



ECONOMY

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PARIS REGION: AT THE CUTTING EDGE OF BIOTECHNOLOGIES AND GENE & CELL THERAPIES

1st in Europe

FOR THE NUMBER OF COMPANIES
IN THE PHARMACEUTICALS SECTOR.

250

HEALTH BIOTECH ENTITIES
IN PARIS REGION.

More than 60

ACADEMIC RESEARCH CENTERS
FOR THE DEVELOPMENT
OF BIOTECHNOLOGIES.

PARIS REGION IS A HUB OF SCIENTIFIC EXCELLENCE AND FURTHERMORE HOME TO NUMEROUS COMPETENCIES IN THE STRATEGIC SECTOR OF NEXT-GENERATION BIOLOGICAL MEDICINES. PUBLIC-PRIVATE PARTNERSHIPS FOR BIOTHERAPY R&D BENEFIT GREATLY FROM THE PRESENCE OF LARGE BIOPHARMACEUTICAL GROUPS IN THE REGION.

Paris Region is Europe's leader for the sciences and particularly notable for its multitude of actors in the health biotech sector, an aspect that illustrates the region's attractiveness and competitiveness assets. The entire value chain is present: research, innovation, evaluation, production and commercialization, not to mention the formidable contributions to come as breakthroughs are made in the fields of informatics and artificial intelligence.

INNOVATIVE THERAPIES: UNPRECEDENTED TREATMENTS AND EXPANDING MARKETS

Biological medicines, or "biologics" for short, are a class of innovative therapies born of world-leading and highly promising fields of research, including novel antibodies (bispecifics), gene & cell therapies (advanced therapy medicinal products; ATMPs) and extracellular vesicles. With its investments in the field and the quality of its ecosystem, Paris Region plays a key role in biologics.

The domain of innovative therapies is growing rapidly and achieving considerable breakthroughs in diagnostics, prognostics and treatments for rare brain (adrenoleukodystrophy, Parkinson's disease, etc.) and blood (immunodeficiencies, beta thalassemia, hemophilia, etc.) pathologies, and for numerous cancers (lymphomas, etc.). Within and beyond the focus on rare diseases, there are currently more than 700 clinical trials underway in a broad range of specialties including dermatology, neurology, ophthalmology, oncology, metabolic medicine and infectious diseases (HIV). The stakes are large, both in terms of public health and for industry and the economy. Pharmaceutical groups, with their current R&D models running out of steam, their blockbuster revenue falling and their bottom lines being challenged by generics, are massively investing in these novel research directions and previously unexplored markets.



GENOPOLE
VIVRE L'INNOVATION

**L'INSTITUT
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BIOTECHNOLOGY

Biotechnology is defined by the Organisation for Economic Co-operation and Development (OECD) as “the application of science and technology to living organisms as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.”

BIOINFORMATICS

The OECD defines bioinformatics as “the construction of databases on genomes, protein sequences; modelling complex biological processes, including systems biology.”

GENE THERAPY, CELL THERAPY

Gene therapies treat genetic diseases by repairing or replacing defective genes: functional genes are delivered to and inserted in (e.g., via retroviral vectors) the genomes of affected cells to compensate for the dysfunctioning defective gene. The gene itself is the active pharmaceutical ingredient of the medication. Cell therapy, also called regenerative medicine, uses stem-cell-derived cell grafts to restore the function of tissues and organs damaged by disease, age or trauma.

BIOTECHNOLOGIES AND INNOVATIVE THERAPIES: CORNERSTONE ASSETS FOR PARIS REGION

Paris Region has numerous advantages:

- Field-leading, public and private experts, teams and infrastructures—particularly in the fields of biomarkers, genetic predisposition, biologics and nanobiotechnology¹—notably federated in “major interest domains” (DIM; domaines d'intérêt majeur) for gene therapies (DIM thérapie génique) and for new technological processes such as microfluidics and extracellular vesicles (DIM ELICIT);
- Several already-active centers of excellence (in Paris, Évry-Courcouronnes, Villejuif and Paris-Saclay), which unite academic research, clinical research, business incubators and larger office+lab buildings (“hôtels d'entreprises”);
- A dense network of innovative start-ups and young businesses that are working synergistically with the numerous international pharmaceutical groups also present in the territory. Paris Region leads Europe for the number of businesses in the pharmaceuticals sector²;
- Numerous research hospital centers for the preclinical and clinical evaluation of medical and therapeutic innovations;
- Numerous accompaniment, networking and valorization structures (Medicen Paris Region, EIT Health, Satt, OTT, incubators) to facilitate access to the French and European markets;
- Bioproduction capacities (developed notably by such establishments as Centre Meary, Yposkesi, CellforCure (Novartis) or LFB Biomedicaments) able to ensure particularly complex medicines manufacturing and industrialization processes, which represent a critical crossroad for the development of innovative therapies.

Venture Centre of Excellence EIF-EIT to be piloted from Paris

Paris was chosen for the headquarters of EIT Health. This latter is the health Knowledge and Innovation Community (KIC) of the European Institute of Innovation and Technology (EIT), a European Union

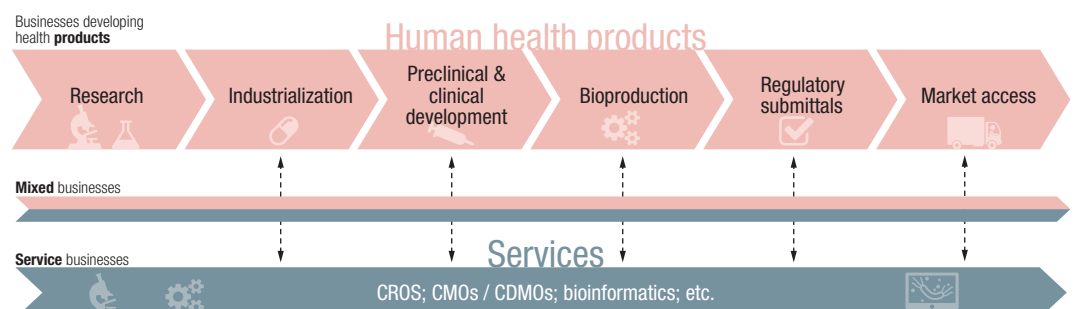
organism whose purpose is to strengthen innovation capacities in a range of domains, including health. In September of 2019, the European Investment Fund (EIF) and EIT Health signed a Memorandum of Understanding for the deployment of a co-investments program, called Venture Centre of Excellence EIF-EIT Health, to attract private investments, particularly for biotech companies. At the EIT Health Summit held 3 December 2019, it was announced that Paris would host the piloting team for the Venture Centre of Excellence program.

Meary: an ATMP production center

The Centre Meary de thérapie cellulaire et génique (Meary center for cell and gene therapies) is integrated within the Paris network of public hospitals (AP-HP), Europe's largest university hospital center, and provides that institution with ATMP production capacities. With support from the region, the Centre Meary provides a full gamut of state of the art services and competencies for the production, validation and distribution of gene & cell and tissue engineering-derived therapies.

Within its healthcare and research ecosystem, the center's kinetics for innovation have produced several world's firsts. It furthermore has established privileged relations with actors in the medical and pharmaceutical industry. Centre Meary has the expertise and means to accelerate the maturation of preclinical and clinical ATMP projects on all crucial fronts: regulatory issues, automation, process optimization, definition of ATMP specifications and quality control. The center has also developed partnerships with Paris Region industrials working in the ATMP sector. These include Astraveus, a pioneer in microfluidics for the production of ATMPs, Honing Biosciences a company developing CAR-T cells³, MadeCell, which provides computer programs specifically developed for ATMP bioproduction activities, and Flash Therapeutics, a specialist in the production of viral vectors for gene therapies.

The health biotechnologies sector and associated businesses



Principal academic research centers (CRA)

- CRA
- Incubator
- CRA + Incubator
- H CRA + Hospital
- H CRA + Incubator + Hospital

Centre Meary: academic bioproduction center

- Single platform
- Several platforms at a same site

1 Agoranol; 2 C.U. des Saints-Pères; 3 ENS Biologie;
4 Sorbonne U. et CRC; 5 IPGG/ESPCI; 6 U. de Paris

Biotech companies

- Biotech or biotech services companies
- Gene & cell therapy companies (pure player or generalist)
- Bioproduction site
- Gene & cell therapy companies + bioproduction site

1 Theravectys; 2 Brainvectis; 3 Horama; 4 Hybrigenics; 5 Astraveus;
6 Honing Biosciences; 7 Springvision; 8 Gensight; 9 Eyevensys; 10 Smart Immune;
11 Everzom; 12 Pathoquest; 13 Alderaan; 14 Ermlum Therapeutics; 15 Step Pharma;
16 Invetys; 17 Scarcell

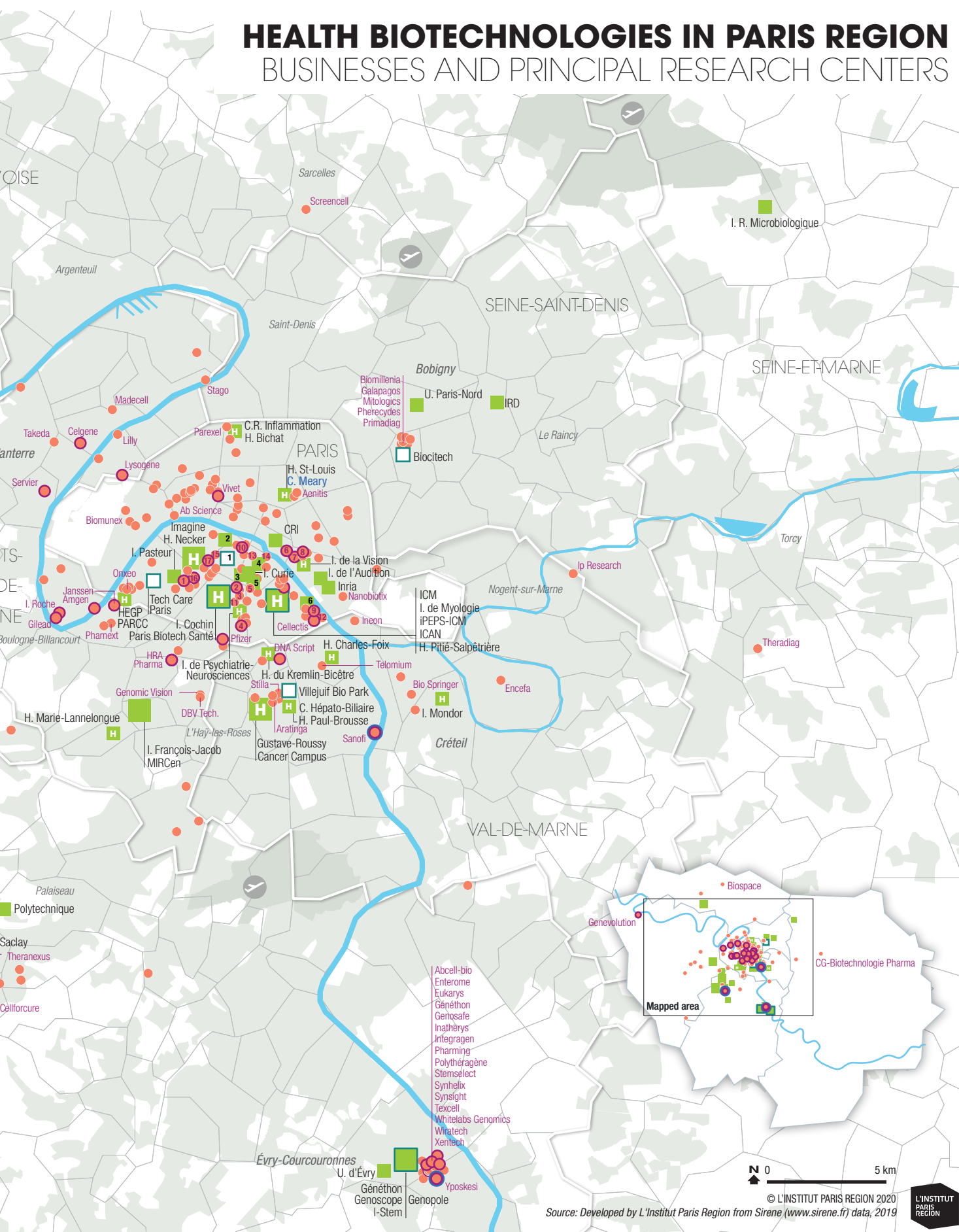
C.: Center
C.R.: Research center
C.U.: University center
H.: Hospital
I.: Institute
U.: University

CEA: French Alternative Energies and Atomic Energy Commission
CNRS: French National Center for Scientific Research
CRC: Cordeliers Research Center
CRI: Center for Interdisciplinary Research
ENS Biologie: École normale supérieure Institut de Biologie (French *Grande École*)
ESPCI: École supérieure de physique et de chimie industrielles (French *Grande École*)
HEGP: Georges-Pompidou European Hospital
ICAN: Institute of Cardiometabolism And Nutrition
ICM: Brain and Spinal Cord Institute
Imagine: Genetic Diseases Institute
Inrae: French National Research Institute for Agriculture, Food and Environment
Inria: National Institute for Digital Sciences and Technologies
iPEPS: Paris-Salpêtrière business incubator
IPGG: Pierre-Gilles-de-Genes Institute
IRD: French National Research Institute for Development
I-Stem: Institute for Stem Cell Therapy and Exploration of Monogenic Diseases
MIRcen: Molecular Imaging Research Center
PARCC: Paris-Cardiovascular Research Center



HEALTH BIOTECHNOLOGIES IN PARIS REGION

BUSINESSES AND PRINCIPAL RESEARCH CENTERS





PARIS REGION: A HUB FOR BIOTECH

Paris Region offers a plethora of world-renowned academic research institutions and a highly fertile ecosystem for the health sector.

More than 60 biotech research centers

In Paris Region, scientific and clinical research in biotechnologies is carried out within prestigious organisms, most notably the French National Institutes of Health and Medical Research (Inserm; Institut national de la santé et de la recherche médicale), which is second only to the American National Institutes of Health⁴, and the AP-HP, Europe's largest university hospital network. Three major higher education centers contribute to world-class learning in life sciences: the Sorbonne University, the University of Paris and Paris-Saclay University. Paris Region stands out also for its concentration of research centers unique in Europe: the institutes Curie, Pasteur and Gustave-Roussy, the genetic diseases institute Imagine, the brain and spinal cord institute ICM, the Institute of Myology, the Institute for Biomedical Imaging, the François Jacob Institute of Biology, Neurospin, the Centre Meary, the Institut de la vision, Genethon, the Institute for Stem Cell Therapy and Exploration of Monogenic Diseases (I-Stem) and the Genomic Therapy Technology Research Accelerator.

A unique network of businesses: more than 250 establishments in Paris Region

L'Institut Paris Region tallied 250 human-health biotech establishments in its namesake (including service providers, contract research, development and manufacturing organizations, and bioinformatics entities).

These businesses are distributed across a range of activities, with more than half of them performing R&D in biotech, and a quarter R&D in other physical and natural sciences. Thus, 76% of Paris Region businesses are active in research and development. The remaining businesses are also often involved in health or—importantly for the sector—in bioinformatics.

The competitiveness cluster Medicen Paris Region, which federates public and private actors in health innovation, represents the majority of this ecosystem. All large pharmaceuticals groups carry out biotech R&D internally or in partnerships, and/or acquire promising biotech start-ups while they are still in their more or less early stages of development. Most of these Paris Region businesses are therefore micro-enterprises or SMEs, while mid-caps remain relatively rare. Biotech companies are evolving toward a mixed business model associating health product development and service offers. This allows them to better weather the difficult periods inevitably encountered in this field due to the high costs and lengthy timeframes needed to develop and obtain market approval for biotech products. As for companies active in bioinformatics, they too are growing and contributing to the excellence of the Paris Region ecosystem.

Geographically, two administrative divisions group more than 75% of these businesses: half of them are located in Paris and the other quarter in the Essonne administrative department. The weight of this latter in biotechnologies is thus particularly important and largely due to the presence of Genopole, but also that of a number of bioproduction facilities such as LFB Biomédicaments and CellforCure in Les Ulis, and Yposkesi at the Genopole site.

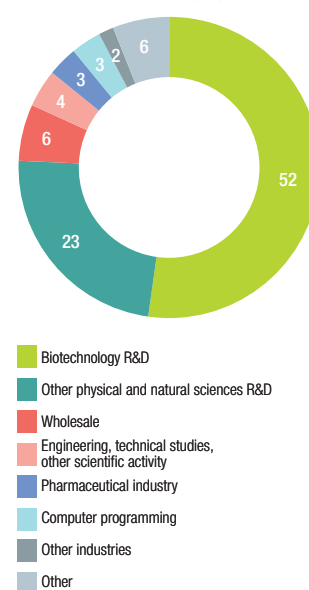
The Genopole biocluster

Genopole is a major actor in gene, genome and cell biotherapies, with entities covering the entire range, from R&D to GMP⁵ production. Genopole was founded in 1998 in Évry-Courcouronnes, just south of Paris. It owes its existence to the mobilization of the French State, the Paris administrative Region, the Essonne Department and AFM-Téléthon (French Muscular Dystrophy Association). Financed mainly by the Paris administrative Region, Genopole oversees ten hectares of land and real estate wherein academic laboratories, biotech companies, a business incubator, and the University of Évry-Paris Saclay are united.

Left: the genetic diseases institute Imagine in Paris.

Right: the histology-anatomic pathology platform at Genopole in Évry-Courcouronnes.

Distribution of establishments by type of activity (%) in 2020



The Genopole model is unique in France and a motor for innovation, particularly in its four strategic sectors: personalized medicine, innovative therapies, computational genomics and industrial biotechnology. The biocluster's renown, built upon 20 years of experience, has earned it a number of international distinctions, such as the Outstanding Research Park Award of the Association of University Research Parks, and brought to it a number of foreign companies, such as Illumina and Pharming.

Before all else, Genopole's mission is to attract and retain business and academic talent by empowering entrepreneurship, research and training in the fields of biotechnologies. Its actions follow three main orientations

- Entrepreneurship: Genopole provides accompaniment for the development of innovative projects (Shaker) and young companies (Booster), and furthermore enables contacts between its accredited companies and investors/corporate groups, all with the goal of accelerating business growth.
- Research: Genopole finances the acquisition of shared-use technological equipment, infrastructures and competencies ("platforms") and the recruitment of postdocs within the site's labs and businesses. It furthermore assists with the creation of research units in the biocluster's laboratories.
- Training: In partnership with the University of Évry (part of Paris-Saclay), Genopole accompanies the creation of new life sciences training curriculums.

Paris Region is both a hub of scientific excellence and a place where the production of advanced therapy medicinal products is taking form. The region is symbiosing and strengthening its capacities and competencies in the ATMP sector, including in professional training; creating new employment & activities; catalyzing biopharmaceutical projects through public/private R&D partnerships; and finally harnessing that R&D to enable joint activities with the pharmaceutical groups present in and about Paris. Because business financing remains a key issue, the region's objective is to pursue growth in available capital to accompany the continuing development of these Paris Region companies. ■

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1. Applies the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics, etc. (OECD definition)
2. Source: Medicen Paris Region.
3. Chimeric Antigen Receptors of T cells. "(...) CAR-T cells are a novel therapeutic option bringing new hope for certain blood cancers. [These gene therapies are] manufactured from the patient's T lymphocytes, which, once modified genetically and reinjected, are able to specifically recognize and destroy cancer cells." Excerpt from a French National Authority for Health press release dated 27 May 2019.
4. In terms of the number of publications in high-impact scientific journals. Source: Inserm.
5. Good Manufacturing Practices. Describes the minimum standard that a medicines manufacturer must meet in their production processes. (EMA definition)

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RESOURCES

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