France

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Agenda

1. **Main issues and executive summary France**
   a. Executive summary
   b. Key recommendations
   c. France context specificity: **Biotherapies**

2. **Tackling the talent gap and the talent crunch in biomanufacturing in Europe**
   a. Academic Ecosystem: **Academic forces & labor market**
   b. Talent policy: **National Council of Industry**
   c. Success story: **Mabdesign Academy**
   d. Opportunity: **creation of Campus Biotech Digital**

3. **Research to innovation**
   a. Innovation capabilities
   b. Innovation policy: **the Ile-de-France Region**
   c. Success stories: **BIOASTER**
   d. Opportunities: **Recovery plan & PIA4**

4. **Business to Innovation**
   a. Business ecosystem mapping
   b. Access to Finance
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5. **Conclusion & recommendations**
   a. Conclusion & next steps: **Good practices identified and highlights**
   b. EIT Health footprint radar: **France**
   c. References

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Part II

Main issues and executive summary

France

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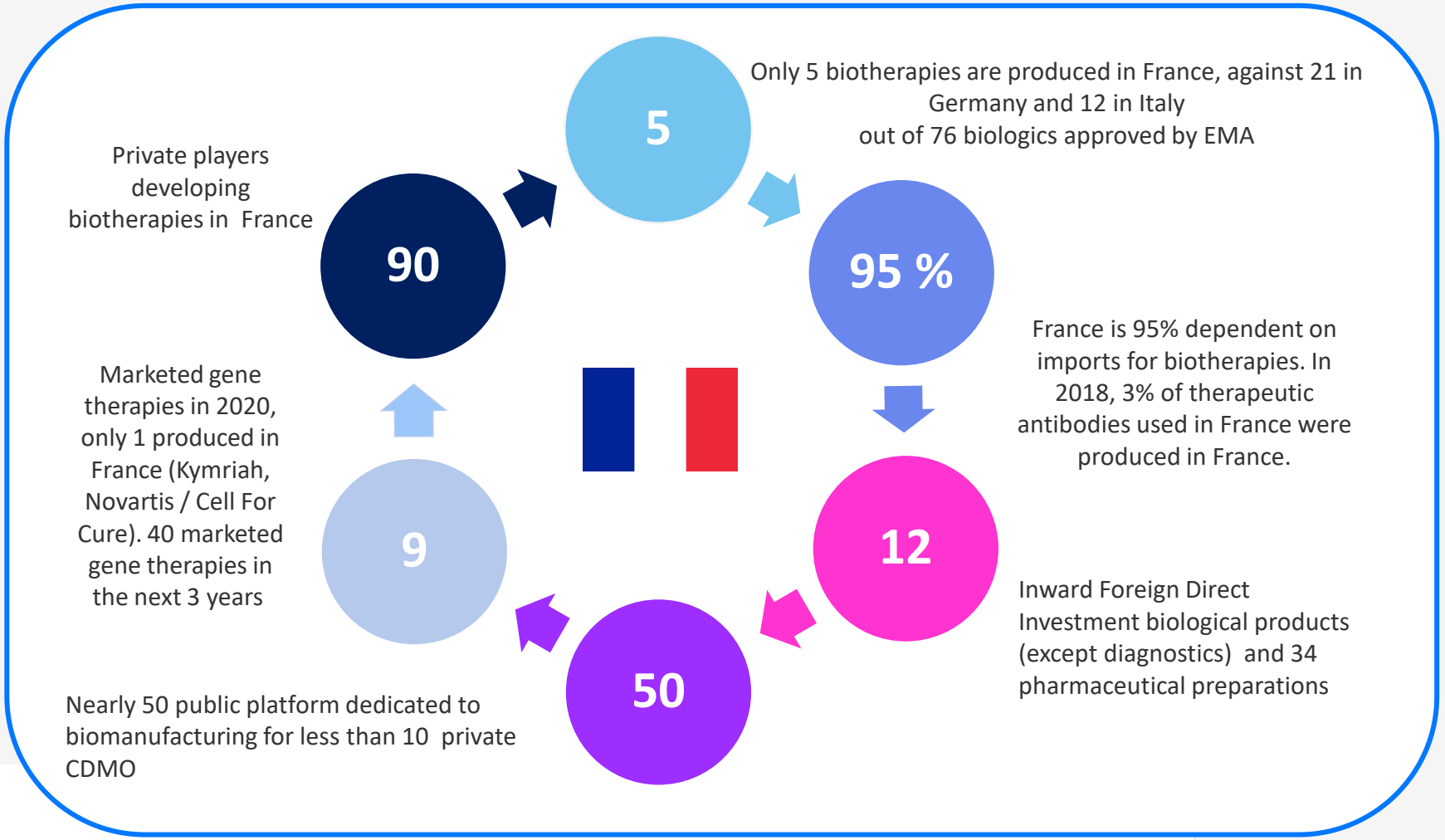
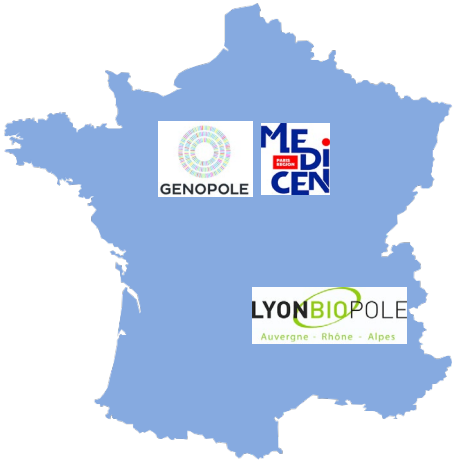
France

« France, a rich ecosystem for new biotherapies but with major lack on tech provider and ambitious CDMO for biomanufacturing. »



BioClusters Contributors



Focus

- **Historical position as a leader for classic vaccines** with a cluster (Lyon Biopole) and leaders (Sanofi-Pasteur, Institut Pasteur)

Executive summary

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France

	Pain points	Success stories	Opportunities
Education	• Nearly 50 public platform dedicated to biomanufacturing **but without national organization**, ambitious HR and internal innovation to develop new disruptive technologies	• A strong academic and clinic tissue in emerging therapies (**Cell and Gene therapies)** • **Strong competencies** in modelling, process engineering, sensors, synthetic biology/ genetic engineering and industrial biotechnologies on bacteria, yeast or micro-algae	**Campus Biotechnology and Digital Accelerator** (Sanofi, BioMerieux industrial partners, schools, start-ups).several spaces for **process design thinking** **Innovation digital training centre** (such as flight simulators) with digital twins, virtual & augmented reality, optimized control rooms with AI & robots
Innovation	• Need to explore **new source of cells and differentiation process** to create new cell therapies • Need to support the development of **new therapeutic vaccines**	**Aenitis Technologies is a French spin off ESPCI** ParisTech, a research engineer's school in Paris and The National Center for Scientific Research (CNRS). **Aenitis** Technologies is developing innovative separation, manipulation and filtration of biological elements solutions, based on acoustophoresis technologies.	• **A rich ecosystem** of private and academic actors developing biotherapies, especially for **therapeutic antibodies** • Strong growth of next generation Abs as ADCs and bispecific Abs in clinical development (some are marketed)
Business	• No/few supplier of equipment, consumable and raw materials • Only 10 private CDMO of small size • Not enough private investments in promising start-ups	**TreeFrog Therapeutics** has developed C-Stem™ : a proprietary technology platform that provides an end to end 3D scalable solution that will dramatically reduce treatment costs	• **creation of a national structure in charge of the French bioproduction strategy** with the aim of creating an aligned industrial sector and the marketing of disruptive technologies - industrialization. It may take the form of an **Alliance of industrial and academic players (Alliance France Bioproduction - AFB).**

Key recommendations

eit Health
eit Manufacturing
CEBR Council of European BioRegions
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NB : We would like to thank D&C Consultants which delivered the bioproduction report to the CSF-ITS/ CSF BioProd from which we extracted relevant data and the Ile de France Region who provided a large part of the data, mapping & recommendations presented in this report for France.

Contributions

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France

National specificities

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French context [CSF – ITS Bio-Production initiatives | Nov. 2020]

"France has a solid pharmaceutical sector with many players and a fundamental research ecosystem that is an internationally recognized source of R&D. But despite these qualities, since 2004 France has lost 3 places in the European ranking of drug-producing countries while it held a leading position. Although no study makes a formal diagnosis, we can observe significant differences in certain key development factors: lack of visibility of the industrial offer compared to Germany or Italy, weak structuring of our sector compared to United Kingdom and during the industrialization of projects, lack of support for funders and national regulatory authorities compared to the United Kingdom and Belgium.

The development of the production of biological drugs is a strategic axis of economic development for France which initially gave rise to the establishment of a Bioproduction initiative within the framework of the strategic sector contract signed by the State and health industry on February 4, 2019, and the **establishment by the Innovation Council of a major challenge "Biomedicines: increase yields and control production costs" in January 2020 ".**

For nearly 2 years, the actors involved in the sector have been able to organize themselves into an active and diversified network, around more than 100 public and private actors, by mobilizing significant human and financial resources (D & Consultants study with more than 50 interviews, **LEEM** study, exchanges with **France Biotech** and the **CSF-ITS BioProd** alongside **Pole-Pharma** and the, launch of an AMI (expression of interest) by all the Sectors, several conferences around these themes organized by the Competitiveness Poles and **CSFs Security and Electronics industries** Clusters, etc.). "

*Extract from **CSF-ITS – INITIATIVE TECHNOLOGIE DE RUPTURE POUR LA BIOPRODUCTION***

Only 5 biotherapies are produced in France,
against 21 in Germany and 12 in Italy
out of 76 biologics approved by EMA

France context specificities

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CSF-ITS BioProd strategic initiative

Opportunity

the Strategic Committee for the Sector for Health Industries and Technologies (CSF - ITS) set for the first time in February 2019 in its Strategic Sector Contract, the framework of an extended **collaboration between public and private actors, for an ambition of 500 million euros, prior to the construction of a federated sector around one objective: to make France the European leader in bioproduction.** The action plan proposed to achieve this revolves around 5 priorities:

1. **Creation of a scientific and industrial steering structure** for the sector, the "Alliance France Bioproduction".

2. **Support for research capable of producing the innovations of tomorrow,** and support for the development and industrialization of major technological innovations of today, aimed at drastically reducing the production costs of these biotherapies thanks to processes using the best of digital innovations.

3. **Consolidation of a network of industrial integrators** with the aim of facilitating and accelerating the passage of an innovation (product / technology) from its experimental stage to an industrial proof of concept stage.

4. **Improving the attractiveness of France**

5. **The development and maintenance of key skills in France** by setting up and consolidating initial and continuing training courses, adapted to future technological developments.

Jacques Volckmann, Chairman of the Board of the CSF-ITS Bioproduction Initiative.

Emmanuel Dequier, Director of the Grand Défi Biomédicaments

"Our goal is clear: to make France a leader in bioproduction. We have unparalleled potential in this area, in particular thanks to the network of industrial integrators developed in the regions. Today, we are accelerating the momentum to provide patients with the most innovative treatments, as quickly as possible.

This is the meaning of the roadmap set by the Sector Strategy Committee which will lead to the structuring of the entire sector to bring about the breakthrough innovations necessary for our ambition. "

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Clusters Network working together to support Bioproduction initiatives

Since 2019, Medicen acts as a copilot of the CSF ITS Bioprod Strategic Initiatives and as a national representative of health innovation clusters.

Health Innovation clusters develop in partnership with Grand Défi Biomédicaments, LEEM, France Biotech **the French Bioproduction Tour 2021** that aims to show each regional key assets and promote national bioproduction initiatives.

> 7 regional steps
> +100 key players mobilized
> +1500 Attendees

Focus on France Bioproduction Congress

In June took place the **France Bioproduction Congress** co-organised by **Polepharma** and **Medicen** that brougth together key players of bioproduction ecosystems including academic laboratories, SMEs, CDMOs and Pharma companies (either French or Foreign – eg Pfizer, Merck,…).

Key datas of 2021 edition :

+500 registrations
+350 attendees
+25 sponsors
+14 institutional partners

The next edition will take place in Paris on 2022.

Opportunity

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Part II.A

Tackling the talent gap and the talent crunch in biomanufacturing in Europe

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Academic forces & Labor Market

The HealthTech industry represents **50,000 direct and indirect jobs, and by 2030 could generate an additional 130,000 jobs in France.**

Because of the highly technical nature of the sector and the need for specific skills, HealthTech is part of a flourishing ecosystem of experts and suppliers.
85% of HealthTech firms outsource services, thereby generating a significant number of indirect jobs.**84% of HealthTech companies are intending to recruit in 2021,** mainly for R&D positions.

France also has differentiating public and private skills in process engineering, unique at the international level in modeling and artificial intelligence, microfluidics, analytical tools and synthetic biology.

SUP biotech

Université Paul Sabatier TOULOUSE III

Université Paris Sud – Faculté de Médecine – Université Paris-Saclay

IFSBM INSTITUT DE FORMATION SUPÉRIEURE BIOMÉDICALE

estbb Biology - Biotech school of Lyon

IMT FORMATIONS INDUSTRIES SANTÉ ET BIEN-ÊTRE

Bordeaux INP ENSTBB – ENSTBB FORMATION CONTINUE BIOTECHNOLOGIES ET PROCÉDÉS DE BIOPRODUCTION INNOVANTS

eit Health

eit Manufacturing

CEBR Council of European BioRegions

Institut Mines-Télécom

LANCEMENT DU 4e PROGRAMME D'INVESTISSEMENTS D'AVENIR

The Institut Mines-Télécom supports companies throughout the innovation cycle regardless of their stage of advancement. In particular, it hosts 200 startups in its incubators. Its partnership research contracts represent on average more than € 70 million per year. To support economic development in the regions

IMT is a national science and technology institute whose activities are carried out by 8 grandes écoles in the major regions. As part of the France Relance plan and the first wave of its support for R&D employment, the Institut Mines-Télécom (IMT) appears in 4th position among public operators involved in supporting scientific employment in as part of its partnerships with businesses.

The key themes of IMT echo government priorities as affirmed in PIA4. IMT positions its expertise in line with the major flagship themes that structure its research: **health engineering; risks & cybersecurity; AI, digital twins; networks and IoT, production systems; the industry of the future**

«. With this system, which not only preserves the skills of research collaborators in the private sector, but also supports young people who want to pursue a career in research in connection with companies, we are contributing to the future of the country. »

Odile Gauthier, General director de l'Institut Mines-Télécom

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Academic ecosystem

National Council of Industry - objectives

Context

- The emergence of **new areas of digital skills and tools** (data governance, data transparency, data security, etc.) bring need for integrating digital competence.
- The most frequently cited occupations are **biostatisticians and data scientists.**
- Historically recruited from clinical or marketing departments, today a **data scientist is increasingly in demand both for the management of a new production process and for the analysis of data from biomedical research.**

The evolution of the skills needed for healthcare professionals can be explained by the integration of industry 4.0 solutions into the processes of the sector and the emergence of digital technologies

- **8 key technologies impact the value chain of the business: cloud, cybersecurity, IoT, AI, big data augmented reality, digital simulation, robotics**.
- From this perspective, in terms of initial training, it seems relevant to be able to set up **multi-skills schemes, which carry multi-disciplinary measures** (decommissioning of sectors and specialties).
- With regard to continuing education, skills blocks should be built with schools and training bodies, based on the collection of the needs, according to an interactive, transparent and permanent process, which should enable the **identification of new skills needs and the needs for the evolution of the training offer.** The aim will be to adapt the certification strategy accordingly

Biotech Skills Plan for France in 2025

The main objectives of the project are:

1. Find a forward-looking vision of biotechnology;
2. Identify the qualitative and quantitative impacts on organizations, issues and human resources needs;
3. Find the initial and continuing training needs and verify the suitability of the existing offer;
4. Develop recommendations and an action plan in terms of human resources (trades, skills) for LEEM and the various players in the sector

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Mabdesign Academy

MabDesign is a membership organization dedicated to the creation of a unique environment that allows the economic **development and growth of the French industrial sector in the field of therapeutic antibody and immunotherapy.**

Issued from governmental and health industry recommendations, MabDesign was created in November of 2014 by the determination of three pharmaceutical companies **(LFB biotechnologies, Pierre Fabre, Sanofi) and 5 regional bio-clusters (Atlanpole Biotherapies, Cancer-Bio-Santé, Eurobiomed, Lyonbiopôle, Medicen Paris Région). MabDesign is strategically located in Lyon, at the heart of Europe.**

MabDesign Training assisted the following companies in increasing the skills of their teams to respond to the changes in the industry.

MABDESIGN academy

IMT FORMATIONS INDUSTRIES SANTÉ ET BIEN-ÊTRE

Biomedicine developability assessment : From R&D to industrialization

- **Overview of CMC (Chemistry Manufacturing Controls) activities for mAbs product development (from Clone to Clinic phase 1 and 2)**
- **CMC Strategy**
  - TPP
  - Quality by Design
  - CoG (Cost of Goods)
  - Gantt
- **Analytical development**
  - Regulatory strategy
  - Analytical development and validation
  - Analytical Methods for In-Process, release and Stability testing
  - Analytical Methods for measuring Purity and product related impurities
  - Reference standard
- **Cell Line development**
  - Host cells selection
  - Cell Line development activities
  - Preparation and characterization of Cell Bank
  - Key decisions and Risks associated with Cell Line development
- **Cell culture, Development and scale-up**
  - Growth and productivity assessment
  - Media and Feed optimization
  - Cell culture optimization and scale-up
  - Planning for process change
- **Purification Development and Scale-up**
  - Removal of contaminants
  - Specific unit for mAbs Purification (Centrifugation, filtration protein A, virus inactivation, ...)
  - Scale-up
- **Formulation Development and Stability**
  - Degradation Pathways
  - Excipients
  - Formulation development
  - Stability studies
- **Drug Product development**
  - Bulk DS
  - Container
  - Aseptic filling
  - Lyophilization
  - Release testing
- **Process Validation**
  - A brief overview to phase 3 and commercialization.

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Success story Education

The French bioproduction sector announces the creation of Campus Biotech Digital, a platform unique in the world for bioproduction training

Opportunity Education

Covering the entire bioproduction chain, Campus Biotech Digital will use various innovative digital solutions to promote understanding of processes and the appropriation of professional practices.
The Campus is managed by a leading industrial consortium (bioMérieux, Novasep, Sanofi, Servier)

The Campus is financed by an exceptional public / private partnership including €11,75 million as part of the "Engineering of vocational and on the job training and innovative offers" financing program by Caisse des Dépôts on behalf of the French State, to which in addition, there is a support from Opérateur de Compétences interindustriel (OPCO 2i), Région Ile de France as well as Pharma Companies grouped into Consortium for **an investment of more than € 30 million**.

Opening of the first training courses in spring 2021

Covering the entire bioproduction chain from design to delivery of the product to the patient, Campus Biotech Digital uses

- various digital tools reproducing essential production elements (**digital twins, serious games, immersive reality, virtual reality and augmented reality)**
- and cognitive approaches supported by **artificial intelligence to promote understanding of processes**.

The training courses, inspired by those provided by flight simulators to train airplane pilots, will generate real added value unique in the world in bioproduction on several levels:

- The acquisition of **new skills by employees**
- The arrival on the **labour market of young graduates and retraining employees,**
- The training of experts for **breakthrough innovations**
- **Learning communities** to developp of networks, start-ups and cooperation

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Part II.B

Research to

Innovation

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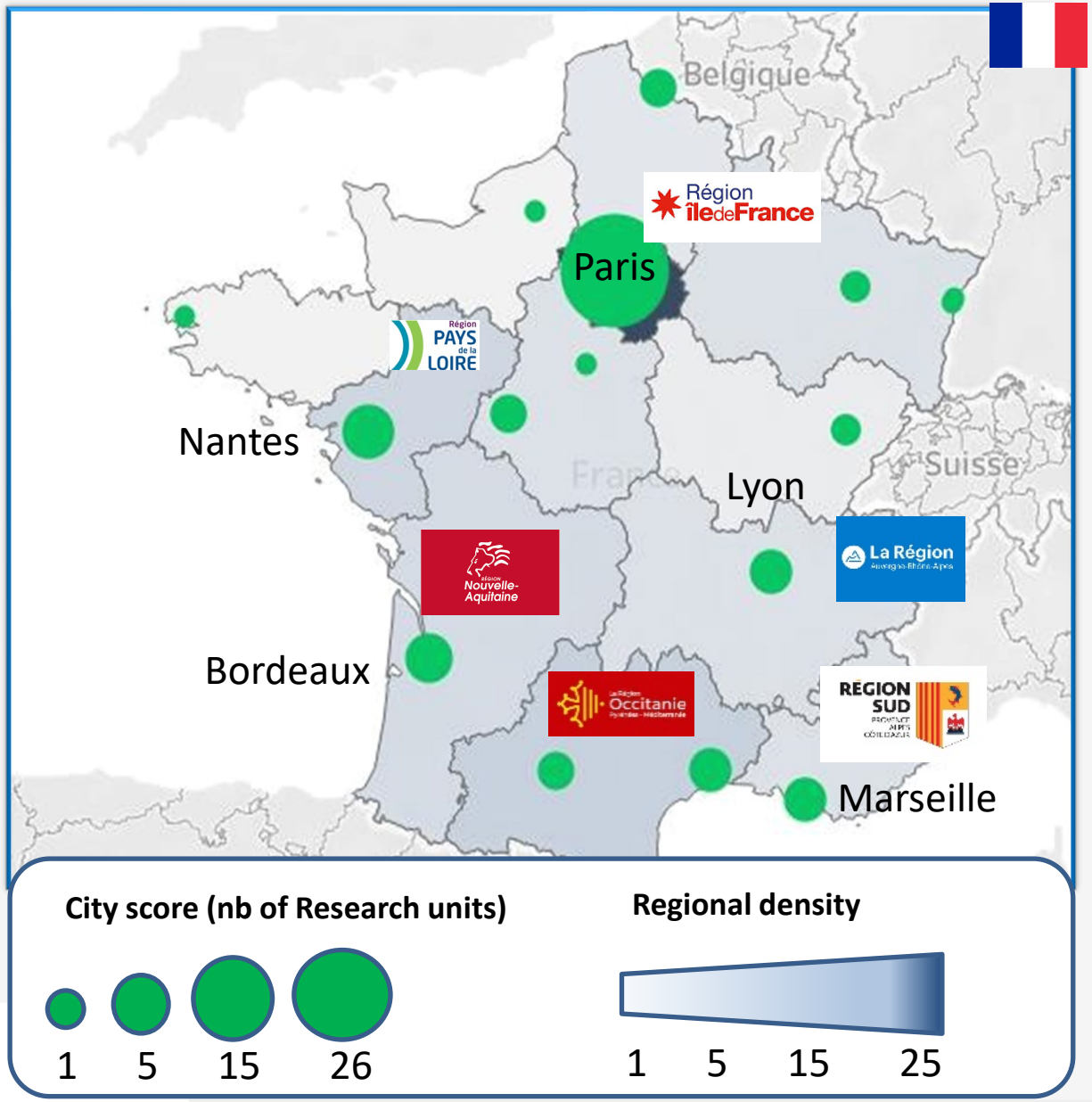
Academic players in biotherapy in France

Work from the best research organizations such as the French **Atomic Energy and Alternative Energies Commission (CEA),** the **National Center for Scientific Research (CNRS)**, **the National Institute for Computer and Automation Research (INRIA),** the **Pasteur Institute** or the **National Institute of Health and Medical Research (INSERM**) as well as those of certain **university hospital centers (CHU)** are references on many subjects (HIV, genomics, oncology, etc.).

France has a recognized network of players developing biotherapies, particularly in the field of therapeutic antibodies, but also in the field of cell and gene therapy thanks to strong academic and clinical expertise. **French academic and clinical research, with nearly 100 research units, in the field of biotherapies is rich and is mainly concentrated in 3 regions** : Ile de France, Pays de la Loire and Occitanie with international excellence in cell and gene therapy and vectorization. Laboratories such as the IRMB, the Imagine Institute, I-stem and the CEA are particularly recognized in the field



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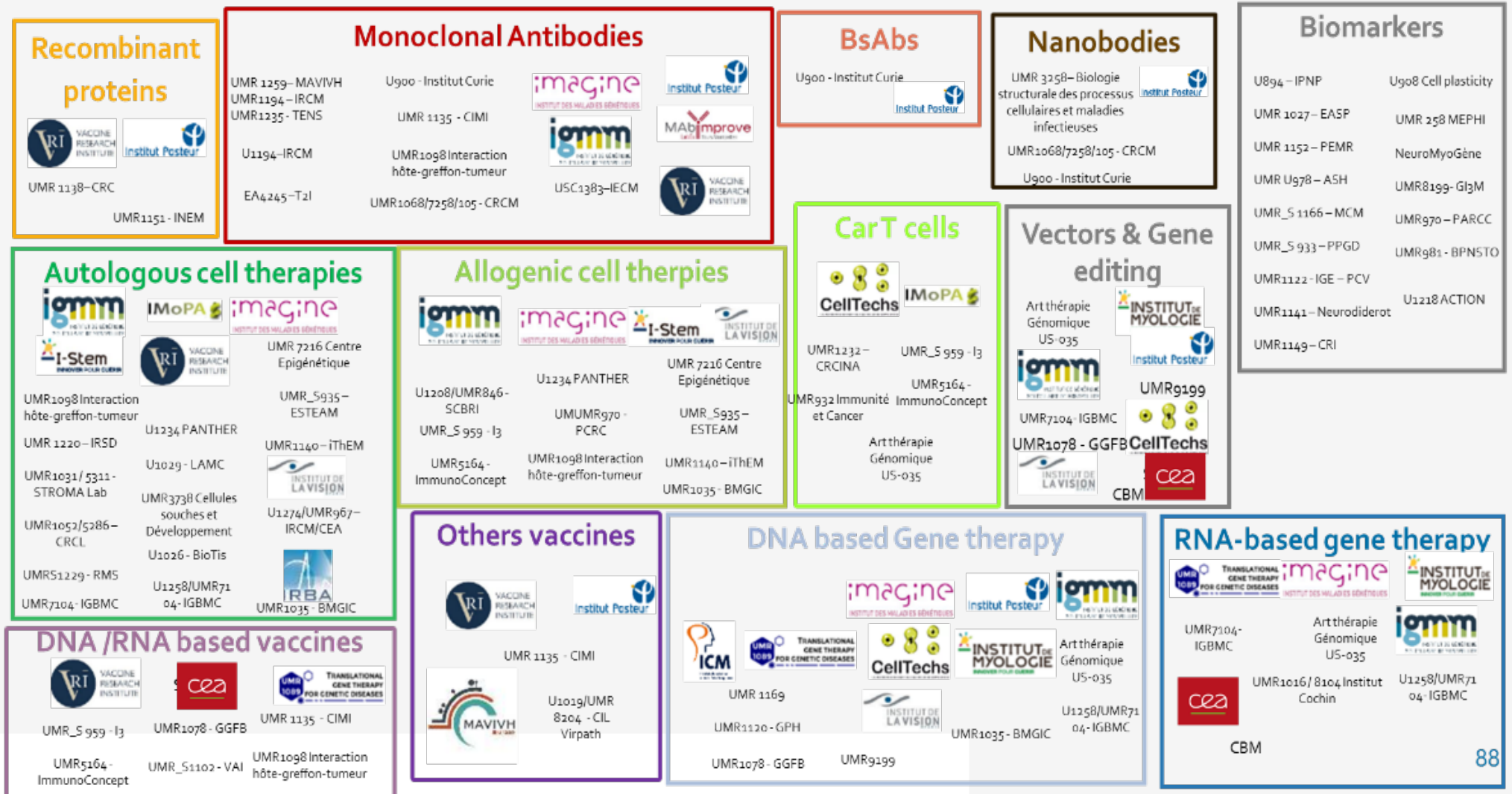
Academic players in biotherapy in France



Innovation capabilities

eit Health eit Manufacturing CEBR Council of European BioRegions

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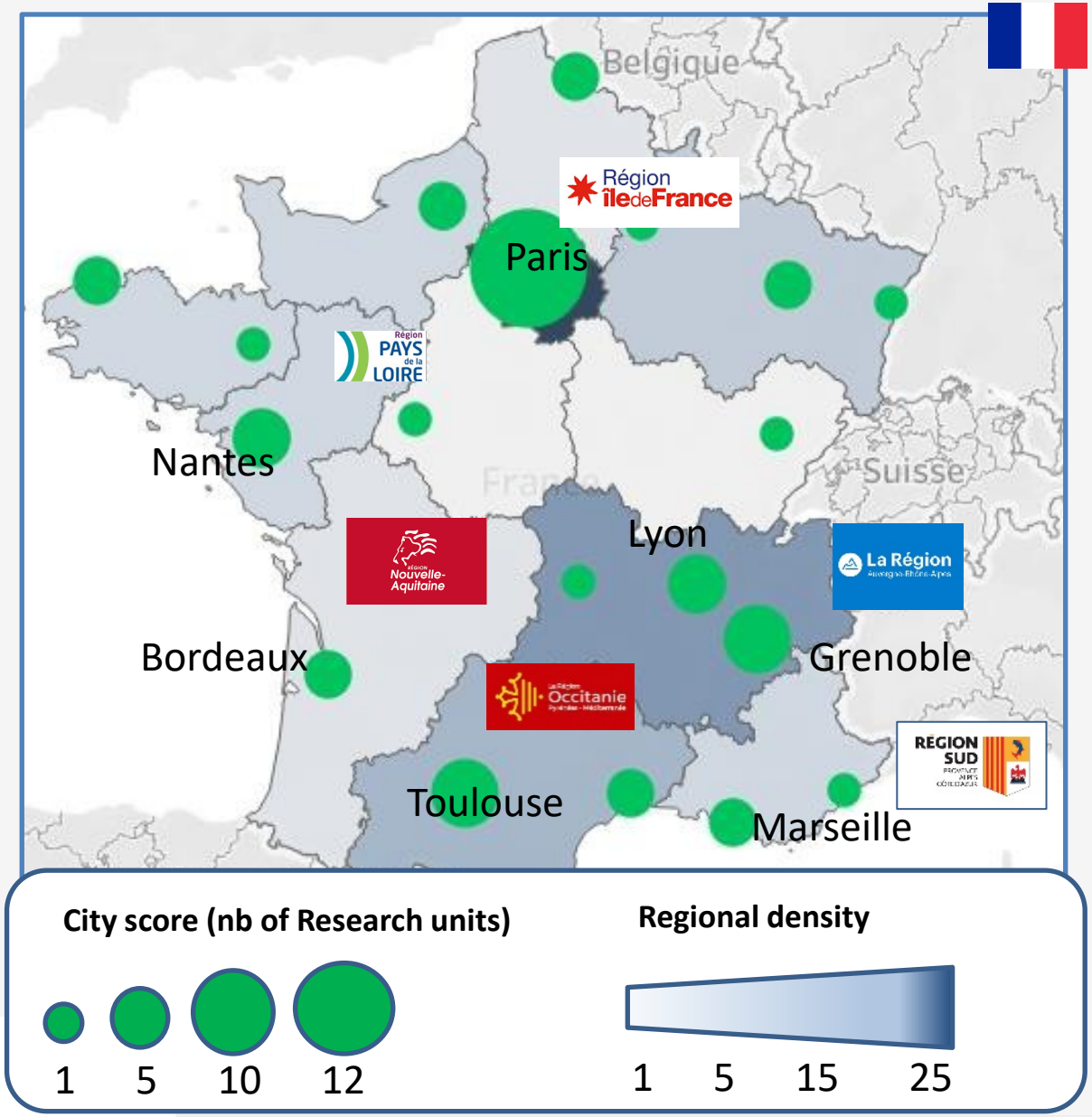
Players as Tech provider for Biomanufacturing in France

France also has differentiating public and private skills in process engineering, unique at the international level in modeling and artificial intelligence, microfluidics, analytical tools and synthetic biology.

For example, academic or private-associative actors: Bio3 à Tours, CEA, Centrale Supélec, ESCPI, INSERM, CNRS/INSIS, Généthon, Institut de Myologie, Institut Pasteur, IPGG, IRT Bioaster, TWB, etc. ; **Clinical actors**: AP-HP, EFS, IHU, etc. ; **Private actors** : Altran, Dassault Systems, Flash Therapeutics, Novasep, Sanofi, Servier, ST Microelectronics, Texcell, Transgene, V-Nano, Yposkesi, etc.



Innovation capabilities

Academic players as Tech provider for Biomanufacturing in France

Innovation capabilities

Bioreactors modelization & Safety

Bio CO2re

EA4038 LGPM

I-CLeHS / IPPG

UMR 144 Biologie cellulaire et cancer

LRGP

ProBioGEM

cbmn

BIOASTER

ibisc

LAGA

UMR7502 - Equipe BIGS

leti ceatech

twb

Process engineering

2PM

GEPEA

LISBP

CBI

UMR 6602 Institut Pascal

EMBRC FRANCE

UMR 1163 Biodiversité et Biotechnologie Fongiques

UMR6286 - UFIP

C2N

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femto-st SCIENCES & TECHNOLOGIES

UMR 8640

ERRMECe

3D Bioprinting

UMR 168 Laboratoire Physico Chimie

Laboratoire Microfluidique Physique et Bio-ingénierie

UMR6229 ICMR Institut de Chimie Moléculaire de Reims

icb ims UMR 5306

BIOTIS

bio institute

ease

CPE

Education

Cell growth optimization

Process optimization software and numeric tools

Vectors and cell transfection tools

Robotics

Purification/capture

Analytics

Cell free system

Cells screening

Microfluidic

Algae engineering

UMR 6047

list ceatech

LS2N

Laboratoire Paul Painlevé

GENCI Le calcul intensif au service de la connaissance

litis

I2BC

EMBL

ibs

isbg

imm

CBS

LMGM

UMR 8030 Génomique métabolique

PF3PR / Institut pasteur

USR 3505 - ITAV - Projet Imactiv-3D

LAMBE

LCB

IBMM Institut des Biomolécules Max Mousseron

UMR 8197/U1024 "Institut de Biologie de l'ENS"

UMR 6270 Laboratoire PBS

Data Management

Cells engineering

Micalis

MSC

eit Health

eit Manufacturing

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A strategic priority for the Ile-de-France Region

Go further, following the Smart Health Strategy and the health crisis

- Federate and structure regional initiatives
- Engage in the construction of an ambitious strategy from innovation to industrialization 2021-2026 around biotherapies and bioproduction.

A long-standing commitment to research

- Research support displayed by funding dedicated to research projects on stem cells, biotherapies, gene therapy, n to networks of researchers and research centers
- Support for ecosystem coordination and federation structures (Genopole, Meary Center, etc.)

Funding already effective for innovation and economic development

- Innov'up device, AAP Ile-de-France, leader in Bioproduction,
- Sesame Sector Leader PIA
- Collaborative places: Sanofi Vitry on antibodies

Track record

Location	Biological products (except diagnostic) (inward FDI)	Pharmaceutical preparations (inward FDI)
Greater London	22	36
Paris (Region)	12	34
Munich (Region)	7	17

Size of industry - Data

Location	Companies in biopharma
Greater London	313
Munich (Region)	205
Paris (Region)	70

Industry cluster

Tier 2 sub category	Weight	Paris (Region)
Size of industry	40%	3dt
Track record	25%	2nd
Industry specialisation	25%	3rd
Research and development capabilities	5%	2nd
Export competitiveness	5%	2nd

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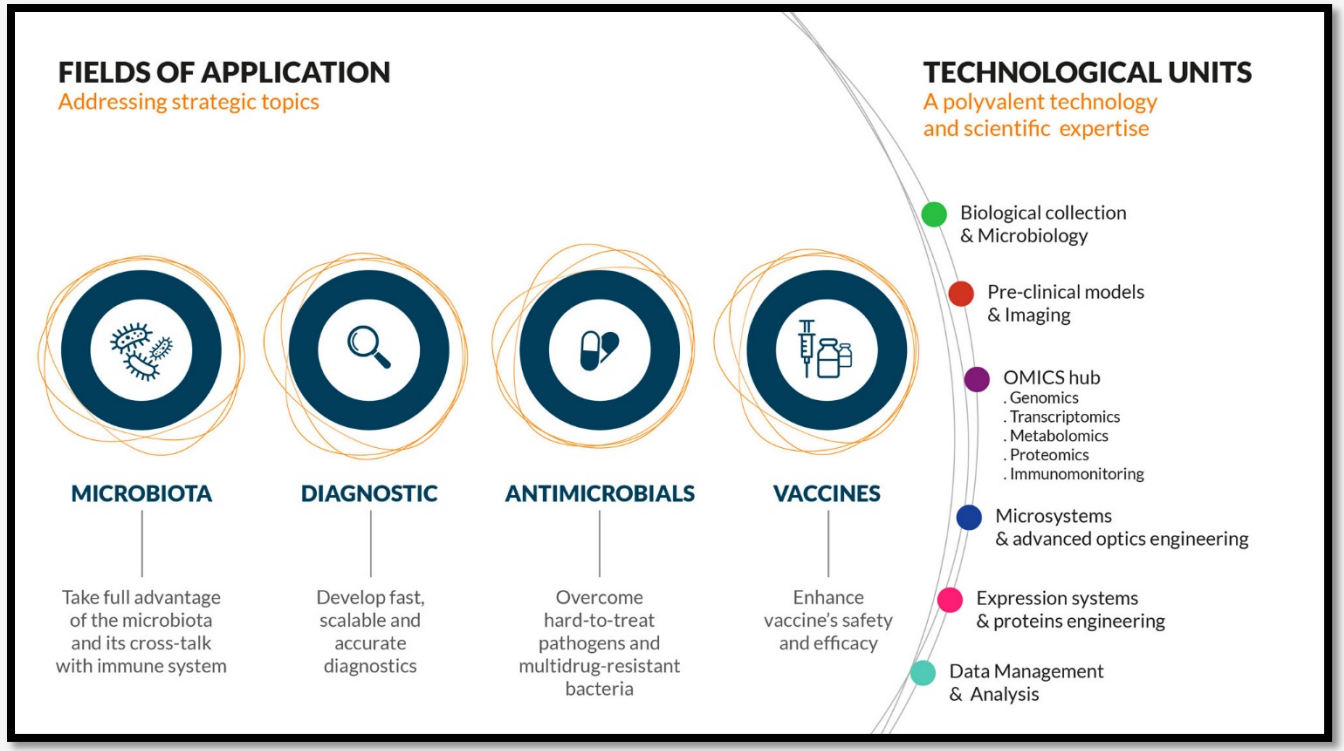
Innovation policy

BIOASTER, a new model for technology innovation in microbiology

Complementary and co-localised scientific and technological expertise,
using advanced platforms dedicated to microbiology to create new synergies.

BIOASTER
MICROBIOLOGY TECHNOLOGY INSTITUTE



Fight antimicrobials resistance.

Improve vaccines safety and efficacy.

Quickly diagnose infections at patient bedside.

Take full advantage to human and animal microbiota.

In order to overcome technological bottlenecks and explore new avenues, BIOASTER is leading collaborative projects that bring together academics, start-ups, SMEs and industrial groups.

Success story Innovation

eit Health

eit Manufacturing

CEBR
Council of European BioRegions

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Recovery plan & PIA4

The 2020-2022 economic recovery plan, presented last September, **devotes 6 billion euros to the health sector as part of the Ségur de la santé.**

It also includes an envelope of 600 million euros of targeted investments for "industrial relocation" by 2022 in five sectors deemed strategic, including health with the establishment or extension of pharmaceutical manufacturing sites.

In detail, the funds of the PIA4 presented on January 8 will be divided into two main "priorities":

1. **7.5 billion euros to "irrigate ecosystems of higher education, research and innovation“**

1. **and 12.5 billion euros to "build acceleration strategies targeted on priority sectors and innovation and technologies".**

Health as a common thread
The health sector is present in the two main priorities presented.

"Thanks to the PIA4, **the State thus guarantees long-term and predictable structural funding for ecosystems and higher education organizations (research universities, laboratories of excellence, etc.), research and innovation (university hospital institutes, institutes technological research ...),** to make France the most fertile and attractive breeding ground in Europe for students, teachers, researchers and entrepreneurs. so-called 'structural' innovation ”.

Likewise in the part relating to the acceleration strategies targeted on priority sectors and innovation and technologies (12.5 billion euros), over 2021-2023**, the PIA will mobilize 2.6 billion euros. on "priority investment strategies" for economic independence, for example concerning artificial intelligence (AI), the cloud, cybersecurity, quantum technologies, digital health, the bioproduction of innovative therapies, the fight against infectious and emerging diseases**.

This second part of the PIA consists in targeting a few so-called "priority" markets and technologies and in supporting companies and research laboratories in the various stages of their development.

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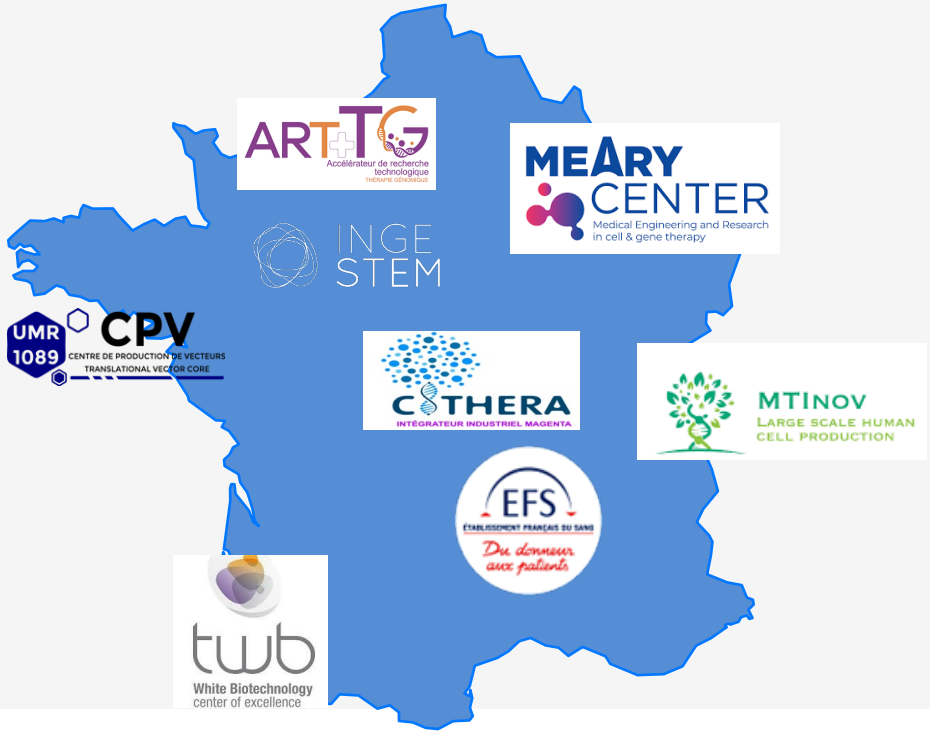
Opportunity Innovation

Grand Defi / Pre-Industrial Platform

The Grand Défi "Biomedicines: improving yields and controlling production costs" labeled various technological platforms which are becoming the industrial integrators of the Grand Défi.



Evotec Starts Construction of Its Toulouse Biomanufacturing Facility

Evotec began construction of its J.POD® 2 EU biologics manufacturing facility at its Campus Curie in Toulouse, France. J.POD 2 EU, Evotec's second cGMP biomanufacturing facility, will use technology from its wholly-owned subsidiary, Just – Evotec Biologics, that utilizes small, automated, highly intensified and continuous bioprocessing operations housed inside autonomous cleanrooms.

J.POD® 2 EU will be Evotec's first commercial biomanufacturing facility in Europe. The construction of Evotec's first J.POD® 1 US in Redmond, WA, is expected to be operational later this year.
The build-up of J.POD 2 EU will be supported with up to € 50 million from the French government, the Occitanie Region, Bpifrance, the Haute-Garonne prefecture as well as Toulouse Métropole. The total investment that Evotec plans to undertake is currently estimated at approx. € 150 million.

"The global availability and accessibility of highly effective biotherapeutics has been Just – Evotec Biologics' mission right from the start," said Werner Lanthaler, PhD, CEO of Evotec. "The ongoing coronavirus pandemic has underlined the need for flexible and nearshore biomanufacturing capacities. We are very grateful that through the support of the French government as well as all local institutions, we can now continue to deliver on this mission with the construction of Europe's first J.POD® facility. This is critical for society."

Opportunity Innovation

eit Health eit Manufacturing CEBR Council of European BioRegions

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Part II.C

Business Innovation

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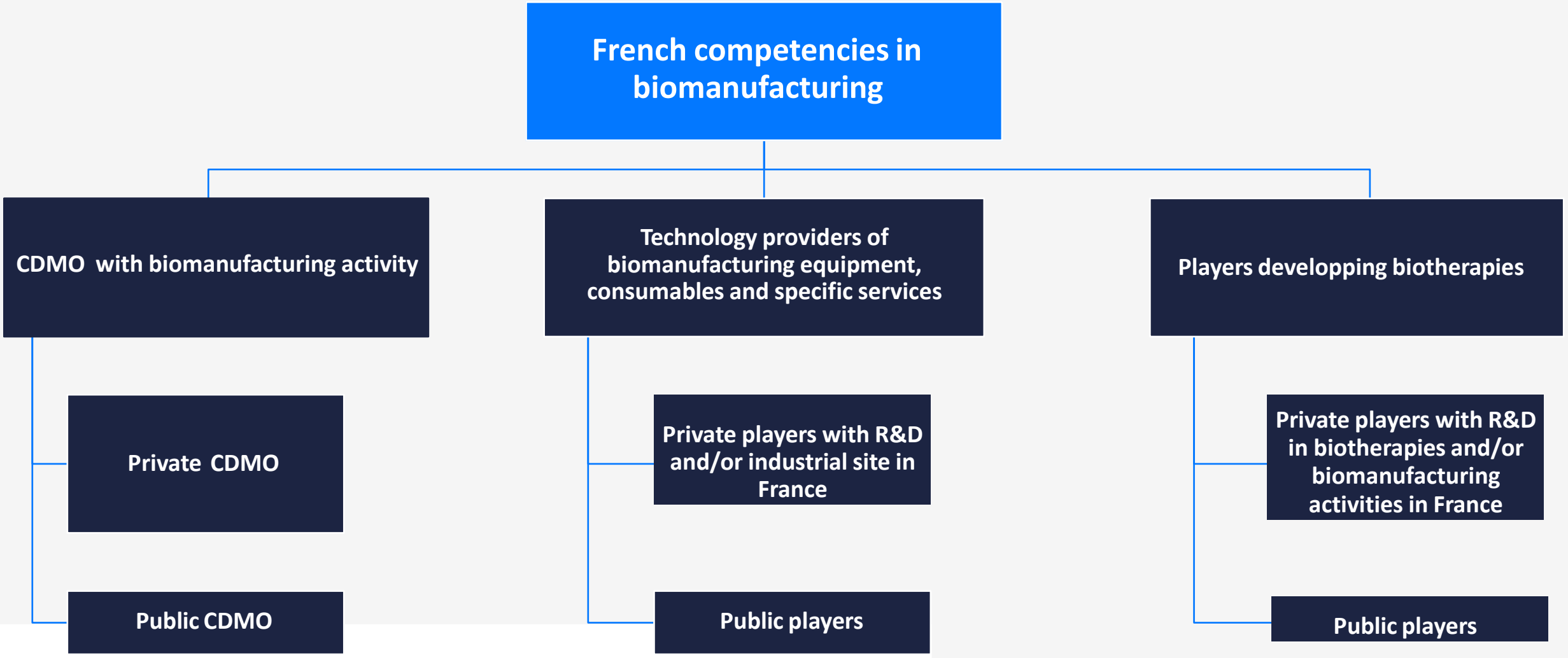
Cartography of French competencies
Description of type of actors



Business ecosystem mapping

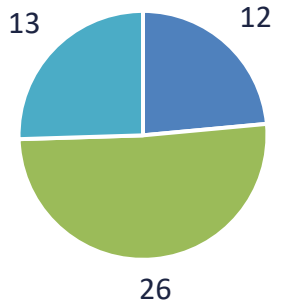
Funded by the European Union

Source: Directory of poles, clusters and regional agencies, LEEM reports on biomanufacturing and innovative therapies, Internal database at D&C, Winners of Bpifrance competitions

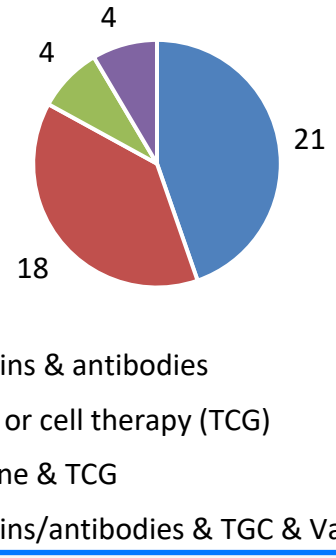
Positioning of CDMO on biomanufacturing value chain

Business ecosystem mapping

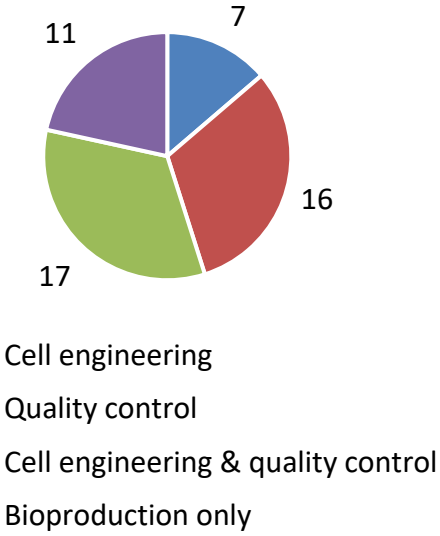
CDMO breakdown according to bioproduction type



CDMO breakdown according to biotherapy type



CDMO breakdown according to specialty



Nearly 50 public platform dedicated to biomanufacturing but without national organization, ambitious HR and internal innovation to develop new disruptive technologies for less than 10 private CDMO…

….But a strong private and public competencies in analytical and biosafety for biotherapies

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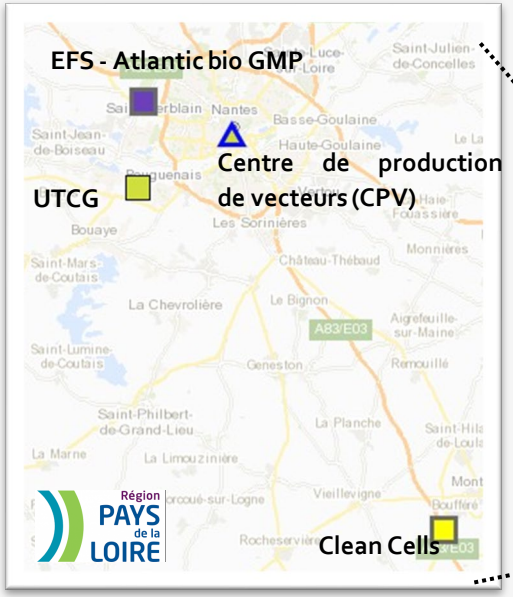
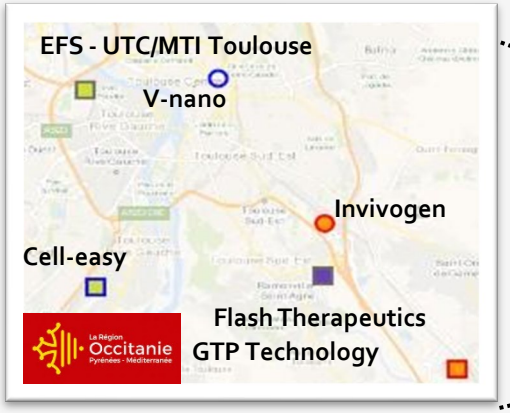
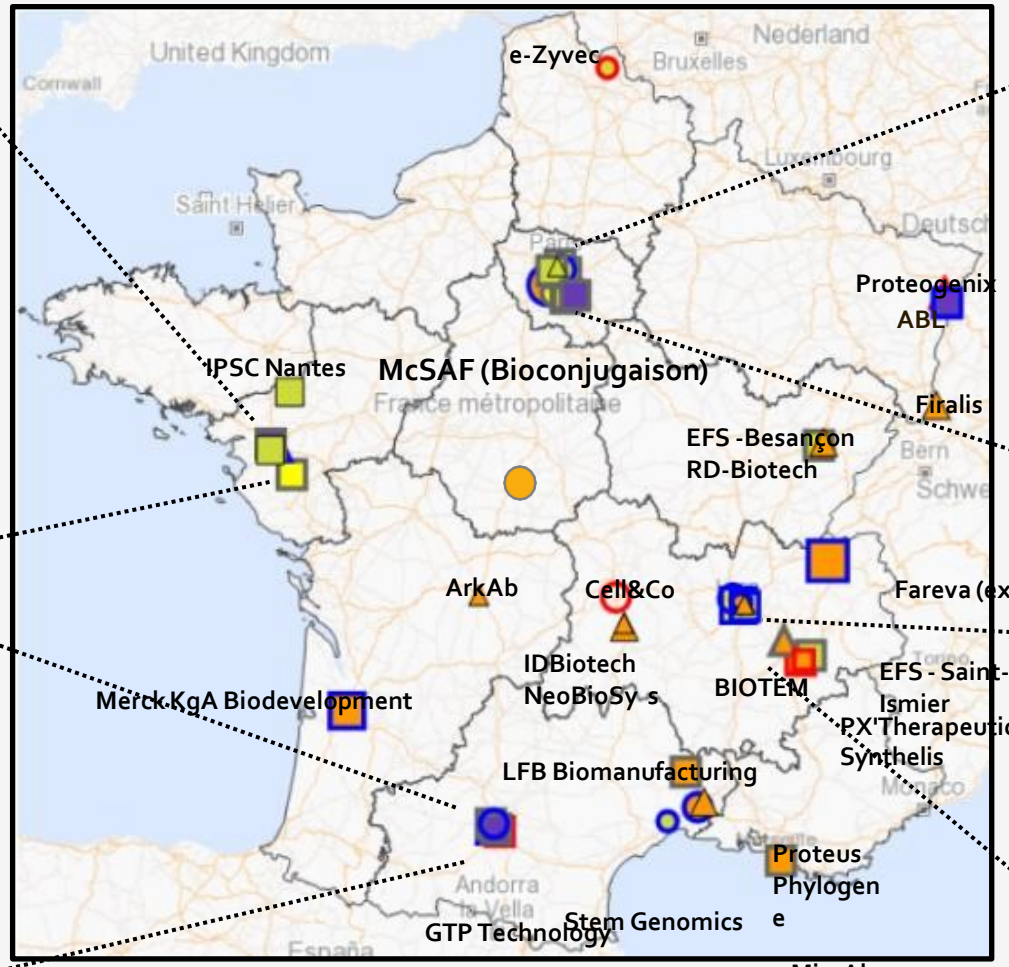
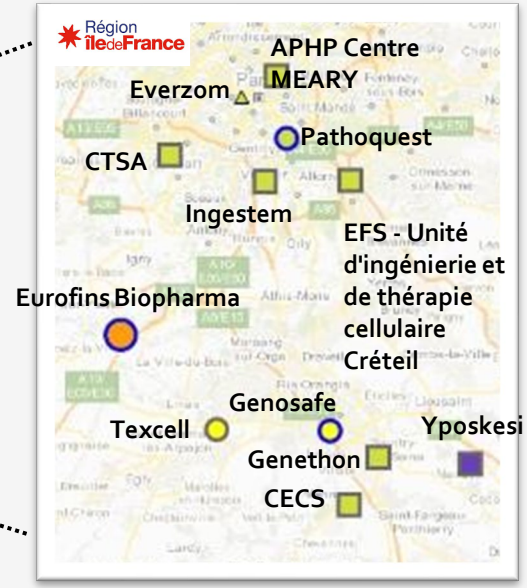
CDMO players in biomanufacturing in France composed of only 10 private CDMO of small size

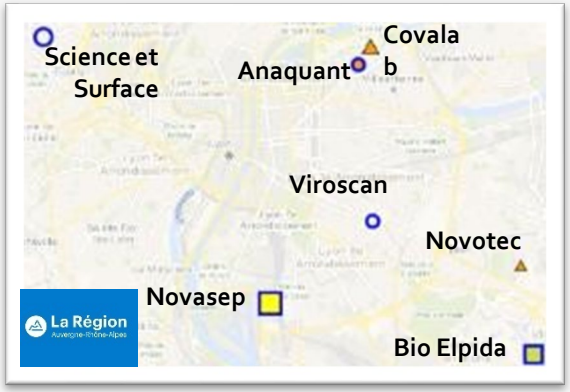
Business ecosystem mapping











Type of specialty

- Cellular engineering
- Cellular engineering & control quality
- Quality control
- Production only

Type of biotherapies

- Protein & antibodies
- Vaccines & GCT
- Protein, antibodies , GCT & vaccines
- Gene & cells therapies GCT
- other

Biomanufacturing GMP / Non GMP

- No biomanufactring capabilities
- GMP
- Non GMP

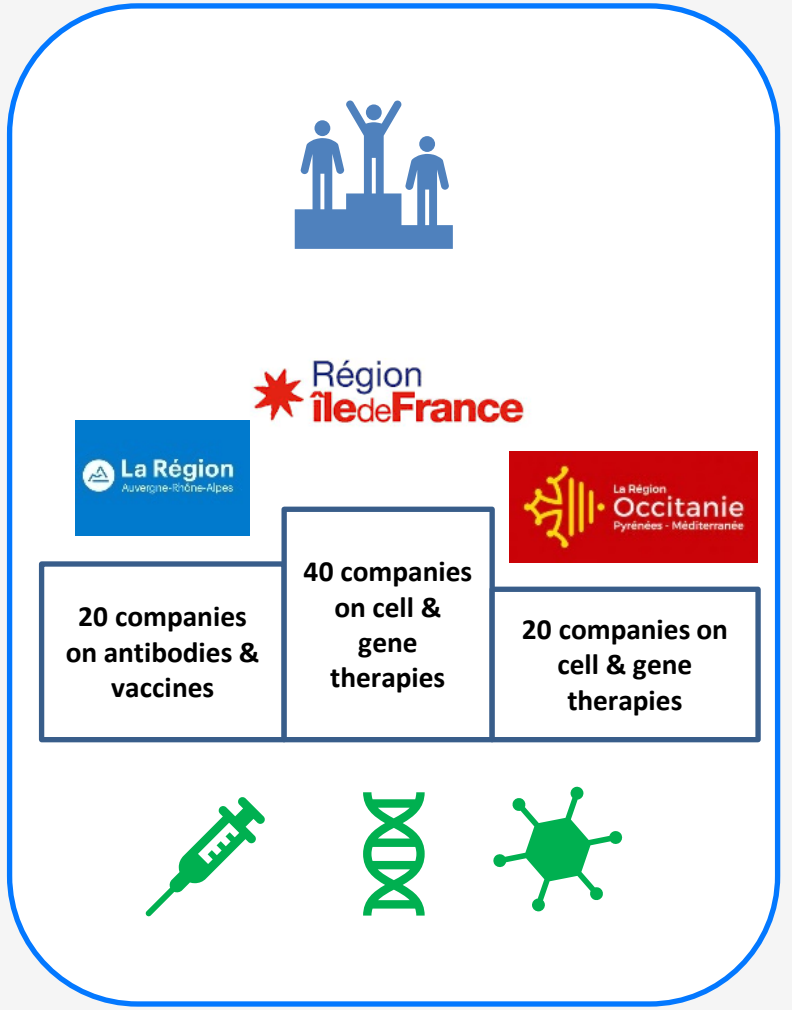
Positioning of French 90 private players by biotherapies

France has a recognized network of players developing biotherapies, particularly in the field of therapeutic antibodies, but also in the field of cell and gene therapy thanks to strong academic and clinical expertise.

It should be noted that the low supply of bioproduction for third parties leads these players to have their biotherapies produced abroad for clinical batches and, by continuity, for commercial batches.

These players are mainly in Ile de France, Auvergne Rhône Alpes and Occitanie.

- The Ile de France thus has a rich and varied fabric of players developing biotherapies with nearly 40 companies mainly positioned on the development of gene therapy and therapy based on CAR-T cells and therapeutic antibodies.
- The Auvergne Rhône-Alpes region, with nearly 20 companies, is more active in therapeutic antibodies and proteins and vaccines.
- Occitanie, also with nearly 20 companies, is mainly present in ITNs with cell and gene therapy.



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Positioning of French 90 private players by biotherapies

Opportunity

Recombinant proteins

LFB ★ SANOFI ★
IPSEN
ANGANY
erytech
MED-INN-PHARMA LABORATOIRE INNOVANT
Tridek - One

Monoclonal Antibodies

NOVARTIS ★ Pierre Fabre SANOFI ★ SERVIER ★
Alderaan Biotechnology ciloa DIACCURATE Innovative Immunotherapy encefa ElsaLys Biotech
GAMAMABS PHARMA Galápagos HiFiBiO THERAPEUTICS iDD biotech
iMAb innate pharma OGD2 Pharma odimma OREGA Biotech ImCheck therapeutics
OSE Immunotherapeutics NETRIS Pharma SKMAB xenothera

Bispecific Antibodies (BsAbs)

SANOFI ★ SERVIER ★
BIOMUNEX pharmaceuticals ElsaLys Biotech
evotec innate pharma
OREGA Biotech OSE Immunotherapeutics

ADC

Pierre Fabre ★ OGD2 Pharma

Nanobodies

SANOFI ★ Fab'entech
iMAb Theranyx

Autologous cell therapies

angegenesis CELLPROTHERA DISCOVERY CELL CULTURE TRANSPLANT smart immune
erytech ORGANIC VACCINES
poietis SCARCELL THERAPEUTICS Symbioken

Allogenic cell therapies

SANOFI ★ angegenesis evotec
GO LIVER Therapeutics medXcell

CarT cells

NOVARTIS ★ SERVIER OGD2 Pharma
aratinga.bio Honing BIOSCIENCES
medXcell NKar THERAVECTYS

Antibodies for IVD

BioSpeedia b cell design
GENCLIS SurgiMab
Diaclone RD-Biotech

DNA /RNA based vaccines

evotec In Cell art SANOFI ★
APCure AIVA ciloa
invectys KARCINOLYS
odimma ONCOVITA OSIVAX
STIMUNITY transgene VAXON Biotech

Others vaccines

gsk GlaxoSmithKline Only F&F SANOFI ★
Adjuvatis CALIXAR
imaxio PHERECYDES PHARMA Telomium
ViroCoVax valneva

DNA based Gene therapy

SANOFI ★ Alma Bio Therapeutics
BRAINVECTIS eyevensys
EUKARYS flash THERAPEUTICS GENETHON GenSight
HORAMA LYSOGENE
Sensorion
SPARINGVISION Vivet THERAPEUTICS

RNA based Gene therapy

SANOFI ★
Dynacure medesis
flash THERAPEUTICS MESSENGER BIOPHARMA ONXeo

Private actors with biomanufacturing capabilities ★

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Biomanufacturing Capacity

The Biomanufacturing sector of producers is fragile.

It includes actors that are not very visible but multiple of public platforms, less than 10 so-called Mid-sized biomanufacturers (Including ABL Europe, LFB Biomanufacturing, Merck Biodevelopment, Fareva ex Pierre Fabre CDMO, and Yposkesi), only 9 factories for the own production of 3 pharmaceutical players (Sanofi, Novartis and Servier), for the production of a limited number of biotherapies.

But only 5 biotherapies are produced in France against 21 in Germany and 12 in Italy out of the 76 authorized in Europe. France is 95% dependent on imports for biotherapies.

ABL inc. ADVANCED BIOSCIENCE LABORATORIES

LFB S.A.

SANOFI

NOVARTIS

Pierre Fabre

YPOSKESI

MERCK

Opportunity

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Private players as Tech provider for Biomanufacturing activities in France

Business ecosystem mapping

Stem cell engineering/ Genomic expression system characterization

ALTRA Bio, Biofacet, bgene, GENOMIC VISION, DEINOVE, XEGEN, WHITELAB GENOMICS, EUKARYS, MAbSilico, IMEAN

Vectors and cell transfection tools

ciloa, DNA SCRIPT, OZ BIOSCIENCES, Polyplus, Polytherapene

High yield cell line selection

BioTek, BioCytex, Biomillenia, Biosciencia, cellenion, MilliDrop, SCI PIO, X'PROCHEM, Miltenyi Biotec

Cell line engineering

ADISSEO, GenoScreen, HELIXIO, INTEGRAGEN, yposis, jmp, OWKIN, Seqone, MALTIS, MethodOmics, SOPHIA, TRAASER

GENETHON

Stem cells provider

BIOPREDIC, LYMPHOBANK, Phenocell

Cell culture system

4Dcell, CELLPROTHEC, GENETHON, GPC, PIERRE GUERIN, macopharma, NETRI

Cell culture raw materials /inputs

3D MATRIX, HEMARINA, Solabia, ABCell-Bio, CellMade, ICELLTIS, NVH Medicinal, Procelys

Smart Lab

ASTRAVEUS, Creative, iLsa, TreeFrog

Microfluidic

ELVESYS, FLUIGENT, Klearia, VULKAM, Cherry Biotech, microlight3d

Single use tech

MERCK, sartorius stedim

Analytics

bertin TECHNOLOGIES, BioMeca, Lipofabrik, SCALPS, Geno Splice, CYPRIO, NANObiose, INNOPSYS, burkert, CYTOO, promise, iPRASENSE, STILLA, resolution spectra systems, GENETHON, MERCK

DSP Chromatography

affilogic, BIO-RAD, KROMATON, novasep, LIBIOS, GENETHON, YPSO FACTO

DSP Ultrasonic technologies

DAICEL, aenitis, NovAliX, SYNETUDE

Viral safety

BIOMERIEUX, indicia, myriade

Data management

Thermolabb, EXPERT SYSTEM, IBM, intel, Atos, DEXSTR, Microsoft, SWORD, EXACT CURE, DASSAULT SYSTEMES, altran

Process sizing

MERCK, 3C FRANCE

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D&C CONSULTANTS

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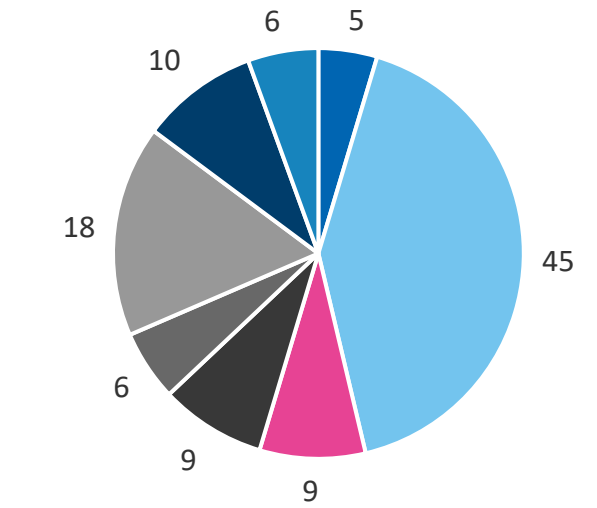
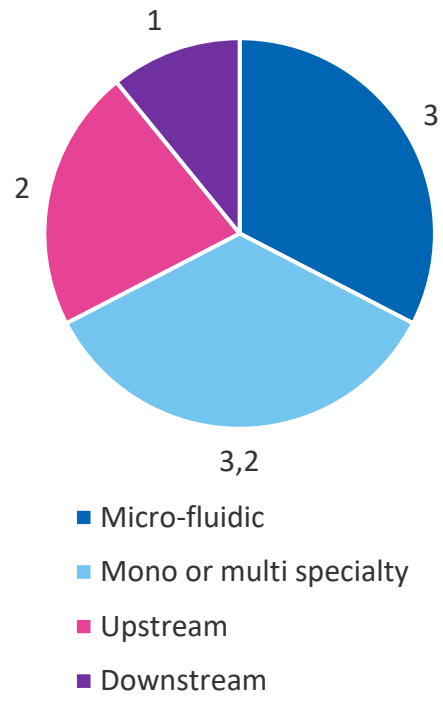
Private players as Technology providers for Biomanufacturing activities in France

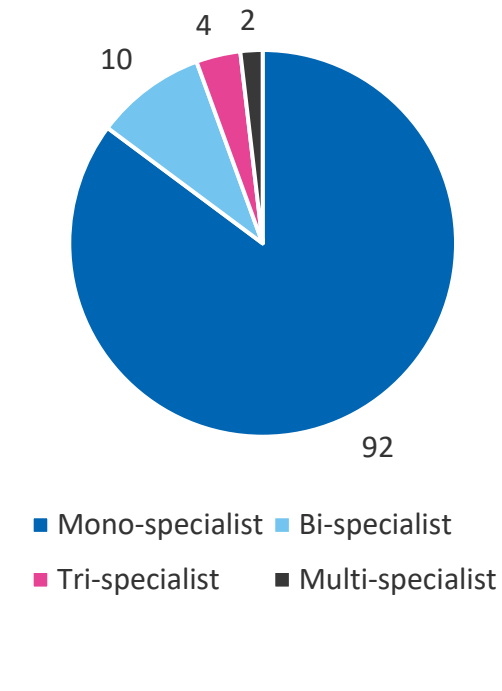
Tech providers speciality breakdown



Second specialty breakdown



Tech providers breakdown according to specialty number



Business ecosystem mapping

Funded by the European Union

Access to Finance

Regarding private investments, we can mention in particular

- **Sanofi**, which announced a new flexible vaccine plan in France (€ 600M) as well as the support of the digital biotech campus project,
- but also **Novartis**, which finalized its € 100M investment in Huningue and completed the integration of CellForCure with the ambition of tripling the workforce by the end of 2020,
- **Yposkesi, recently acquired by a Korean investor,** which invested € 50M between 2018 and 2022 for capacity development for commercial gene therapy products and the establishment of a production unit for cell therapy products with 150 jobs planned,
- as well as **Servier,** which is finalizing its Bio-S biomolecules plant near Orléans with € 65M invested.

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Support for companies with state-guaranteed loans.

Increase in innovation funding:
€420 M for health in 2020, nearly three times more than in 2019.
New programmes introduced to support R&D projects: vaccines and therapies with strong government support for clinical trials in France.

Funding for increased production capabilities or relocation for curative and preventive therapies and also for molecules used in COVID-19 treatment that were in short supply.

Innovation capital:
€126 M invested in 2020 in 32 transactions.
Health is one of the key sectors of the Recovery Plan launched in 2020, which supports industrialisation and relocation to promote national sovereignty.

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French Manufacturing Plant Launches to Make Cell Therapy Cheap and Scalable

TreeFrog Therapeutics's beta encapsulation system

According to TreeFrog, the key bottleneck in cell therapy research today is the cultivation of pluripotent stem cells – self-replicating cells which can form to grow any part of the human body. These cells are fragile and difficult to grow, and **current cell therapy programs are limited by manufacturing capacity, cell processing costs, and cell quality.**

To address this challenge, TreeFrog Therapeutics developed C-Stem™; a 3D cell culture system that enables the mass production of stem cells with short lead times, while preserving genomic integrity. **With C-Stem, TreeFrog aims to significantly lower the cost and accelerate the production of stem cells**

"Today, our C-Stem™ technology reduces manufacturing costs by ten-fold, while dramatically improving batch-size, yields and genomic quality. All our efforts are now focused on bringing this technology to the clinic as fast as possible, by advancing a pipeline of cell therapies in co-development with leading pharmaceutical companies"**Maxime Feyeux, co-founder, CEO & CSO of TreeFrog Therapeutics.**

Invetech

David Kneen, Invetech's Vice President, Cell Therapy

TreeFrog Therapeutics and Invetech Expand Partnership to Transition High-throughput Stem Cell Encapsulation Technology to GMP System for Commercial-scale Cell Therapy Manufacturing

"TreeFrog approached us with a very novel, early-stage technology that has progressed extremely fast and shows incredible promise," remarked **David Kneen, Invetech's Vice President, Cell Therapy**. "In under 18 months, our combined teams have transitioned C-Stem™ from a bench-top proof-of-concept, to **a closed and automated beta production system**. It's been a great collaboration driven by our shared vision of commercializing this technology **to enable the mass-production of cell therapies for patients in need**."

Success story Business Creation

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Part VI

Conclusions and

next steps

France

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European Union

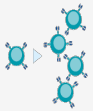
Conclusion: Biotherapies, a major issue of sanitary independence

France is 95% dependent on imports for biotherapies

- In 2018, **3% of therapeutic antibodies used in France were produced in France**
- Strong growth of next generation Abs as ADCs and bispecific Abs in clinical development (some are marketed)

- **Historical position as a leader for classic vaccines** with a cluster (Lyon Biopole) and leaders (Sanofi-Pasteur, Institut Pasteur)
- Need to support the development of new therapeutic vaccines

- **9 marketed gene therapies in May 2020**, only one produced in France (Kymriah, Novartis / Cell For Cure)
- Major role of French research in the development of 8 of these gene therapies
- 40 marketed gene therapies in the next 3 years



- **No real commercial success for cell therapy**
- Need to explore new source of cells and differentiation process to create new cell therapies

Recommendations from CSF-ITS – INITIATIVE TECHNOLOGIE DE RUPTURE POUR LA BIOPRODUCTION

With 2 priority areas, in the short term: the roadmap defined will aim to develop technological solutions to meet the challenges of bioproduction, namely **the deployment of Industry 5.0 in factories with continuous monitoring for the prescriptive control of bioprocesses with priority axes on biosensors, microfluidics, simulation and edge artificial intelligence and new high yield and industrializable expression systems**

- **Measure 1:** Ensure the visibility and attractiveness of the national bioproduction sector - Establishment of the France Bioproduction Alliance
- **Measure 2**: Develop and industrialize major technological innovations through collaborations between stakeholders in accordance with the CSF roadmap.
- **Measure 3**: Facilitate the industrialization of disruptive technologies. In addition to this, you need to know more about it.
- **Measure 4**: Support the development of the bioproduction sector through the implementation of ambitious financing tools.
- **Measure 5**: Ensure the development of skills in bioproduction.

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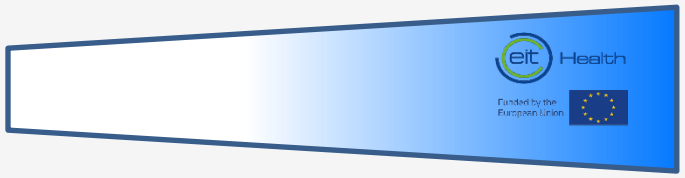
EIT Health French Network Footprint

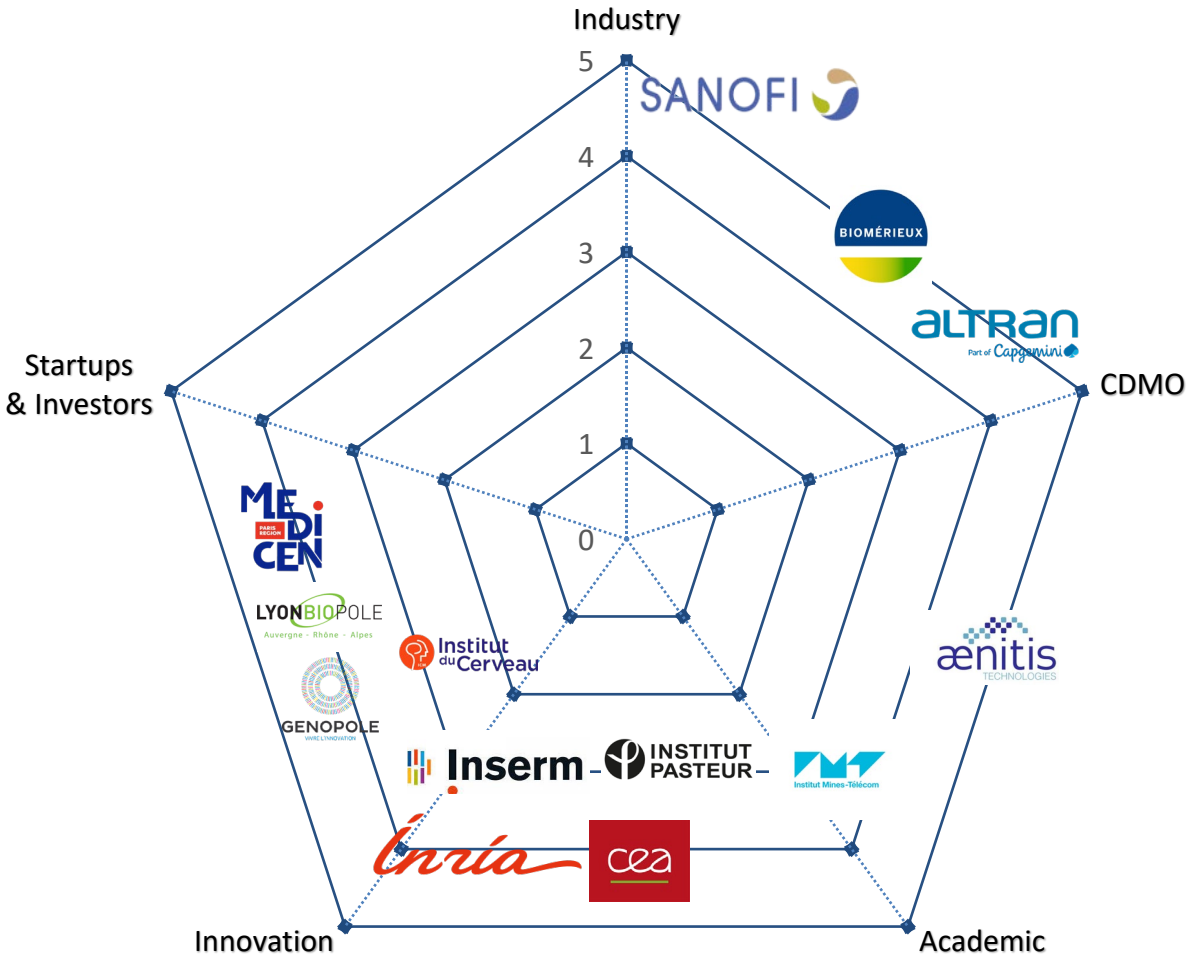
1. Industry
2. CDMO
3. Academic
4. Innovation
5. Start-ups & Investors

Scoring - Partners engagement with EIT Health

Neutral High



French radar



EIT Health footprint radar

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REFERENCES

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- Panorama France Healthtech 2020
- Plan HealthTech : état des lieux et pistes d'évolution pour les biotech française
- Etude sur une filière de bioproduction – LEEM
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- Partners-LEEM-Cartographie-de-la-Bioproduction-en-France
- Innovation en santé : soignons nos talents
- Création de l'Alliance France Bioproduction : Faire de la France le leader européen de la bioproduction à l'horizon 2030
- 4eme Programme d'investissements d'avenir : 20 milliards d'euros pour l'innovation dont plus de la moitié mobilisée pour la relance économique.
- Labellisation des intégrateurs industriels par le Grand défi "Biomédicaments"
- Plan compétences Biotech/innovations Santé 2020
- Plan healthtech du vivier aux grandes réussites

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