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Biotechnologies: Europe struggles with China-US rivalry

EXECUTIVE SUMMARY

Biotechnology companies play a vital role in improving the survival of patients facing difficult-to-treat diseases, as well as preserving their quality of life. Innovation is essential for the pharmaceutical sector in general, and for this segment in particular, which manipulates complex biological systems. The most challenging diseases, often rare and affecting specific populations, notably children, require a thorough understanding of the underlying biological mechanisms. In addition, these pathologies require personalized treatments, based, for instance, on the patient's genetic profile. The development of such therapies has been made possible thanks to advances in the fields of "omics"[1] and big data analysis.

Boasting a large and relatively well-funded market, Europe[2] is one of the main centres of medical research and production. However, it is losing ground against the United States, its historic competitor, and against China, whose biotechnology sector, which is crucial for health independence, has developed rapidly in recent years. The European continent even seems to be falling critically behind the United States in establishing an effective and integrated ecosystem to stimulate innovation, which would notably facilitate patients' early access to innovative therapies. The United States is widening the gap by taking advantage of the symbiosis between universities, research centres, funding agencies, private partners (VCs), clinical trial facilitators and manufacturers. These partnerships between multiple players in the biotechnology value chain thus make it possible to promote the survival of companies which must overcome numerous regulatory obstacles before being able to generate sales.

At the same time, China has established itself as a strong competitor, striving to develop a biotechnology industry capable of rivalling that of the United States. Europe has consequently found itself caught in a bind, notably due to the smaller size of its biotechnology "clusters" and an environment less conducive to entrepreneurs in the sector. These challenges have been exacerbated by the flight of talents to destinations with a stronger base in research and development. The lag has therefore lengthened on the continent – not so much in the production of knowledge, but above all in the transformation of this knowledge into industrial projects. The obstacles to the creation of biotechnology companies of critical size, financed by European funds, and with staff largely trained in the continent's universities have so far prevented the creation of large European biotechnology companies. This situation exacerbates the region's almost exclusive dependence on its large pharmaceutical laboratories (Sanofi, Merck, GSK, etc.) for innovation.

1 - "High-powered technologies used for holistic analysis of the molecules that make up the cells of living organisms." EFSA.
2 - Europe, here, is made up of the countries of the European Union, as well as the United Kingdom and Switzerland.

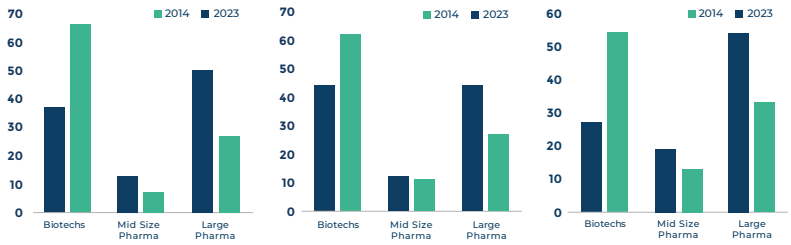
The world of biotech is buoyant

A key segment for meeting patient needs

Biotechnology companies, more commonly called biotechs, occupy an important place in the global pharmaceutical landscape. These players participate in the discovery of new therapies, thanks to their agility and above all to their belonging to an ecosystem of research, development of their clinical trials and financing. Their activity is based on the application, also called translational research, of discoveries from basic research made in university to therapeutic areas in order to meet the diverse needs of patients. Its applications have led to the development of biological drugs[3], the share of which is constantly growing in drug sales. Hence, according to EvaluatePharma, the overall market share of these treatments reached 37% in 2022, compared to 24% in 2014.

In terms of research and development (R&D), biotechs have established themselves as major players, accounting for almost two-thirds of phase I[4] clinical trials in 2023 compared to one third in 2014 **(Chart 1)**. The progress of these players has mainly come at the expense of the major global pharmaceutical laboratories, whose share in these initial clinical trials fell from 50% to 27% in the space of nine years. It should be noted, however, that biotechs have a 12-percentage point lower share in phase III compared to phase I, because their therapies are bought "at the end of the process" by these same large pharmaceutical laboratories when they have proven their effectiveness.

Chart 1 - Share of clinical trials by phase and type of enterprise (%), 2014 vs. 2023



Sources : IQVIA, Coface

The impact of this sector can also be measured through technological advances which have not only saved lives, but also improved the quality of life of many patients. Hence, Genentech's Herceptin, approved by the American Food and Drug Administration (FDA) in 1998, has considerably improved the survival of patients developing breast tumours with a particular genetic profile. Additionally, this advancement has paved the way for personalized medicine. Since then, other drugs have generated sales exceeding a billion dollars annually, such as the blockbusters Enbrel from Amgen or Sovaldi and Harvoni from Gilead/Pharmasset.

Biotechnology companies stand out by participating in the development of molecules targeting difficult therapeutic areas, including those affecting restricted populations such as rare childhood diseases, the financial benefits of which for the founders can be difficult to understand. According to IQVIA, clinical trials initiated by biotechs represent 30% of the pipeline for these diseases. They reach 68% for oncology. In this area, certain needs remain unmet, with mortality still high for several types of tumours.

A segment highly dependent on public funding, venture capital and partnerships with pharmaceutical laboratories

Biotechs have capital requirements to finance clinical trial phases, in addition to marketing, communication with practitioners and production expenses. They must have ample liquidity for many years before being able to generate sales, these being conditional on obtaining a market approval from regulators.

Financing by venture capital proves to be a tool adapted to take into account these uncertainties and support over the long term a mobilization of capital without immediate returns on investment, especially at the start of the creation of a biotech. Venture capital funds are looking for molecules with a "high risk – high return" profile, allowing them to tolerate certain failures inherent to biotechs. Their role here is that of a catalyst. The expected gains are then able to offset losses from failed investments in other companies. Obviously, not all venture capital funds have the same appetite for risk: those who are less risk-averse will invest earlier, while others will prefer to acquire more data before making a financial commitment, therefore intervening when therapy reaches certain milestones. When the biotech company reaches these later stages, it is common for these funds to find themselves competing with larger biotechs, or even large pharmaceutical companies. This in turn increases the amounts invested.

VC funds also play a mentoring role towards biotech leaders. The managers of these funds often have long experience in the sector, having themselves founded certain companies. This allows them to capitalize on their expertise and, most often, on their scientific training, to help "clear the way". In addition, these players operate in an ecosystem, a geographic cluster, which provides significant assistance by facilitating connections not only with other researchers and investors, but also with suppliers. This network training enables knowledge and good practices to be shared, which makes it possible to better navigate the hazards of clinical research.

In 2023, biotechs managed to mobilize nearly USD 162 billion from investors in 2023, according to CrunchBase. One third of this amount was allocated to American companies, while Chinese biotechs occupied second place with 12% of the amount. European companies came in third place, with a share of 7%.

In addition to VC funds, the contribution of national medical research institutes, particularly in the United States with the National Institutes of Health (NIH), is also significant. These entities mainly focus their participation through the financing of fundamental research, in universities, of which certain biotechs are "spin-offs". Consequently, in 2022, the NIH spent nearly USD 8.6 billion to initiate research in biotechnology, compared to 5.7 in 2013.

Europe loses steam vis-à-vis the United States and China

Europe, a major scientific player

BioNTech, a German biotech allied with the American pharma company Pfizer, was the first company to offer an authorized vaccine to fight the COVID-19 pandemic, which propelled it to prominence in the vaccine order stakes along with its financial ally Pfizer. This example, far from being unique, illustrates the importance of the European contribution to the biopharmaceutical sphere on a global scale. By way of illustration, an OECD study demonstrates European strengths[5]: behind the United States, the United Kingdom, France, and Spain respectively occupy second, third and fifth place in the world in terms of number of active medical biotechnology companies[6].

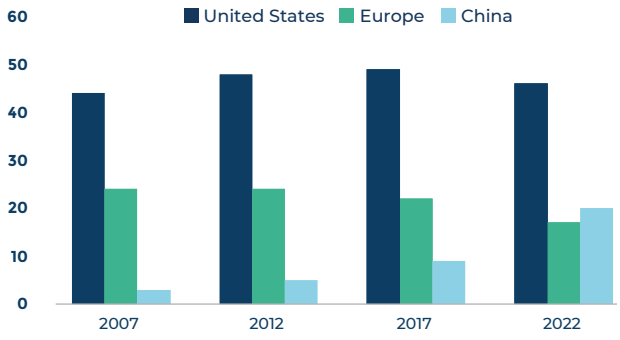
3 - Also called large molecule drugs, because they are produced from living entities.
4 - Before being dispensed to patients, a drug must follow three phases (I, II and III) which make it possible to determine its effectiveness and toxicity on groups of volunteers. The competent medical authority may or may not issue an approval at the end of phase III. A fourth phase is planned to measure possible side effects over the long term and in real life conditions.
5 - *https://www.oecd.org/innovation/inno/keybiotechnologyindicators.htm*
6 - *https://www.labiotech.eu/best-biotech/top-biotech-countries/*

The intensity in R&D, the degree of specialization in certain therapeutic areas (oncology and neurology for example), and the predominance of geographical research clusters such as Manchester and Oxford in the United Kingdom, and the Paris and Lyon regions in France, contribute to the emergence of these companies. In addition, Europe has a trained workforce capable of participating in innovation development. Yet again according to the OECD[7], of all higher education graduates, more than 36% had a STEM (Science, Technology, Engineering and Mathematics) diploma in Germany and 26% in France, while in the United States, they represent only 20%. The latter, however, manage to attract graduates from other regions of the world, particularly Europe and Asia (mainly China and India). The European continent has renowned universities in the field of biomedical research, whose researchers publish in the main peer-reviewed scientific journals. On that score, according to EuropaBIO, an association that defends the interests of European biotechs, the European Union, the United Kingdom and Switzerland published 310 papers in these journals, between 2018 and 2021, while the United States and China published 266 and 104, respectively.

It should be noted, however, that in Europe, Switzerland and the United Kingdom accounted for almost one third (91 out of 310) of these publications. The tradition of research and innovation in these two countries, their research infrastructures, and a favourable regulatory framework for international collaborations have made them strong contenders on the continent. However, the concentration in these two countries outside the EU raises longer-term questions about the robustness of European fundamental research. Clinical applications are closely dependent on advances in fundamental research, which currently come from research centres located in non-EU countries. This could therefore lead to a possible "two-speed-research Europe" with a division between a "centre" connected to other international clusters, and a "periphery" that is likely to lag further behind.

By initiating 17% of clinical trials (phases I to III) in 2022, European biotechs are doubtless still actively participating in biotechnology advances. However, while the United States has held on to first place, Europe has, in five years, ceded second place to China, which now represents 20% of these tests compared to 9% in 2017. (**Chart 2)**. The loss of clout to China's benefit can be explained by a certain lack of clout on the part of this European "periphery".
In addition, the continent is having trouble in transforming its advances in basic research into marketable clinical applications. The presence of research centres with a trained workforce does not seem capable of producing companies with a critical size, adequate and local financing, or of marketing new therapies and developing a European manufacturing base.

Chart 2 - Share of clinical trials (phase I - Phase III) by country of origin of biotechs

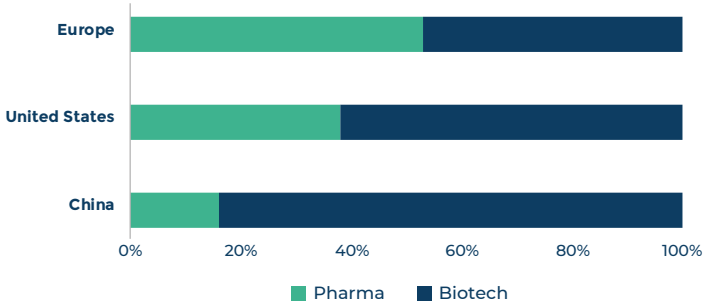


Sources : IQVIA, Coface

Innovative companies that fail to flourish

Europe continues to rely on its historical heritage, symbolized by the strong presence of large pharmaceutical laboratories **(Chart 3)** and a large network of world-renowned universities. However, the European situation, where nearly 60% of clinical trials are initiated by pharmaceutical laboratories, contrasts with that of the United States and China, where most trials are now carried out by biotechs. However, the most innovative therapies are found in the field of biological medicines.

Chart 3 - Share of clinical trials (from phase I to approval) by region



Sources : IQVIA, Coface

Innovation is therefore found in emerging biotechnology companies that are generally small and which in Europe have difficult access to financing from venture capital funds. Hence, according to Pitchbook, European biotechs (including the European Union, the United Kingdom and Switzerland) only managed to secure between 18% and 41% of the funds invested by venture capital between 2013 and 2022, whereas American biotechs have always been able to take the lion's share, with percentages varying between 49% and 63%. The United Kingdom and Switzerland obtain more than 80% of European funding, reinforcing the observation, described above, of an opposition between the "centre" and the "periphery".

Continental Europe does not have significant venture capital hubs sufficiently integrated with university research centres, major providers of emerging biotechs. This therefore encourages them to look abroad, starting with the United States. The example of BioNTech is an illustration of this, since the company benefited in 2019 from a funding round made up of four Asia-Pacific funds, three American and only one German. According to EuropaBIO, European venture capital funds are reluctant to finance biotechs during preclinical and phase I trials, when the risk is greater and the return on investment is still difficult to assess precisely. American biotechs, for their part, see VC funds concentrate 56% of their financing during these phases compared to 30% for European biotechs.

European investors prefer to concentrate their financing at the "end of the cycle", during phase III (25%) and that of commercialization (23%), when the risks have been well controlled, demonstrating a stronger aversion to risk than their American counterparts. For a European biotech founder, notably French or Italian, the main challenge is therefore to succeed in securing funds for phase I and II clinical trials. Faced with this challenge, European biotechs are turning to foreign financing in order to guarantee an adequate flow of financing. This approach allows them to benefit from funds to move towards the marketing of their products. Subsequently, they can also obtain further financing through partnerships with large pharmaceutical laboratories or through IPOs, particularly in the United States. On that score, according to S&P, 22 European biotechs chose the New York Stock Exchange to carry out their IPO between 2018 and 2021, compared to only 13 in all European markets combined, including London.

7 - *https://cset.georgetown.edu/article/the-global-distribution-of-stem-graduates-which-countries-lead-the-way/*

China, a biopharma heavyweight in the making

China has strived for over 20 years to become a centre of excellence in biomedical research, through various supporting plans and initiatives. For example, the twelfth five-year plan (2011-2015) explicitly placed biotechnologies in seven emerging strategic sectors[8].

For example, in oncology, at the end of 2021, nearly 84% of molecules developed by biotechs in the clinical trial phase in China entered the "me too" category (similar to pre-existing drugs, but with a patented improvement) or "me better" (drugs whose effectiveness is greater than the original drug). Some 11% of these molecules are developed with foreign players and target new mechanisms of action and only 6% are developed exclusively by Chinese companies, with innovative mechanisms. Chinese biotechs are therefore moving up the value chain, starting from partnerships with international players before turning to the development of more innovative molecules, relying on key areas such as precision medicine thanks to the applications of genomics, as well as an increased integration of artificial intelligence in the detection of therapeutic candidates.

These companies depend on private financing to continue their clinical trials, as well as the marketing phases, particularly internationally. They particularly need access to venture capital financing, which allowed them to raise nearly USD 19 billion in 2021 and 8.9 billion in 2022. The Chinese biopharma industrial base is able to respond to the challenges of the medical supply chain, with the presence of CROs (Contract Research Organizations), which provide laboratories and biotechs with services related to the conduct of clinical trials, as well as CDMOs (Contract Development Manufacturing Organizations), known as of manufacturers in France, of adequate size and in sufficient number, and who have proven themselves with pharmaceutical laboratories. However, Chinese biotechs will still have to overcome several hurdles, not only to participate in international trials, but also to consider the unique features linked to biotechnologies (know-how, workforce skills, etc.).

The United States goes head-to-head with China

The United States is the leading country in the biotechnology segment, both in terms of research and innovation, and financing of the latter, as well as for marketing and communication. These aspects are crucial to demonstrate the effectiveness and safety of therapies to scientific societies and practitioners, and key in placing these therapies on the "front line" against competing products.

The United States has several large biotechnology centres – hubs – where scientists develop companies from research initiated in university medical centres. Public funding plays a catalytic role, particularly during the translational research phase. Private financiers (large biotechs, pharmaceutical laboratories and venture capital funds) subsequently take over to participate in the financing of clinical trials and production and marketing. Hence, the country has nine major hubs, more than the EU, Switzerland and the United Kingdom combined. In order of importance they are: Boston, San Francisco, New York/New Jersey, Washington, San Diego, Philadelphia, Los Angeles, North Carolina, Seattle and, last, Chicago. These hubs facilitate synergies between fundamental and applied research, entrepreneurship, financing and scaling up.

American senators wishing to thwart China's rise in biotechnology and maintain their lead through more restrictive legislation, have targeted technology exports and investments from venture capital funds in Chinese biopharma companies, via the draft "BIOSECURE Act" bill, which was introduced before the Senate in January 2024. The proposed legislation aims to prohibit American public health entities from contracting with biotechnology companies, including CDMOs and CROs, from "hostile" countries, including China. The bill, however, faces opposition from sector players, in particular the American professional association of biopharma companies, the Biotechnology Innovation Organization, BIO. American medical companies or those with activities on American soil particularly fear having to sever commercial ties with these companies from "hostile" countries before securing contracts with American medical entities. The bill was therefore amended at the beginning of May 2024 to grant the American companies concerned a longer period to disengage from their relations with Chinese companies, to avoid jeopardizing the ongoing trials[9].

China-US trade tensions affect many areas of activity and do not spare the biotechnology segment. The European biotech ecosystem, the main topic of this study, must be able to secure the space to consolidate its place. It boasts undeniable assets to meet to the challenges posed by major demographic and societal changes affecting the world population. The region has quality research centres, a qualified workforce, and a recognized presence in therapeutic areas of interest such as oncology and neurology. In addition, it benefits from a process for regulating clinical trials and market authorizations that are centralized in a single authority. In order not to be left behind by American and Chinese competitors, European biotechs could however greatly benefit from better conversion of the results of fundamental research into clinical applications, while attracting funding from venture capital investors and industrial partners, particularly European ones. This would facilitate the development of suitable production capacities, including those in collaboration with large pharmaceutical laboratories. The latter have recognized drug development expertise and significant financial resources capable of facilitating the support of European biotechs in their growth.

8 - *https://www.fondapol.org/app/uploads/2020/06/etude-ma-aifang-fondapol-biotech-chine-va-2020-02-25-3.pdf*
9 - *https://www.bio.org/gooddaybio-archive/updated-biosecure-act-language-released-house-committee-action-expected-next*

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