novo Nordisk… Many of the largest pharma companies have their headquarters in Europe and a lot of the top universities are on the continent.

With $21B of venture capital raised by European life sciences companies between 2016 and 2021, Europe seems to be a must on the international stage. But the region lags far behind the US, which accounts for 68% of the global venture capital flow and is still the main hub for new therapeutics.

The US market accounts for 64.4% of sales of new medicines launched between 2016 and 2021, while the European Market was only at 16.8%. (IQVIA MIDAS, May 2022). This figure highlights the hegemony of the US in the global life sciences sector and their lead in innovation.

On the other hand, the BRICS (especially China and India) are on the rise and are gradually moving into second place in the life sciences industry, overshadowing Europe. To demonstrate, while the US and European markets grew by 5.6% and 5.8% respectively during the 2016-2021 period, the Brazilian and Indian markets registered a growth of almost 12%. During the 2017-2021 period, the pharmaceutical R&D expenditure in China grew at an annual rate of 12.9%, 4.4 points over the US. In comparison, the annual growth rate of pharmaceutical R&D expenditure in Europe over the same period was only 4% (EFPIA, 2022). This increase in R&D efforts is already paying off: in 2021, China launched almost the same number of new substances as Europe (IQVIA MIDAS, May 2022).

In this highly competitive landscape, Europe faces some challenges if it wishes to remain competitive worldwide. Europe is often compared to countries such as China or the US, but it encompasses several countries with very different situations, economies, and policies. By looking into greater detail about what makes European countries attractive for the life sciences industry, we can highlight the good practices and emphasise the under-used potential of some regions. As part of LEAP-BIO, a COSME project aiming to address a lack of intermediary services towards IP licensing and exploitation in some key-target European regions/countries, we will take a closer look at Spain, Portugal, Italy, France, and the Wallonian region (Belgium) with a view to comparing the practices of southern and central European countries to those of northern Europe.

Lastly, we will examine the trends in life sciences to better understand the hottest topics and challenges that European countries must deal with.

Europe: a breeding ground ecosystem with an under-used potential

Europe can count on world-class hospitals and research centres to create new innovations that can be game changers. In 2018, Europe produced more than 1.75 million life sciences-related publications, more than the United States or China. In terms of quality, with 32% of the top 50 Universities located across Europe, the continent is the world's second hotspot for academic excellence, immediately behind the United States (McKinsey & Company, 2019).

The average European scientist is also more competitive than the average American scientist, with only Chinese scientists being cheaper worldwide. (Glassdoor, Savills)

At first glance, Europe appears to be one of the most competitive places for life sciences deals. However, Europe is far behind China and the United States in terms of new patents: almost three times fewer patents in Europe compared to the United States in 2018, ten times fewer than China (McKinsey & Company, 2019).

These figures highlight the leading role of Europe in life sciences research, along with its lack of efficiency in translating those materials into new biotech companies and/or licensing deals.

One must keep in mind that Europe is not a homogenous region, and that this general assessment varies greatly between countries.

Europe remains a highly fragmented landscape, and the high-level academic ecosystem is concentrated primarily in Western and Northern Europe, namely the United Kingdom, Germany, France, Switzerland, the Netherlands, Belgium, and Sweden. These academic clusters are also the main hub for the establishment of biotech companies, rendering Europe very polarised: half of the European biotech companies created between 2012 and 2019 are based in France, Germany and the United Kingdom, and the UK alone account for 35% of those new businesses (McKinsey & Company, 2019).

Conversely, Belgium, Switzerland, and the Netherlands are booming in the life sciences market, although their baselines remain lower.

France and Germany, alongside southern European countries such as Italy and Spain, have a similar or even higher number of academic publications than the United Kingdom, Switzerland, Belgium, and the Netherlands, though this is not reflected in the number of patents and biotech companies.

These statistics highlight the strong academic orientation of certain European countries, with high-quality research, but which does not translate into the creation of biotechnology companies on their territory (Figure 1). This could also show the lack of technological transfer and the difficulties of dealing with intellectual properties between actors.

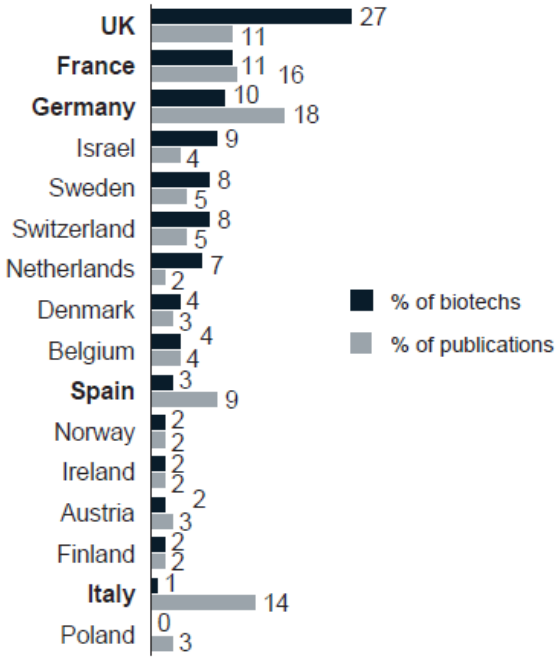

Figure 1: Contribution of European countries in terms of number of biotech companies and academic publications between 2005 and 2019.

Countries with many publications (>9% of total publications) are shown in bold.

The effort on academic research (quantified here by the number of publications) does not translate evenly to the number of biotech companies in the countries. (Source: McKinsey and Company, 2019)

From this global overview of Europe, we can distinguish 4 main types of countries:

- "Translation-effective" countries, with the United Kingdom as the main representative, but also followed by Belgium (especially the Flemish region), Switzerland, the Netherlands, and to a lesser extent the Nordic countries. These countries are highly effective in translating innovation into biotech companies. They are the powerhouse of Europe's dynamic in the life sciences market.
- "Under-performing" countries, namely France and Germany are still major players in the European landscape thanks to their strong academic baseline, but are not as efficient as their neighbours in terms of technological transfer opportunities.
- "Academic-focused" countries, for example Italy and Spain which are active in terms of publications, though they fail to translate this into biotech companies.
- "Underinvested" countries, mainly in eastern Europe where R&D and academic research expenditures are low and technological transfer opportunities are rare.

To keep Europe competitive on a global scale, it seems mandatory to develop new tools and policies to help countries with a great academic breeding ground. These countries have room for improvement and the LEAP-BIO project represents a real opportunity to fill the gaps with northern European countries, leading to a more competitive European life sciences industry.

The regions targeted by the LEAP-BIO project are France, Italy, Portugal, Spain, and the Wallonia region (Belgium). As described above, these regions have different profiles.

Despite its deceleration over the past decades, France has still an important ecosystem, with 947 biotech companies and 881 fully integrated pharma companies in 2023 (Biotechgate, 2023). France is investing in ambitious projects to improve its competitiveness, such as international "Bioclusters", technological hubs inspired by the

Boston Biocluster that aims to bring together academic research and public actors. Venture financing in the life sciences is also increasing in France to help new companies to develop. The Private equity rounds in 2022 reached $997M compared to $852M in 2021, with fundraising such as DNA Script SAS ($200M) and ImCheck Therapeutics SAS ($102M).

Italy has strong academic research and a blooming manufacturing ecosystem, especially in the Lombardy region that accounts for 29.5% of the turnover of the Italian Life Sciences value chain (Report no. 7/2022, Assolombarda). In 2022, 823 biotech companies were active in Italy (BioInItaly, 2023). However, as shown on Figure 1, the translation from academic to biotech companies remains below its potential.

R&D investments in Spain doubled between 2009 and 2019 (Labiotech.eu,2019), making the country one of the fastest growing in the European Biotech industry. With 587 companies in 2022 (Biotech Gate, 2023), such as Aelix Therapeutics and Oryzon Genomics, Spain is slowly filling the gap with other European countries. However, the venture funding of biotech companies remains well below its neighbours, with $129M in 2022 (Biotech Gate, 2023).

The Portuguese biotechnology industry consists of 98 firms with a sector turnover of 36.5M€ in 2019 (P-BIO, 2021). These companies are three times smaller than the average EU Biotech firm in terms of number of employees. Portugal's biotech industry's growth is limited by difficulties in gaining access to funding and support to deal with intellectual propriety protection. Hence the lack of real breakthroughs in life sciences. Most innovations in Portugal are essentially based on generic drugs (structural changes of the chemical composition) and not brand new substances (Alevar et al., 2022)

Wallonia's life sciences industry is not as dense as Belgium as a whole, but with 35 entities for 3.6 million inhabitants in 2017, Wallonia has a higher density of companies per inhabitant than France and Germany (BioWin, 2020). The pharmaceutical industry accounts for 3.24% of Wallonia's economy. Local entities are stepping up financial support with R&D incentives such as tax credits and the creation of clusters to support new companies.

What are European Life Sciences Trends?

The European biotech industry, unlike the US, is highly focused on services or supporting technologies (drug-discovery tools, contract research organizations, contract management organizations, etc.), which account for 44% of all EU biotech entities (McKinsey & Company, 2019) and 48% of French biotech firms (Biotech Gate, 2023). This specialization in services may explain in part the low number of new substances coming from Europe.

When one looks into greater detail at the distribution of biotech subsectors, most French companies work on small molecules (16% of all French biotech firms), immunotherapy (12%), antibodies (11%), and Cell and Gene therapy (10%) (Biotech Gate, 2023). At the European level, cell and gene therapy is the hottest topic in terms of publications (38% of European life sciences publications from 2012 to 2019) and patents (39% of European life sciences patents from 2012 to 2019), led by the UK and Germany, and to a lesser extent, Italy, Spain, and France, while Belgium is lagging behind in this field (Biotech Gate, 2023).

The leading therapeutic areas in the European industry are oncology and the central nervous system (CNS), accounting for 42% of biotech companies and half of all investments in 2018 (McKinsey & Company, 2019). To a lesser extent, Immunology and Parasitology are also important asset pipelines, especially in “translational-effective” countries such as the UK and the Netherlands (Biotech Gate, 2023).

The European life sciences sector relies on an open innovation approach, meaning that the industry is growing with partnerships and/or licensing (research collaboration, joint ventures, licenses, etc.). The recent COVID-19 pandemic has been a catalyst for the creation of new opportunities, leading to a record number of deals in 2020. 2021 registered a small decrease, but the number of deals remains high and interestingly, new deals between early-stage startups are becoming increasingly common, allowing alternative funding compared to traditional deals with big pharma. However, this new paradigm leads to more aggressive intellectual property in earlier-stage deals, with real challenges for biotech companies linked to an academic institution and that later want to collaborate with external partners (Goodwill, 2022).

Hence the need for IP support to make the process smoother, and projects such as LEAP-BIO are a first step to improve the competitiveness of European regions and help them reach their maturity.

In Portugal, IP is also an issue as a survey organized by P-Bio highlights that 76% of Portuguese biotech companies surveyed do not have any patents. In Portugal, patents are highly concentrated within just a few companies, and negotiations between small players and the leaders in intellectual property also need to be supported to reach fairer agreements.

Conclusion and Outlook

Europe remains an international hub for the life sciences industry but is now in a global competition with other hubs, namely the US and BRICS. Within Europe, some countries are more active in the local landscape, translating their academic research into blooming biotech companies while other countries have great potential but struggle to create new start-ups.

The open innovation paradigm requires new tools to improve the competitiveness of countries and simplify IP deals. Some regions such as Wallonia have started to implement new policies to create a more dynamic ecosystem and could serve as a model to encourage new countries to boost their life sciences industries.

LEAP-BIO

Study 2 Reshoring, onshoring, nearshoring and outsourcing in Europe for the life sciences industry.

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PARTNERSHIP:

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Introduction – Study methodology

Life Sciences have been affected by globalisation, leading to the offshoring of various links in the value chain in emerging countries such as China or India where the work force is cheaper.

With the Covid-19 pandemic and supply shortage of many vital drugs, Europe's dependency on foreign countries was dramatically exposed and raised concerns in many countries, such as France where an investigative committee headed by the Senate published an alarmist report on the shortage of drugs in France (Report no. 828 (2022-2023), 4th July 2023).

Hence the new "reshoring" trend in many developed countries: globalisation has its limits, especially in a general context of geopolitical crisis, and it seems sensible to have sovereignty by keeping some activities of the life sciences industry "at home", or at least in neighbouring countries. This serves to secure global supply chains in terms of preventing shortages, but also to secure the intellectual property that may be at risk when dealing with external partners.

On the other hand, life sciences are mainly driven by open innovation, and so need to remain open and maintain global cooperation with foreign actors. With the two waves that are currently shaking the industry, new trends, such as "nearshoring" or "outsourcing", are emerging.

We will examine these trends and see how they translate to the European landscape.

As part of LEAP-BIO, a COSME project aiming to address and solve the lack of intermediary services towards IP licensing and exploitation in some key-target European regions/countries, we will highlight some examples in Spain, Portugal, Italy, France, and Wallonia (Belgium).

Outsourcing: a pragmatic solution in an “Open Innovation” life sciences industry

Since the 1990s, life sciences companies have changed their strategy from traditional “in-house” research to a more open strategy based on outsourcing. With the rise in drug development costs and the emergence of biotechnologies, requiring more and more specialised knowledge, it is more efficient and cost effective to collaborate with external partners rather than to keep an extensive internal R&D team that may be outdated in a couple of years. To further reduce the cost of drug development, some actors may choose to deal with Asian actors, such as India or China. However, these countries are often accused of poor IP protection. For example, the European Union requested a consultation with China at the World Trade Organization on 7 December 2022.

Some companies chose to work at a more regional scale, with a more horizontal approach leading to partnerships aimed at creating new competitive entities.

One concrete example of open innovation with a share of intellectual properties, completed by investment in manufacturing in Europe is ONConcept. This firm was created by pooling the Portuguese CDMO Bluepharma with two German companies, Helm, and Welding. This partnership led to the creation of a European value chain from R&D to market supply with a current portfolio of 20 products, mainly in the oncology field.

In 2023, €30M was invested by Bluepharma, as part of the ONConcept strategy, to create a new manufacturing plant in Eiras, Portugal. This new entity represents one of the largest oral solid high-potency drug manufacturing units in Europe, creating more than 100 jobs. This unit highlights the fruitful potential of such a partnership between German companies, providing new intellectual property, and the Portuguese company, which specialises in production.

This collaboration is a good example of the division of the value chain throughout Europe, with R&D mainly concentrated in Northern Europe (Germany in this case) and production in European countries where labour is cheaper (Portugal in this case).

Reshoring and Onshoring: a new trend for a more secure supply chain

Reshoring involves a company moving its manufacturing operations from a foreign country to the country in which it is based. Pharma companies rely on foreign suppliers, and the recent geopolitical events have made pharma industry more careful about the supply chain, leading to a new trend of reshoring, or onshoring if the company chooses a supplier inside the native country. According to a 2022 survey by Global Data, more than 40% of pharma companies believe that onshoring supply chains will make them more secure; especially for European companies that are more likely to onshore than North American companies.

An example of companies that moved abroad and are now relocating their efforts to their homeland is the Italian Biopharmaceutical group Menarini. After several years of expansion in various countries, resulting, for example, in the acquisition of the Singaporean lab Invida in 2012 to have a presence in the Asia-Pacific region, Menarini chose in 2020, in the midst of the Covid-19 pandemic, to launch a new €150M pharmaceutical plant near Florence, Italy.

Lucia and Alberto Giovanni Aleotti, members of the Menarini Board declared "*We are a proud Italian company. Here we will manufacture drugs which are the essence of the Menarini Group and are used every day by tens of millions of patients in Italy and abroad*." This declaration highlights this company's desire to return to its roots and create jobs in Italy.

Many European governments have launched initiatives to help reshoring through financial incentives. For example, the French state investment bank BPIfrance has a 12% share in EuroAPI, an active pharmaceutical ingredient (API) production initiative leaded by Sanofi launched in 2021 (Policy Department for Economic, Scientific and Quality of Life Policies; European Parliament (PE 740.070; 2023))

At the European scale, in April 2023 the European commission proposed a reform of the EU"s pharmaceutical legislation to offer an attractive framework for drug research, development and production in Europe, especially by lessening the administrative burden and changing the regulatory protection of innovative medicines by combining existing intellectual property rights with another regulatory protection of up to 12 years.

This proposal highlights the need for an IP policy at the European scale to make Europe more attractive in the pharmaceutical industry. Financial incentives are a first step, but these must be combined with a global policy to help reshoring the entire chain value of life sciences industry on the continent.

We have discussed examples of reshoring in manufacturing, but incentives are also needed in R&D and during regulatory affairs. For example, Wallonia (Belgium) provides a wide range of financial support, with a tax deduction of 85% of their income if this income is considered 'innovative' or a reimbursable advance to cover up to 70% of R&D costs, creating an attractive ecosystem for Belgium-based companies.

Nearshoring: an opportunity in an integrated Europe

The European Union was created with the ideal of a free market between countries. However, Europe is not homogeneous and some countries are more competitive than others in terms of labour costs, industrial infrastructures, workforce education, etc.

Some countries are more competitive within the European Union and are ideal place for companies wishing to establish a new manufacturing unit at a lower price, while being at the heart of the European market. Most of the time, APIs are produced in one region, then sent to another manufacturing unit in another country. APIs are often made in Asia, but the current trend is to create new API production units across Europe (Figure1).

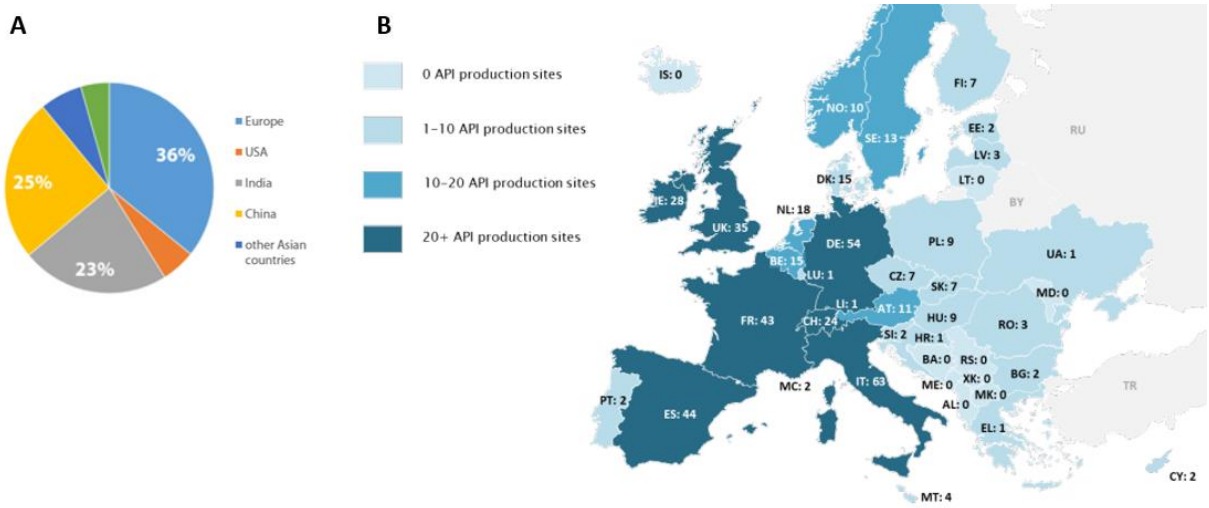

Figure 1: API production in Europe.
A) Distribution of API manufacturers (worldwide, 2019)
B) API manufacturing sites in Europe (2022,2023)
Source: Policy Department for Economic, Scientific and Quality of Life Policies; European Parliament (PE 740.070; 2023)

As Europe's production costs remain high, it seems obvious that not all APIs could be reshored in Europe, and only some critical and complex APIs will be produced in Europe. Also, as the API market relies on an important economy of scale, companies should work at a continental level, not having a manufacturing unit per country.

For example, Novartis (Switzerland), through its subsidiary Sandoz, has invested €50M in 2022 for a sterile API production unit in Palafolls, Spain, to increase its antibiotic production capacities in Europe. The APIs produced in Spain are then sent to other units throughout Europe.

We can see this organisation in other countries such as France and Belgium with GlaxoSmithKline (GSK). Around the major R&D centre of Rixensart in Wallonia (Belgium), manufacturing units are established in Wavre (Wallonia), the largest vaccine manufacturing unit in the world, but also in France with a €390M investment between 2023 and 2025,

supported by the French policy called “Choose France” to attract new foreign investments. The Saint-Amand-les-Eaux (France) site is close to the Belgian border, creating a genuine vaccine hub in the heart of Europe that can be a real asset, with synergy between the R&D centre that creates new vaccines and the manufacturing units exploiting the patents filed only a few kilometres away.

GSK’s strategy highlights the incentives in Europe, with R&D efforts located in Wallonia, where financial supports for R&D are more attractive, along with some production in France with the “Choose France” initiative, targeted particularly at industrial production.

Conclusion and outlook

The Covid-19 pandemic and the current geopolitical situation have been a brutal shock to Western countries, showing our dependency on foreign countries. However, reshoring the entire value chain in life sciences industry without a real strategy and without any incentives seems unrealistic, especially in an industry based on open innovation with a variety of actors and a profit-driven approach in a sector where economies of scale are the standard.

Hence the need for new policies to attract life sciences companies to Europe and have a regional approach with a division of the value chain in different countries through Europe, with a logic of specialisation.