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ENTREPRENEURS IN HEALTHTECH

19TH EDITION
**PANORAMA
FRANCE
HEALTHTECH
2021**

bpifrance

 **EURONEXT**

 **EY** Building a better
working world

"French HealthTech: strengths & challenges on the road to becoming European champion!"

The French HealthTech industry is incredibly vibrant. Innovative health companies of all types (biotech, MedTech, diagnostics and digital health companies) play a central role in developing major disruptive technologies, providing a hotbed of solutions for patients and the health system, while also offering considerable potential for jobs, R&D investment and exports.

The figures compiled in this new edition of "Panorama France HealthTech" produced with the unstinting support of our partners Bpifrance, EY and Euronext are a testament to this. French HealthTech employs over 50,000 people both directly and indirectly. Over 4,000 innovations have been developed by industry stakeholders to improve patients' life expectancy and treatment, ensure early diagnosis and optimize their care pathways. As regards funding, French startups in the industry raised a record sum of €2.3 billion, making 2021 an historic year.

This year, which marks 25 years of France Biotech, a milestone in the development of our ecosystem has undoubtedly been reached. The HealthTech industry boasts numerous strengths including its resilience and vibrancy, increasing global visibility, strong entrepreneurial dynamic, initial successes, and sharing of experience and expertise between the first and new generations of entrepreneurs. Highly ambitious plans to support the ecosystem, foremost of which are the Recovery



Franck Mouthon,

Chairman of



Plan and 2030 Health Innovation Plan, will undeniably contribute to confidence in this dynamic.

Health is now more than ever our fellow citizens' top priority, with major elections on the horizon in 2022. The challenge is now to consolidate this dynamic and prompt the emergence of global leaders by 2030, thus strengthening the standing of the French HealthTech ecosystem, which, true to its scientific, medical and industrial past, must now confirm its place among the leading European health innovation players.

It is up to us as HealthTech entrepreneurs to mobilise fully and

collectively to achieve successes that resonate globally, an essential means of converting tries scored on home turf. Moreover, it is vital to take all public and private stakeholders with us, to foster more extensive skills and competence

"THIS YEAR, WHICH MARKS 25 YEARS OF FRANCE BIOTECH, A MILESTONE IN THE DEVELOPMENT OF OUR ECOSYSTEM HAS UNDOUBTEDLY BEEN REACHED."

networks, and thus achieve a critical mass of like-minded stakeholders all committed to the same goal. It is also crucial for us to work with the public authorities to speed up the adaptation and simplification of the administrative, regulatory, tax, legal, market access and export environment for our companies and strategic financial and industrial partners. ■

A WORD FROM THE MINISTER

"We have taken measures with the Strategic Council for the Healthcare Industries (CSIS) to bring about a radical change in the situation"



P. Bagein

Agnès Pannier-Runacher,
Minister Delegate for Industry
in the French Ministry of the
Economy, Finance and
Recovery

In 2017, we were paying the price for years of inaction which had led to a weak ecosystem of health industries despite our strengths. We are all aware of the diagnosis: France's global share of medical product manufacturing halved between 2005 and 2015, and we were demoted from first to fourth place among European producers.

Since 2017, we have therefore been working within government to make up for 30 years of bean counting in relation to drugs and increase our country's appeal for the health industries.

Since 2018, we have taken measures with the Strategic Council for the Healthcare Industries (CSIS) to bring about a radical change in the situation. These include fast-tracking innovative molecules to market, taking account of innovation and industrial investments in drug price negotiations, and simplifying procedures for clinical trials.

We wanted to take this further with the 2030 Health Innovation Plan announced last summer by the French President, and implement the necessary measures to ensure that France is the most innovative European nation on health. To achieve this, through the plan we will allocate €7.5 billion to supporting the industrialisation of drugs and the development of strategic sectors in the area of health products.

In particular, the 2030 Health Innovation Plan will address biotherapies, an area in which France is not yet able to meet the enormous economic and health sovereignty challenges raised. We will specifically allocate €800 million to this area with ambitious targets for 2025 of France producing a total of 10 biopharmaceuticals, doubling the number of jobs in the sector, and prompting the emergence of five new mid-cap biotechs through our action. Our action must be holistic and not limited to specific company types such as startups. In addition to biomanufacturing, we must also imperatively continue to support the biotech, MedTech and eHealth sectors to encourage the emergence of mid-caps, which are a critical component of our success.

The Panorama France HealthTech 2021 figures, particularly on fundraising, perfectly illustrate the benefits of the measures we have taken. They also reflect the full dynamism of health as an industrial sector of the future. They encourage us to continue tirelessly with the efforts we have been making to support its development.

At stake are patient welfare, our ability to innovate, our economy and our sovereignty. ■

"THROUGH THIS PLAN, WE WILL ALLOCATE €7.5 BILLION TO SUPPORTING THE INDUSTRIALISATION OF DRUGS AND THE DEVELOPMENT OF STRATEGIC SECTORS IN THE AREA OF HEALTH PRODUCTS."


**MINISTÈRE
DE L'ÉCONOMIE,
DES FINANCES
ET DE LA RELANCE**

*Liberté
Égalité
Fraternité*

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METHODOLOGY

Each year, **France Biotech** produces Panorama France HealthTech, a report drawn up on the basis of a dedicated survey and publications by companies in the sector. It does not provide an exhaustive picture. The information was collected from 20 October to 8 December 2021 on the basis of 427 companies. The companies included in the survey meet the following criteria:

► Their core business is in the area of life sciences and their registered office is in France;

► Their research and development spending represents at least 15% of their total costs;

► They have fewer than 500 employees.

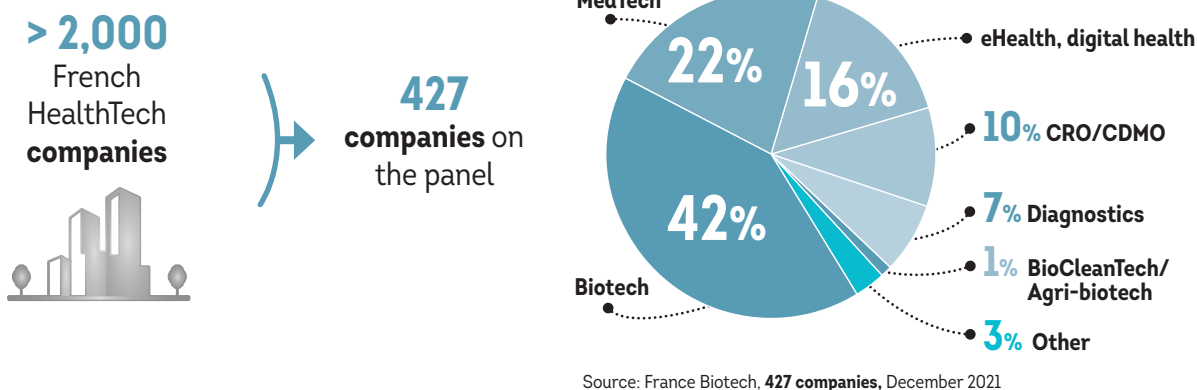
In addition to the data from the questionnaire, a detailed analysis was compiled from other sectoral and financial studies, as well as previous publications and reports by France Biotech, cited in this report.

The survey was carried out in partnership with Bpifrance, EY and Euronext.

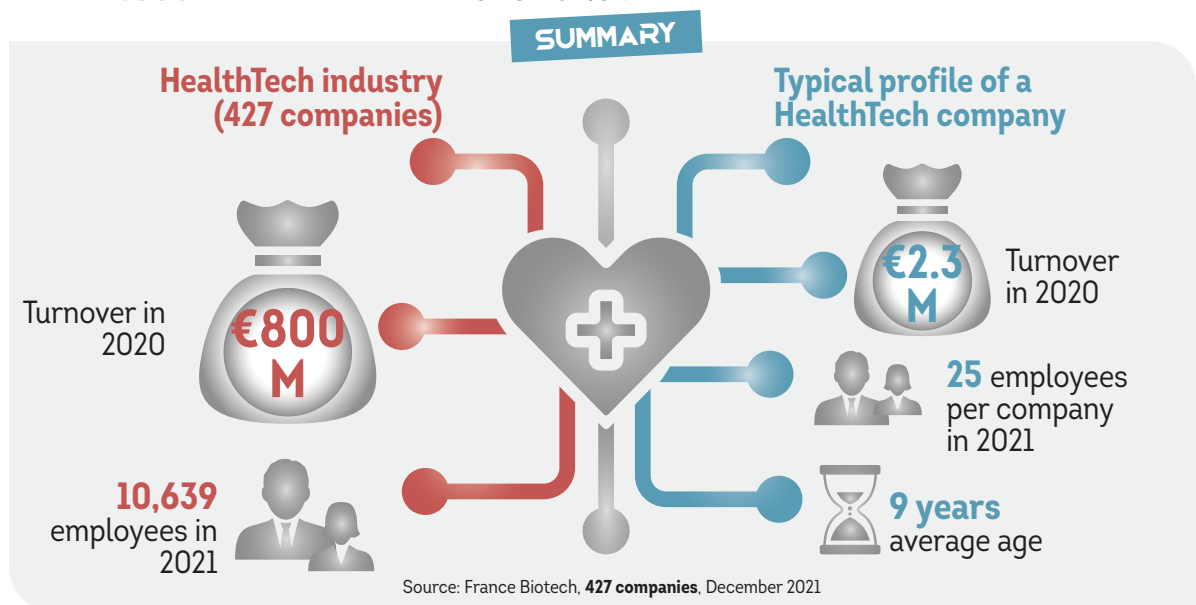
SUMMARY

FRENCH HEALTHTECH: A DYNAMIC AND DIVERSE SECTOR

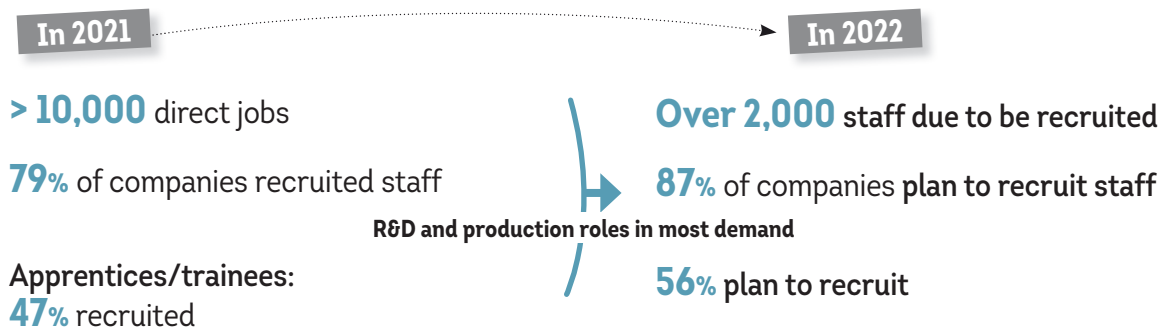
TYPES OF COMPANIES SURVEYED



€800 M TURNOVER IN 2020 (€2.3 M PER COMPANY ON AVERAGE)



AN INDUSTRY THAT CREATES JOBS, MOST OF WHICH ARE HIGHLY SKILLED



SUMMARY

SIGNIFICANT OVERLAP BETWEEN THE MEDTECH AND EHEALTH FIELDS

47% of eHealth solutions developed or marketed **are medical devices (MDs).**



82% of eHealth MDs are CE-marked or CE-marking is pending.

53% of eHealth solutions developed **incorporate artificial intelligence.**

Improved care and follow-up, optimized care pathways and prevention are the main aims of digital solutions developed.

R&D AND INTELLECTUAL PROPERTY (IP), A KEY CHALLENGE AND INVESTMENT FOCUS

- ▶ **49% of HealthTech companies incorporated using research from the public sector** (2/3 of biotechnology companies).
- ▶ **On average, TTOs** (technology transfer organisations) **hold equity in 27% of startups originating from public research** with median equity of 8%.
- ▶ **€1.1 Bn invested in R&D in 2020**, €3.6 M per company on average (+ 20% vs. 2019).
- ▶ **R&D: Top expenditure item** for companies.
- ▶ **69% of HealthTech companies filed at least 1 patent application** (as in 2020) and **54% intend to file one in future** to secure their company's growth.
- ▶ A need for support: **2/3 of companies would welcome the public authorities taking initiatives to support them** with their IP strategy.

A STRONG COLLABORATIVE DYNAMIC IN 2020 AND 2021

EUROPE



> **6,000 licence and partnership agreements signed between 2017 and 2021** by European healthcare stakeholders.

2020 and 2021 were record years in terms of the number of transactions and amounts.

Biotechnology products were highly diverse, representing the majority of collaborations.

FRANCE



Involved in 53% of partnerships, public research stakeholders were the main partners of French HealthTech companies.

The proportion of industrial agreements increased slightly (33% in 2021 vs. 31% in 2020).

1/3 of partnerships were conducted globally and the majority were still R&D collaborations.

French HealthTech companies **primarily collaborated with European partners.**

SUMMARY

HEALTHTECH, A MATURING INDUSTRY WITH GLOBAL AMBITIONS

- ▶ **1 in 5 companies** have at least **one subsidiary abroad**.
- ▶ **No. 1 destination: the United States** (50% of subsidiaries).
- ▶ **50% of biotech and MedTech companies** aged over 10 years have a **global presence**.
- ▶ **50% of medical devices (MDs) are on the market or in the process of registration**.
 - ▶ **Top target markets: no. 1 United States, no. 2 Europe, no. 3 Asia.**

MAJOR DIFFICULTIES PERSIST IN TERMS OF MARKET ACCESS

- ▶ **Only 10% of HealthTech companies** were issued appraisals on development and early market access by the French health authorities
- ▶ **Only 5% were approved for an early-access scheme** (temporary authorisation for use, the Forfait Innovation scheme providing temporary funding to facilitate early patient access to innovative technologies, etc.)
- ▶ **For eHealth companies, access to the market and reimbursement was the chief concern expressed by entrepreneurs** due, among other factors, to a lack of clarity on the funding of solutions and the business model to adopt.

SUMMARY OF 2030 HEALTH INNOVATION PLAN MEASURES

The 9th CSIS (Strategic Council for the Healthcare Industries) reflects **the government's ambition of making France Europe's top innovative and sovereign nation for health by 2030**.

The ambitious fourth Investing in the Future Programme (PIA) representing **€7 billion** aimed at "*innovating, inventing, manufacturing and selling the health products and solutions of the future worldwide*" has been structured accordingly.

THE 7 PRIORITIES OF THE 2021 CSIS

MEASURE 1.

- ▶ **€1 billion** to boost our **biomedical research capacity**.

MEASURE 2.

- ▶ **Invest** in the 3 health fields of the future: **biotherapy** and **biomanufacturing of innovative therapies, digital health, emerging infectious diseases and CBRN threats** (1).

(1) CBRN: chemical, biological, radiological and nuclear.

MEASURE 3.

- ▶ **Make France the leading** European country **for clinical trials**.

MEASURE 4.

- ▶ **Provide patients with fair access to care** and ensure that innovations have a **framework for faster, simpler market access**.

MEASURE 5.

- ▶ Provide a **predictable and consistent economic framework** aimed at **promoting health and industrial sovereignty**.

MEASURE 6.

- ▶ **Support the industrialisation of health products in France** and boost the growth of companies in the sector.

MEASURE 7.

- ▶ **Set up an organisation** to promote and strategically manage innovation in healthcare: **the healthcare innovation agency**.

AN ATTRACTIVE TAX ENVIRONMENT AND POSITIVE SIGNALS ON SUPPORTING HEALTH INNOVATION IN FRANCE

► 3-year extension of the eligibility period for Innovative Young Company (JEI) status

53% of HealthTech companies are currently eligible for JEI status, with the remainder largely ineligible on age grounds.

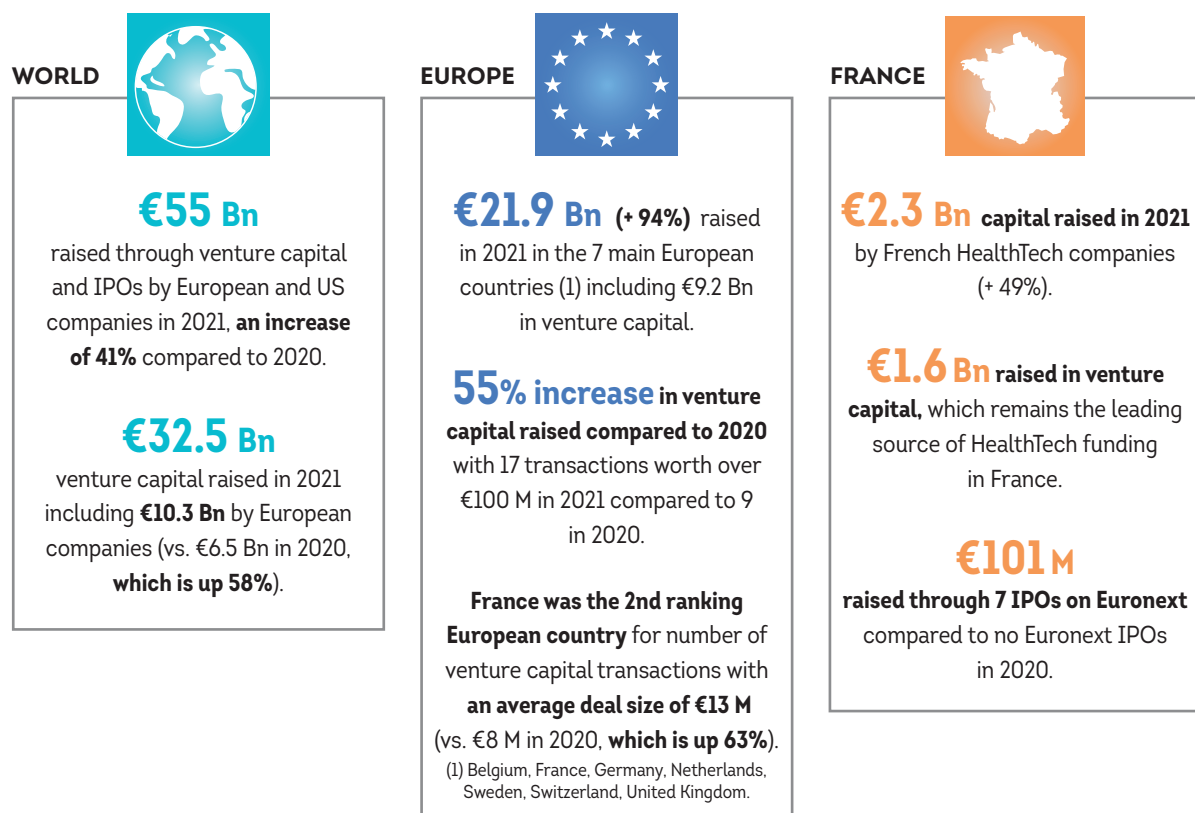
This new scheme provides companies that have been in existence for less than 11 years with JEI status (compared to 8 years previously), which better reflects the time taken to develop innovative health products.

► Introduction of the Research Collaboration Tax Credit (CiCo)

This scheme for HealthTech companies and public/private research partnerships aims to compensate for the abolition of Research Tax Credit (CIR) base doubling for expenditure subcontracted to public organisations.



RECORD HEALTHTECH FUNDRAISING IN 2021



SUMMARY

EXCEPTIONAL GOVERNMENT SUPPORT FOR THE HEALTH INDUSTRY IN 2021

bpifrance

→ An exceptional year with significant financial support for HealthTech stakeholders: **€1.2 Bn was awarded to the sector in grants** to provide approximately 850 projects with innovation and industrialisation support, which is **over four times more than in 2020**. The HealthTech share of total grants rose from 20% in 2019 to **33% in 2021** with a total budget of €3.7 Bn.

→ **The recovery plan** has provided support for investment, modernisation and relocation of the industry.

→ **Launch of the fourth Investing in the Future programme for which €2 Bn has been ring-fenced:** digital health, "biotherapy and biomanufacturing" and Emerging Infectious Diseases (EIDs). Bpifrance set up programmes in 2021 and supported 53 projects with €100 M in

grants. Measures aimed at companies will continue to support these priority sectors in 2022 and help implement the roadmap.

→ Since the outbreak of the crisis, **the government has provided €856 M of funding to companies tackling COVID** (vaccines, diagnostics, treatments).

→ Bpifrance also continued its support through the **Hub** (12 supported startups) and equity investments, with **€158 M equity investment in HealthTech companies and €205 M in HealthTech venture capital funds in 2021**. These include the investment of Bpifrance funds in increasingly substantial Series A rounds: Egle Therapeutics, Emergence Therapeutics, a Series C round: DNA Script, and IPOs: MaaT Pharma.

EURONEXT

2021 HAS STRENGTHENED THE POSITION OF EURONEXT* AS THE number 1 EUROPEAN LISTING VENUE FOR HEALTHTECH COMPANIES

*Euronext includes the Amsterdam, Brussels, Dublin, Lisbon, Paris, Oslo and Milan stock exchanges.

End of 2021



131 HealthTech companies

including
75 French companies



listed on Euronext markets, with
total market capitalisation of €59.6 Bn

In just one year, **the market capitalisation** of French HealthTech companies increased **from €12.9 to €16.2 Bn** (despite disappointing clinical results from several leading companies).

This success was mainly spearheaded by Valneva and its COVID-19 vaccine technology.



A DYNAMIC MARKET IN 2021 FOR HEALTHTECH

After 2020, which focused primarily on revaluing the sector, **2021 was a year of low stock market volatility** in a context where the COVID-19 pandemic appeared under control.

In the wake of rises in the main stock market indexes, **a historic wave of new technology company listings** occurred, particularly in HealthTech, with **17 new listings including 7 in Paris, representing €101 M of a total of €417 M raised**. This has been the **best year** in terms of sums raised and number of transactions **since 2017**.

2021 has proven that European HealthTech companies are capable of raising significant amounts to support their growth once they are listed.

Almost equalling the record sum for the previous year, **just under €1.8 Bn** (vs. €2.3 Bn in 2020) **was raised through a smaller number of transactions** (47 vs. 101 in 2020).

- **5 transactions exceeding €50 M market capitalisation;**
- **19 private placements with a total of €346 M raised** including the French companies Transgene (€34 M), Gensight (€30 M), and Valbiotis (€16 M);
- **7 public offerings with a total of €1.14 Bn raised**, including one for ArgenX amounting to €955 M, and the dual listing of NYXOAH, which, having raised €85 M through its IPO on Euronext Brussels in 2020, raised €78 M through its IPO on Nasdaq.

Listings of new stock market vehicles known as **SPACs** rose significantly in Europe in 2021, with 22 new SPACs on Euronext **including 2 in the healthcare sector**.

A POOL OF ACTIVE GLOBAL INVESTORS

The pool of investors with equity in Euronext-listed HealthTech companies continued to grow (over 700 institutional investors) and internationalise, with US (38.5%) and UK (17.5%) investors most represented. In parallel, **European funds** saw significant increases in

resources in their possession in 2021, with **over €10 Bn raised**, bringing the total to **€88 Bn under management**. Within this ecosystem, specialist **biotech funds raised €745 M in new money**, bringing the total to **€11 Bn under management**.

In 2021, no fewer than 7 IPOs were completed by French HealthTech companies on the Euronext Paris market:



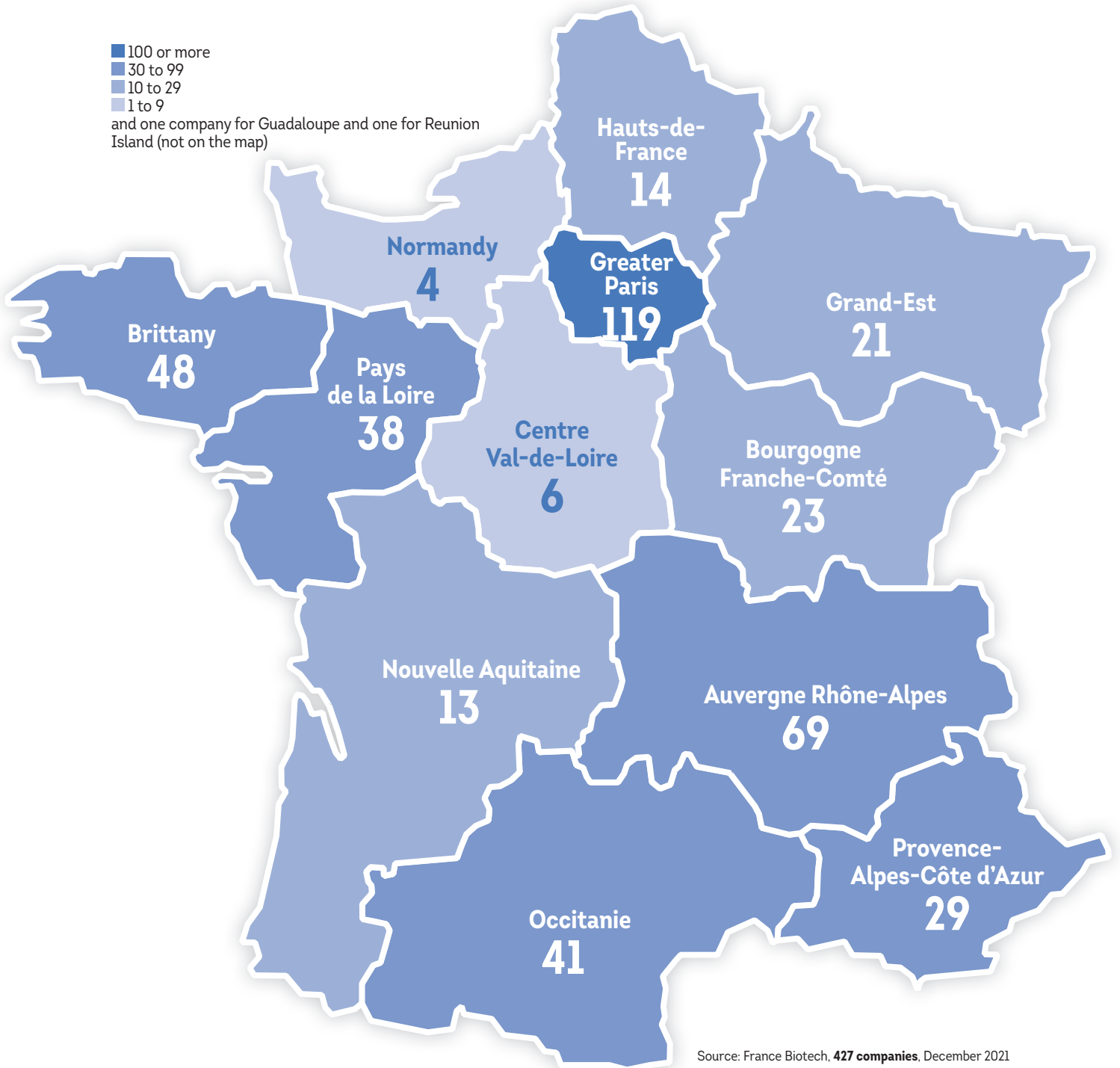
In its contribution to France Biotech's annual Panorama, Euronext provides a guide to stock market listing for heads of biotech companies. Since preparation and planning are of critical importance when applying for an IPO, we have provided you with some initial food for thought in this publication.

SUMMARY

(in numbers of respondent companies)

MAP OF REGIONS IN THE SAMPLE

(in numbers of respondent companies)



As regards the 427 companies that responded to the survey in 2021, Greater Paris was the most densely occupied region hosting 28% of the companies in the panel, followed by Auvergne Rhône-Alpes with 16% of companies. Brittany was in third place, hosting 48 of the respondents, with

the majority of companies based in the Rennes region. PACA and Occitanie are also very dynamic regions for HealthTech, jointly accounting for 16% of the sample. Finally, with 38 respondents, companies in the Pays de la Loire region are also well represented.

A close-up photograph of a person wearing blue nitrile gloves. The person is holding a clear plastic pipette in their right hand, dispensing a small amount of clear liquid into a petri dish held in their left hand. The petri dish contains a red agar medium with a white grid pattern. The background is a plain, light-colored wall.

THE HEALTHTECH INDUSTRY IN FRANCE

1



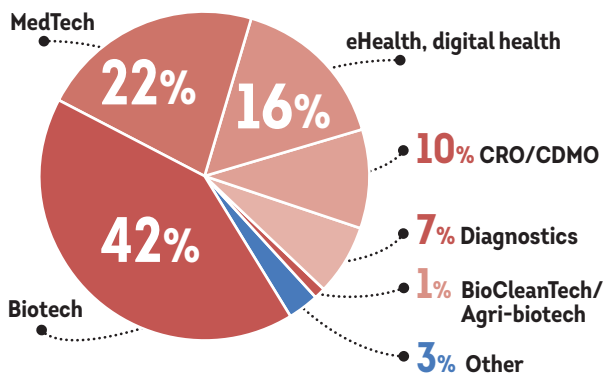
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FRENCH HEALTHTECH COMPANIES

FRENCH HEALTHTECH, A DYNAMIC AND DIVERSE INDUSTRY

France is home to a dense network of HealthTech companies, a significant portion of which are young VSEs. These companies are part of a rich ecosystem of partners and service providers, since subcontracting is a key feature of the sector.

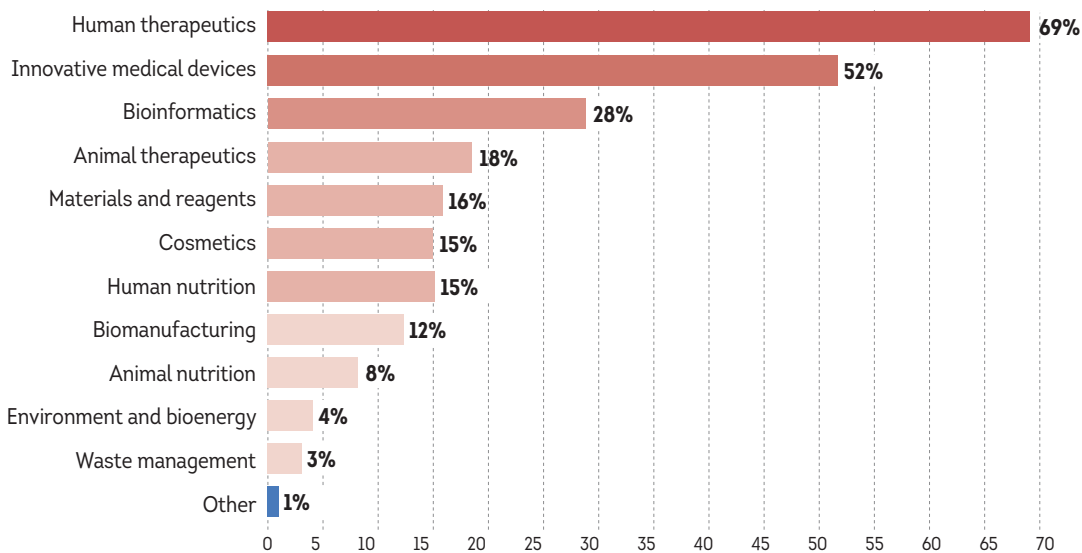
TYPES OF COMPANIES SURVEYED



Source: France Biotech, 427 companies, December 2021

Almost 180 **biotechnology companies represent nearly half of the survey panel**. Companies developing medical devices (known as MedTech companies) account for almost a quarter of it. eHealth companies that often overlap between MedTech, diagnostics and digital health, continued their growth, with around sixty companies representing 16% of the panel. This ecosystem is supported by a network of CROs (Contract Research Organisations) and CDMOs (Contract Development and Manufacturing Organisations).

BUSINESS AREAS OF COMPANIES

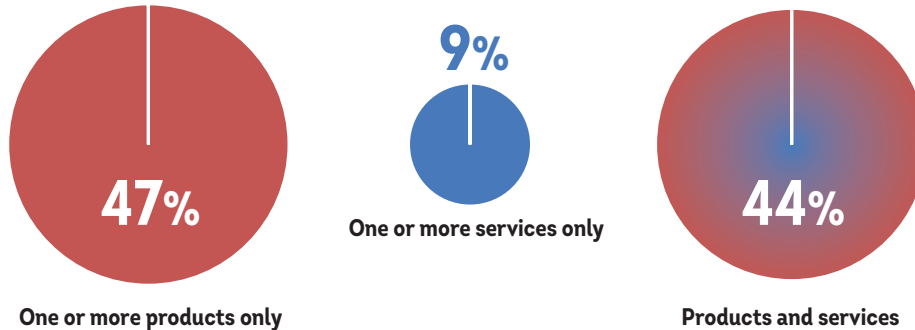


Source: France Biotech, 410 companies, multiple choice questions, December 2021

Although a wide range of fields are represented, the HealthTech industry is mainly focused on human therapeutics (over two-thirds of companies). Companies are also heavily involved in developing innovative diagnostic and therapeutic medical devices, while a quarter of companies

work with bioinformatics, which is used in biotechnology, MedTech and some eHealth companies. **Biomanufacturing saw a 5-point increase compared to 2020, accounting for 12% of applications in 2021.**

COMPANY BUSINESS MODELS



Source: France Biotech, **405 companies**, December 2021

Although a large portion of companies exclusively develops products, another almost equal portion applies a mixed model combining products and services. These companies include certain biotech firms that own technology platforms or offer R&D

services, and MedTech and eHealth companies with an MD component as well as services and software. Companies developing services only are almost exclusively CROs, CDMOs or startups specialising in digital health or drug candidate research.

PROFILE OF COMPANY DIRECTORS



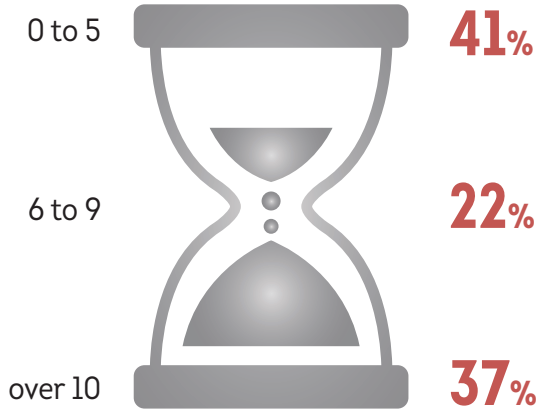
Source: France Biotech, **423 companies**, December 2021



1

FRENCH HEALTHTECH COMPANIES

AGE OF COMPANIES (YEARS)

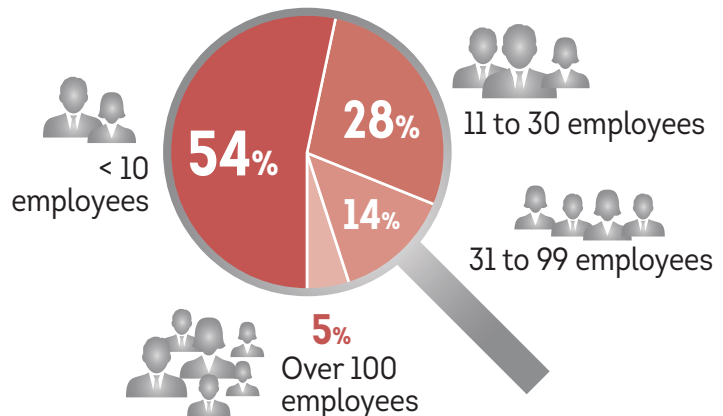


Startups aged under 5 years with an average of 10 employees represent the largest segment (41%) within the HealthTech sector. The trend for startups is counterbalanced by a significant proportion of companies that have been operating for over 10 years, which make up a third of the panel. These more mature companies account for over half (56%) of all HealthTech industry jobs, each employing an average of 40 staff.

Source: France Biotech, **427 companies**, December 2021

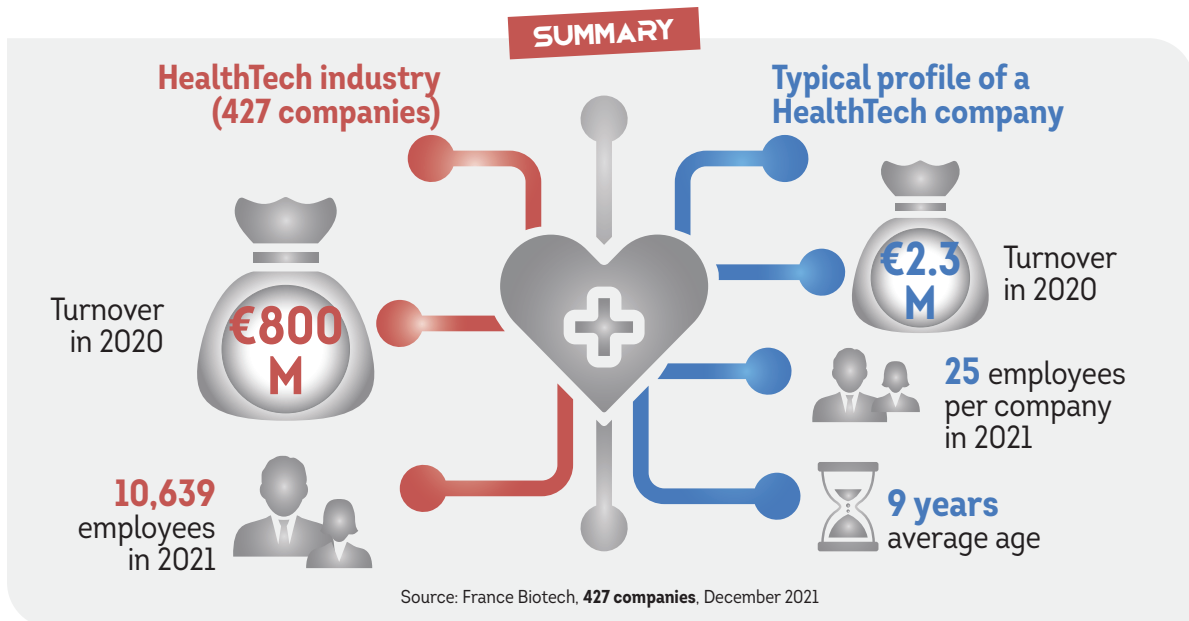
WORKFORCE NUMBERS

The majority of HealthTech companies are VSEs (very small entities) with fewer than 10 employees. However, an increasing proportion of companies (22 firms) now have over 100 employees, almost putting them in the mid-cap bracket. This reflects the industry's growth and increased maturity in France, since only 5 companies of this size were in operation 5 years ago.

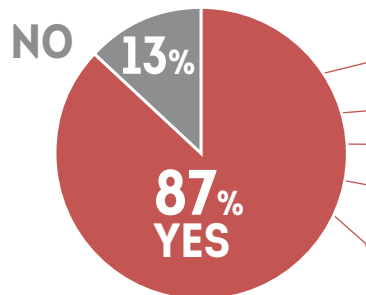


Source: France Biotech, **418 companies**, December 2021

SUMMARY



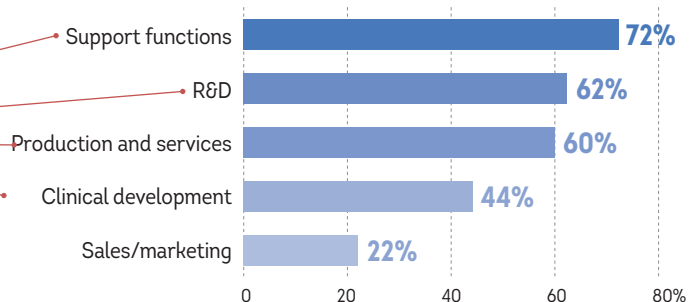
PROPORTION OF COMPANIES OUTSOURCING SERVICES



Source: France Biotech, **414 companies**, December 2021

Subcontracting is one of the sector's key features. Almost all companies (87%) engage in it, regardless of company maturity. The most commonly outsourced activities are support functions such as accounting and human resources. Although a large proportion of R&D is performed

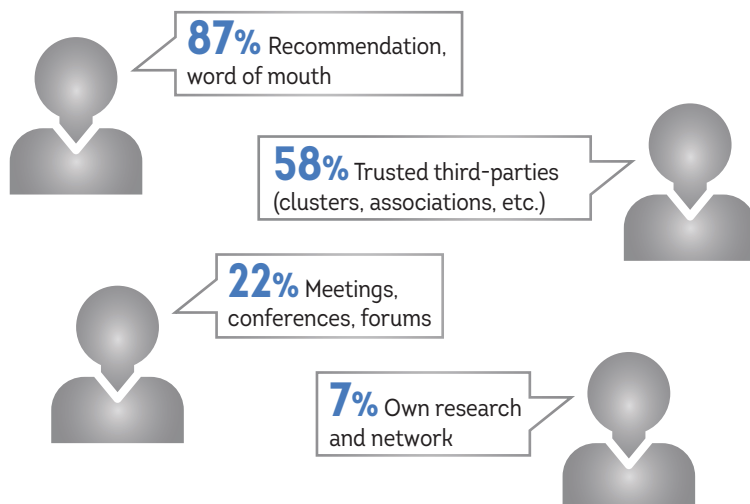
THE MOST OUTSOURCED FUNCTIONS IN HEALTHTECH COMPANIES



Source: France Biotech, **341 companies**, December 2021

in-house, two-thirds of companies outsource some of this type of work as well as production. The HealthTech industry therefore draws on a rich ecosystem of partners and subcontractors.

PREFERRED MEANS OF IDENTIFYING GOOD PARTNERS



Companies that subcontract one or more activities prefer to find the right service provider through word-of-mouth recommendations. Trusted third parties such as competitiveness clusters and trade associations also play an important role in supporting companies with their development and with identifying partners, overtaking meetings, conferences and forums.

Source: France Biotech, **276 companies**, December 2021

SUPPORT FOR COMPANIES

On incorporation, 60% of companies received support through such means as **business incubators or accelerators**.

75% of companies on the panel are **members of a competitiveness cluster**.

➔ French HealthTech companies receive considerable support from dedicated organisations, both on incorporation and throughout their development.



1

FRENCH HEALTHTECH COMPANIES

HEALTH COMPETITIVENESS CLUSTERS

The network of clusters is a key interface for national and regional policy on health innovation

The 6 French health competitiveness clusters:

Atlanpole Biotherapies, BioValley France, Clubster NSL, Eurobiomed, Lyonbiopôle and Medicen Paris Region, were set up in 2005 with over 1,900 members including 1,400 SMEs. This unique and dynamic ecosystem is supported by major corporations, academic institutions, local authorities, hospitals and healthcare institutions.

Projects accredited by the clusters represent over €7 billion of investment and, alone, involve nearly 1,000 members. Over 300 products have been brought to market as a result of completed projects.

Based on these results, the 6 clusters are stepping up their joint action to secure recognition of their members' capacity for innovation and the economic clout of the health sectors they represent.

Health competitiveness clusters are effective actors in the field, which are essential for developing public-private partnerships and supporting companies. Moreover, they are the only parties that bring together all innovation stakeholders throughout the research/development/innovation/production continuum. Their teams' expertise on the sector and their practical know-how are widely recognised at local level due to their action alongside regional councils to promote economic development in their regions.



They are highly involved in the application of public policies at regional level, and also constitute an effective tool for rolling out central government policies in the field.

With the 2030 Health Innovation Plan, central government has adopted a clear and ambitious national strategy whose implementation will rely to a great extent on local stakeholders.

The clusters are best equipped to implement this plan in the field, since its success is also dependent on developing this continuum between research and industrialisation.

Whether through support for innovative companies, identification of promising projects meeting strategic priorities, accreditation, partnership synergies, or attractiveness, the health clusters' actions chime perfectly with government priorities in terms

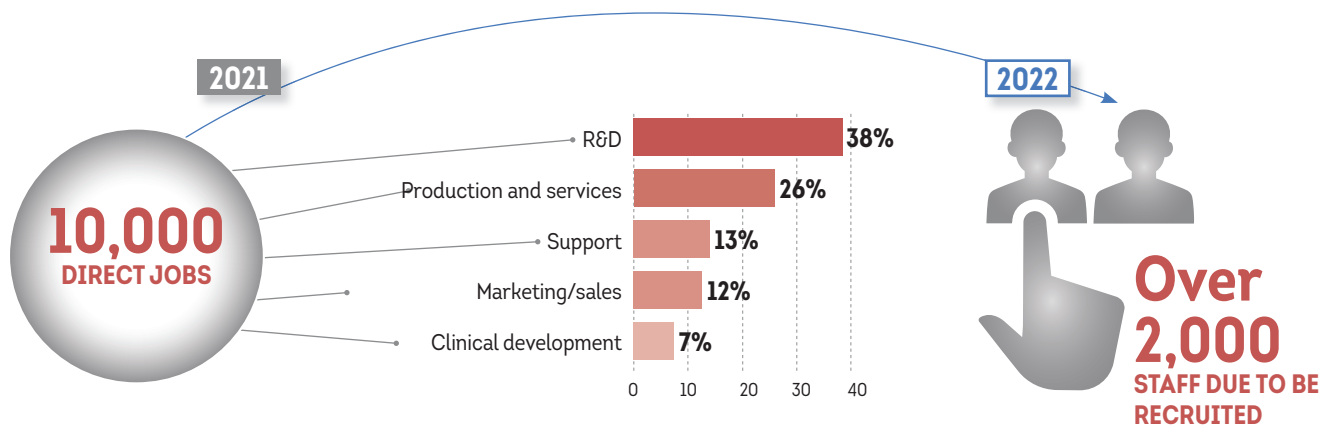
of innovation, industrialisation and health sovereignty, and increase France's influence in European projects such as the IPCEI on Health.

The network of clusters is a key interface for national and regional policy on health innovation in a context where close links between national initiatives and local implementation are an important success factor. The clusters are in a position to apply the national strategy at local level and fast-track projects based on government priorities.

HEALTHTECH, AN INDUSTRY THAT CREATES JOBS

With over 10,000 direct jobs in 2021 and over 2,000 posts due to be recruited in 2022 by companies included in the panel, HealthTech companies have proved particularly dynamic and resilient during the pandemic. 87% intend to recruit staff in 2022.

NUMBER OF DIRECT JOBS IN COMPANIES IN THE SAMPLE



Source: France Biotech, **384 companies**, December 2021

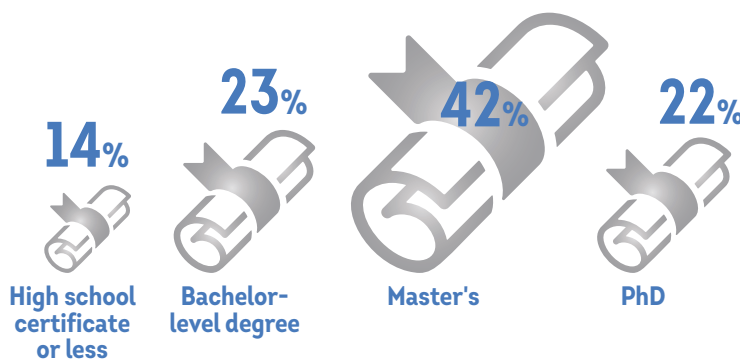
R&D is one of the companies' main activities to which over a third of employees are assigned (38%). Production and services are in second place, currently representing a

quarter of HealthTech companies' wage bills. This area has experienced growth compared to the previous year (20% of employees in 2020).

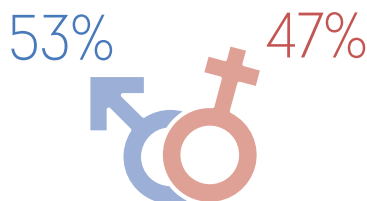
QUALIFICATIONS OF STAFF

Two-thirds of HealthTech employees hold at least a master's degree, proof of a sector largely made up of highly qualified roles and employees.

Source: France Biotech, **400 companies**, December 2021



GENDER PARITY



There is almost full gender parity within HealthTech companies' teams.

Source: France Biotech, **406 companies**, December 2021

A FEW FIGURES

2021
PhD students under the CIFRE co-funding scheme
 are present in 30% of companies

Apprentices/trainees
 are present in 47% of companies

2022
 56% of companies intend to recruit staff

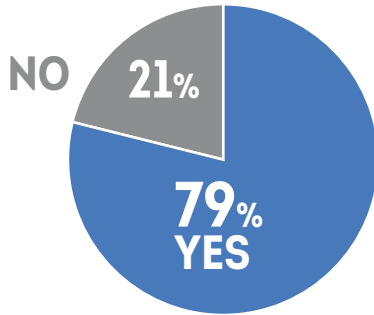


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FRENCH HEALTHTECH COMPANIES

POSITIVE RESULTS FOR RECRUITMENT IN 2021 AND A GOOD OUTLOOK FOR 2022

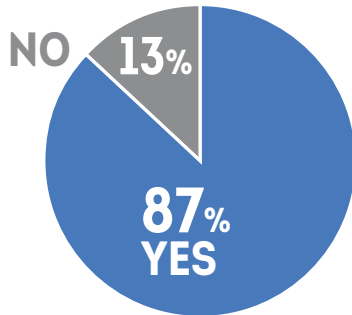
→ Have you recruited new staff in 2021?



French HealthTech is in good shape despite the pandemic and the economic difficulties affecting various sectors. Companies' recruitment levels were high in 2021, with almost all companies (79%) recruiting new staff.

Source: France Biotech, **373 companies**, December 2021

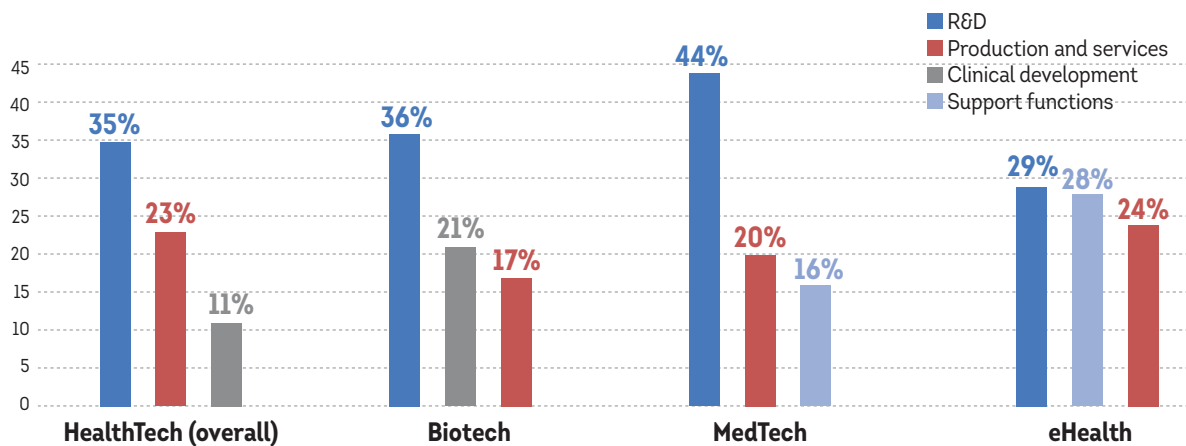
→ Do you intend to recruit new staff in 2022?



This very positive trend appears to have continued and further developed in 2022 with a high demand for human resources. In fact, **87% of companies are intending to recruit in 2022**. This trend is particularly strong in eHealth companies, almost all of which (93%) are planning to take on staff.

Source: France Biotech, **403 companies**, December 2021

POSTS MOST IN DEMAND IN 2022 (% OF VACANCIES)



Source: France Biotech, **196 companies**, December 2021

Companies intending to recruit in 2022 plan to recruit an average of 10 posts per company (compared to 5 in 2021). **There is highest short/medium-term demand for R&D, production/services, support functions and clinical development.**

Over half of new posts in biotechnology companies are in R&D and clinical development, while there is demand for all functions (R&D, support, production) in digital health companies.

HEALTHTECH, AN INDUSTRY WITH GLOBAL AMBITIONS

In terms of both target markets and international presence, French HealthTech companies have global ambitions. Companies accessing schemes enabling early access to the domestic market (temporary authorisation for use, the Forfait Innovation scheme providing temporary funding to facilitate early patient access to innovative technologies) remain rare.

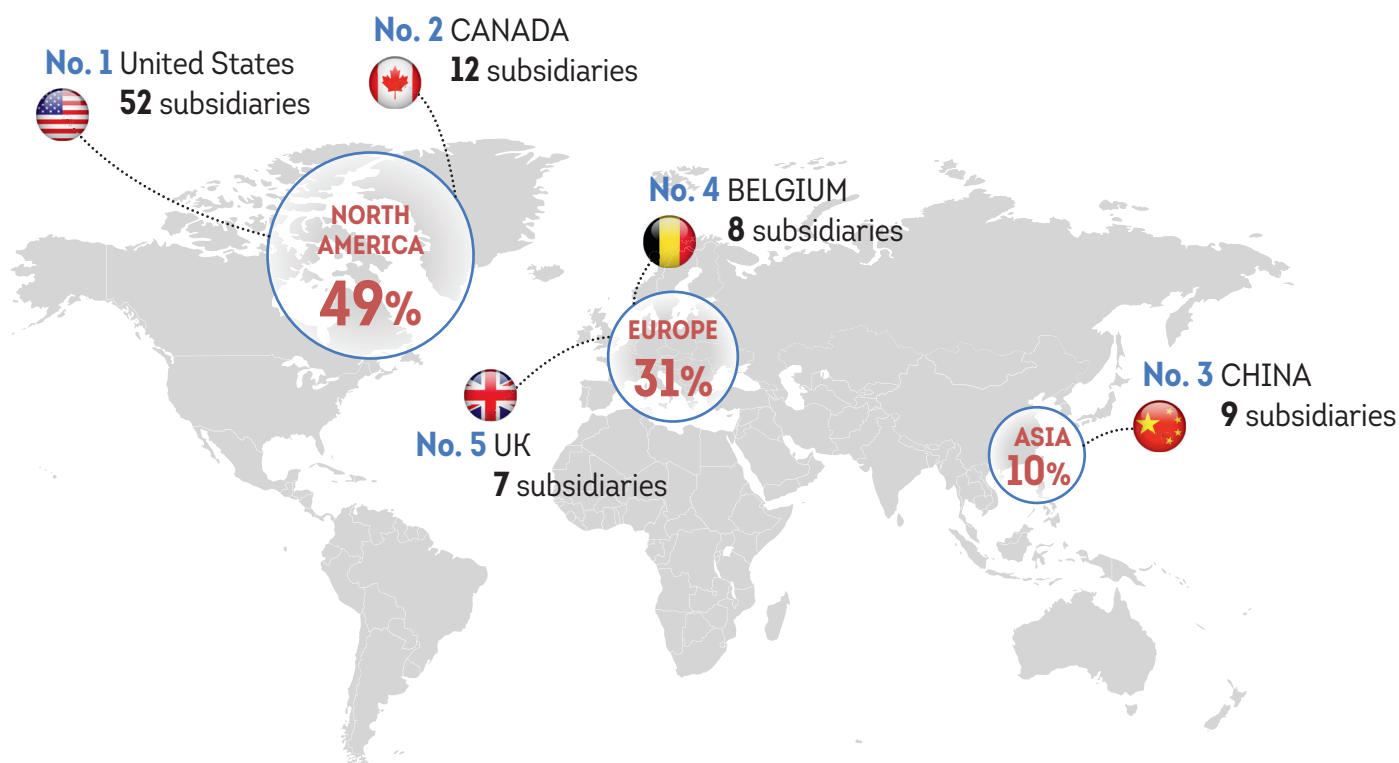


INTERNATIONAL SUBSIDIARIES

1 in 5 companies have at least one subsidiary abroad.

50% of biotech and MedTech companies aged over 10 years have a global presence.

DISTRIBUTION OF HEALTHTECH SUBSIDIARIES ABROAD (% OF SUBSIDIARIES)



Source: France Biotech, **85 companies**, December 2021

Of the 131 international subsidiaries included in the panel of companies, half are based in North America and particularly the **United States**, which continues to be the top country for setting up subsidiaries. **Almost two-thirds of companies with a global presence have at least one subsidiary in this country which remains the world's top pharmaceutical**

market. In Europe, the most targeted markets and countries are France's close neighbours, Belgium and the United Kingdom. Although subsidiaries in Asia are less common (10%), China remains the most attractive country in Asia for subsidiary set-up with 9 subsidiaries, ahead of Japan (3) and Singapore (1).

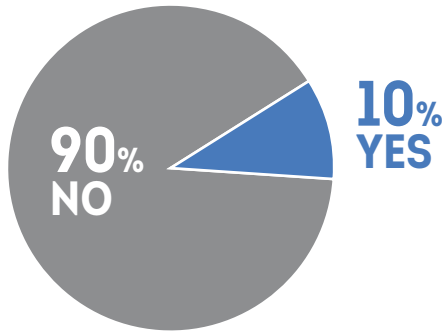


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FRENCH HEALTHTECH COMPANIES

MARKET ACCESS AND MARKETING

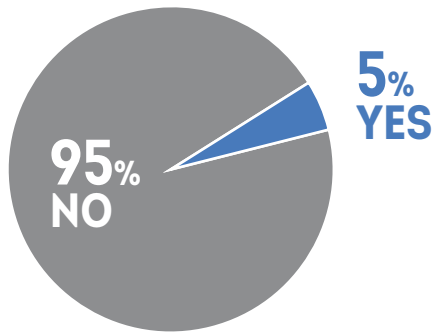
→ *Have the French health authorities issued you an appraisal on development and early market access?*



Appraisals on development and early market access issued by the French health authorities to HealthTech companies are rare, having **only been issued to 10% of HealthTech companies.**

Source: France Biotech, **372 companies**, December 2021

→ *Have the products you develop or market been accepted for early market access schemes?*



- 29% Forfait Innovation
- 24% Early access outside France
- 18% ATU
- 18% Article 51
- 12% RIHN
- 6% ETAPES

Source: France Biotech, **323 companies**, December 2021

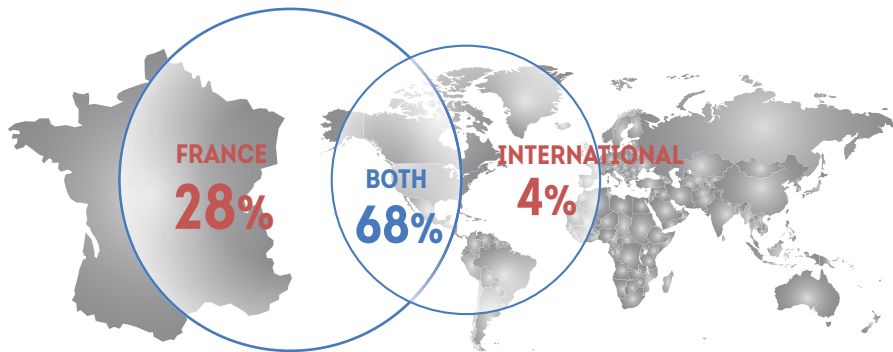
Only 5% of companies benefited from an early market access scheme, the most common examples being the "Forfait Innovation" and international early access schemes (including the FDA's Fast Track scheme and the United Kingdom's "Promising Innovative Medicine Status" scheme), followed by French temporary authorisations for use (ATUs) and the scheme under Article 51 of the French Social Security Financing Act.

KEY MARKETING FIGURES

54% of HealthTech companies already have one or more products on the market

50% of medical devices (MDs) are on the market or in the process of registration.

TARGET MARKETS FOR FRENCH HEALTHTECH COMPANIES [% OF COMPANIES]

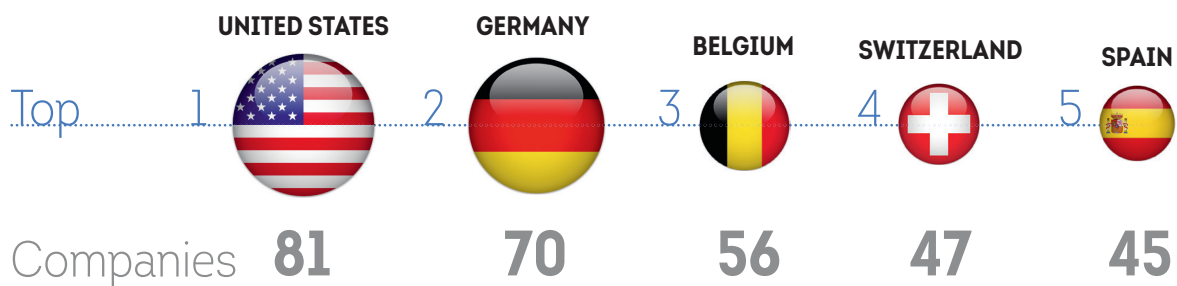


HealthTech companies seek early global expansion and immediately target international markets, with 68% of companies at marketing stage operating within both the French and global markets. Only 28% target the domestic market only, most of which are companies specialising in eHealth/digital health.

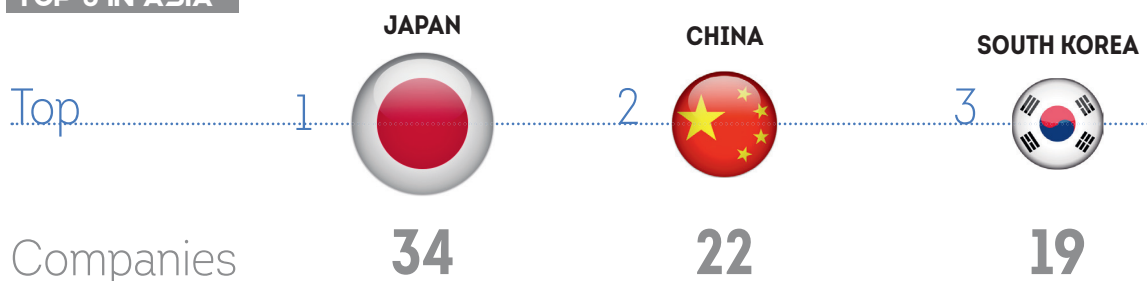
Source: France Biotech, 401 companies, January 2022

TARGET INTERNATIONAL MARKETS [% OF COMPANIES OPERATING IN THESE MARKETS]

TOP 5 TARGET COUNTRIES AT INTERNATIONAL LEVEL



TOP 3 IN ASIA



At global level, the **United States is the top target market** with 81 companies operating in this market, representing over half of all the HealthTech companies that market their products and solutions globally. **Europe remains a key HealthTech market, with Germany, Belgium, Switzerland and Spain topping the ranking**, followed closely by the United Kingdom and Italy. The Japanese health market

ranks third globally and first in Asia, with a quarter of global companies marketing their products and solutions in this country. China is a vast, rapidly expanding market whose growth is ongoing, attracting increasing numbers of French HealthTech companies.

Source: France Biotech, 139 companies, January 2022



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FRENCH HEALTHTECH COMPANIES

3 QUESTIONS FOR...

Thomas Kuhn, Co-Founder and Chief Executive Officer of Poxel

"Market access for your drug candidate needs to be considered on initiation of clinical trials"

2021 was a pivotal year for Poxel whose first Imeglimin product was brought to market in Japan in September. The company developed Imeglimin, the first molecule in a new class of drugs constituting a genuine innovation in terms of therapies available for treating diabetes. Imeglimin delays the switch to insulin in type 2 diabetes treatment by targeting mitochondrial dysfunction (sugar).



Thomas Kuhn began his career with Merck KGaA in 2000 where he held various positions in clinical development, mainly in the therapeutic area of type 2 diabetes and was responsible, in particular, for forging partnerships with Japanese pharmaceutical companies. Between 2004 and 2007, he directed Merck's global R&D projects with two products in Phase II clinical trials and all the life cycle management projects primarily for Glucophage®, the current reference in diabetes treatment. Following Merck's acquisition of Serono in 2007, Thomas Kuhn was part of the team which refined Merck Serono's strategy for divesting from the diabetes therapeutic area. Thomas Kuhn initiated and concluded the project for the transfer of Merck Serono's assets under development in diabetes to a new legal entity called Poxel. Since this transfer, Thomas Kuhn has been Poxel's Chief Executive Officer. He holds a pharmacy degree from the University of Lyon I (France) and an MBA from Ashridge Business School (UK).



Poxel is a biopharmaceutical company that develops innovative treatments for metabolic diseases including non-alcoholic steatohepatitis (NASH) and rare diseases such as adrenomyeloneuropathy. The company was incorporated in 2009 and has been listed on Euronext Paris since 2015. Its registered office is in Lyon and it has subsidiaries in Boston and Tokyo. It currently employs approximately 60 staff.

How did you plan the development of Imeglimin and its market access?

We conducted two clinical development processes in parallel: one for Japan and the other for Europe and the United States, due to the major differences that exist between the diabetes markets in these regions. In total, we conducted 28 clinical trials with 2,500 patients. Japan is a very pragmatic country in which very rapid progress can be made. In Europe and the United States, the authorities require more information. It takes longer and costs more to develop products.

At the end of Phase II and in preparation for Phase III, we signed two partnership agreements, one with Sumitomo Dainippon Pharma (SDP), a Japanese pharmaceutical company with a leading position in the diabetes market, to develop and market Imeglimin in Asia (Japan, China, South Korea, Taiwan and 9 other countries), and the other for the United States and Europe with Metavant (Roivant Sciences), a newcomer to this market when the contract was signed, but which has since changed its strategic priorities. Poxel therefore recovered the rights for Imeglimin in the United States and Europe, and is seeking a further partner for this region to continue its development.

In terms of price setting and reimbursement rates, Japanese market access conditions are similar to those in France. Diabetes is classified as a "priority disease" in Japan and all treatments are reimbursed by the local social security system. To access the market, we had to assess the efficacy and safety of Imeglimin on its own as monotherapy and combined with other treatments available in Japan. SDP took care of price setting and reimbursement with the Japanese authorities, and also promoted this new treatment to general practitioners and specialists using its sales force of 800 pharmaceutical sales representatives specialising in diabetes.

Our partner SDP has marketed Imeglimin since mid-September 2021 under the name "TWYMEEG®".

In financial terms, it's a very standard partnership with an upfront payment of \$42 M on signing and subsequent milestone payments. Marketing of

the product will bring us two types of revenue – royalties indexed to turnover and payments linked to the fulfilment of sales thresholds.

Is market access similar for your other two products for NASH and rare diseases?

Market access is different for both these diseases. NASH is a huge market whose outlook equals that of diabetes and for which a therapeutic solution is currently lacking. Moreover, while it is relatively simple to diagnose diabetes based on a blood test, this is not the case for NASH, which currently requires a liver biopsy. There are still no newcomers to the NASH market. It is virgin territory and the entire market access environment remains to be built. Our trials are being conducted in the United States, where market potential is strongest.

"WE HAVE SERIOUS AMBITIONS FOR THE ASIAN MARKETS WITH OUR PRODUCT IMEGLIMIN, A NEW THERAPEUTIC WEAPON DELAYING THE SWITCH TO INSULIN IN TYPE 2 DIABETES"

As regards adrenoleukodystrophy (ALD), a rare hereditary metabolic disease, the number of patients throughout the world is estimated at between 444,000 and 644,000. Market access for this condition is once again very different. We work with highly active ALD patient associations which contribute to the development of each new product. There are also dedicated centres of excellence for each rare disease.

What are your next milestones?

As regards the treatment of NASH, the results of the Phase II trial of our drug candidate PXL065 are due for publication in Q3 2022. Phase II results for ALD will be revealed in Q4 2022. We are expecting Imeglimin to be brought to market in Asia between 2024 and 2026 with timings varying by country. ■

Franck Grimaud, President & Chief Business Officer of Valneva

"Valneva is one of the few European biotech companies to manage the entire vaccine manufacturing process"

Valneva is one of the few European biotech companies to manage the entire vaccine manufacturing process, from discovery to marketing via preclinical and clinical trials. One of the special features of this market is that private and public markets coexist. For some of our products, we currently apply for public tenders (our COVID vaccine candidate) and for our



Franck Grimaud is the co-founder and former CEO of Vivalis, and was previously responsible for Groupe Grimaud's development in Asia. He has over 25 years' business development experience in life sciences companies. He holds an MBA from the University of Ottawa (Canada).



Valneva specialises in the development and marketing of prophylactic vaccines for infectious diseases. It is a truly European company with its registered office in France, research laboratories in Vienna, Austria and Saint-Herblain, France, and production infrastructure in Scotland and Sweden. Valneva is a pure player for vaccines with a portfolio of 5 products: A Japanese encephalitis and cholera vaccine (IXIARO®/JESPECT® and DUKORAL®) that are already on the market and 3 vaccine candidates for Lyme disease, Chikungunya, and the SARS-CoV-2 virus. Valneva employs over 700 staff. Its turnover of €348.1 M in 2021 has increased significantly since 2019. The company has a dual listing on Nasdaq (\$107.6 M raised in May 2021) and Euronext Paris on which it has recently joined the SBF 120 in Compartment A.

travellers' disease vaccines (Japanese encephalitis/cholera), we work with private operators including travel clinics, specialist pharmacy chains and wholesalers.

What are your market access strategies for your various vaccines and vaccine candidates?

Valneva generally prepares market access for its products from Phase II. It markets its own products in high-income countries and, for low and middle-income countries, signs marketing agreements with local pharmaceutical firms for specific geographical areas. There is sometimes also an intermediate stage where we carry out the active part and fill and finish is performed locally. An overall assessment is necessary to determine the most critical factors for market access: competitive advantages, competition with local producers, working alone or with a partner for a geographical area, and disease incidence.

We signed a marketing agreement in 2009 allowing Novartis to market our Japanese encephalitis vaccine. We subsequently decided to set up our own sales team in 2015 to market our vaccine directly.

At present, we sell it directly in 9 countries (in Europe and North America) which generates 85% of revenue for this vaccine. We signed a partnership agreement with Biological E, an Indian pharmaceutical company, to market it in India, an endemic area. This partnership also includes production of our vaccine. Phase III results for our Chikungunya vaccine candidate were very positive and we intend to initiate the registration process this year in the United States and Europe with a view to directly marketing it in 2023. As regards low and middle-income countries, we have already signed a partnership agreement that includes technology transfer with the Instituto Butantan, a Brazilian producer of immunological products, covering development, production and marketing.

While our Lyme disease vaccine candidate was in Phase II in 2020, we signed an exclusive global agreement with Pfizer to jointly fund Phase III and market and distribute the vaccine in Europe and North America. Phase III will be launched in 2022 with initial marketing planned for 2025.

Our final candidate is the only inactivated COVID-19 vaccine in clinical development in Europe. We have signed an agreement with the European Commission to deliver up to 60 million doses of this vaccine by 2023, 24 million of which are to be supplied as of April 2022 if the vaccine is approved. Finally, we have also signed an initial agreement with Bahrain in the Middle East to supply 1 million doses. We hope to sign further agreements with countries seeking to offer an alternative in their portfolio to help convince sceptics. We firmly believe that, as is currently the case for influenza, certain populations will need to be vaccinated annually with an inactivated vaccine offering a good tolerability and safety profile.

"OUR FINAL CANDIDATE IS THE ONLY INACTIVATED COVID-19 VACCINE IN CLINICAL DEVELOPMENT IN EUROPE"

What are your next milestones?

For VLA2001 (the COVID-19 vaccine), we are considering various combinations with two variants, a COVID/influenza vaccine and a vaccine for children and teens. We are also working on developing homologous and heterologous boosters, formulations and packaging (single pre-filled syringe). The COVID vaccination market is sure to shift towards the private sector as we have seen with the influenza vaccine.

Valneva may experience growth in the next year or so, as the company will potentially be marketing 5 products. We must continue to innovate through new vaccine candidates in our product portfolio. ■



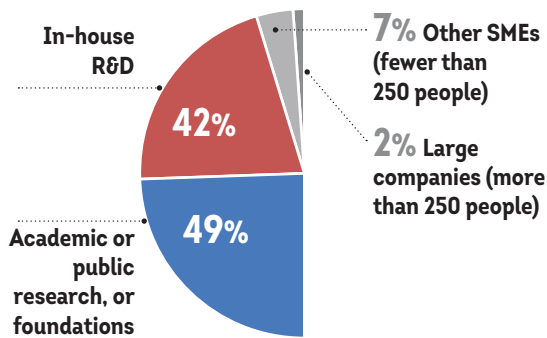
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FRENCH HEALTHTECH COMPANIES

R&D AND INTELLECTUAL PROPERTY A KEY CHALLENGE AND INVESTMENT FOCUS

R&D is essential to HealthTech companies, accounting for 63% of their expenditure on average. Their intellectual property management strategy remains a key challenge.

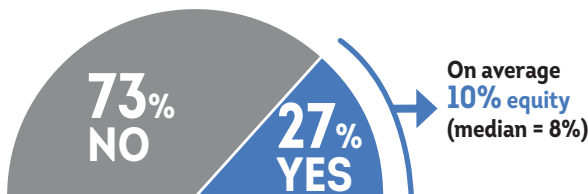
ORIGIN OF R&D AT COMPANY INCORPORATION



Research conducted in public and academic organisations is a key component leading to the incorporation of French HealthTech companies. **Half of the companies (49%) were spin-offs from public research.** Two-thirds of biotechnology companies fall within this category. Following incorporation and during development phases, in-house research plays a predominant role, with 83% of HealthTech companies developing their products and solutions based on research conducted internally.

Source: France Biotech, 423 companies, January 2022

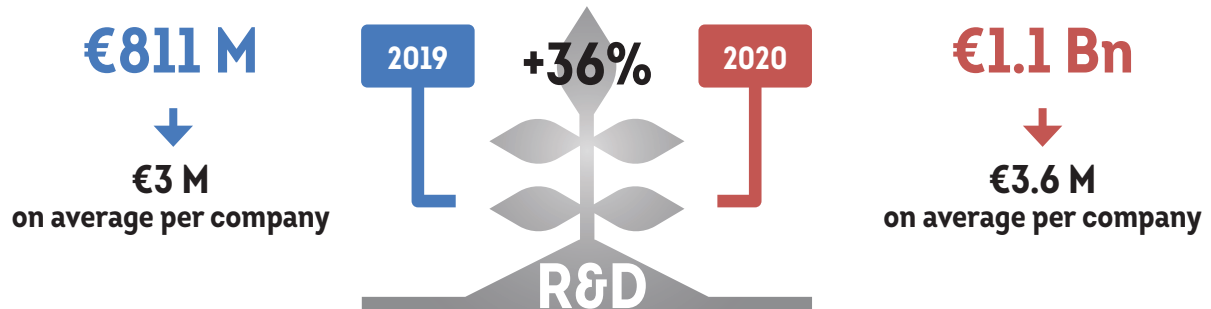
COMMERCIALISATION ORGANISATIONS HOLDING EQUITY IF THE COMPANY HAS ACADEMIC ROOTS



Commercialisation organisations (universities, technology transfer acceleration companies (SATTs), research organisations) acquired equity in 27% of companies whose R&D originated from academia or the public sector, with average equity of 10%.

Source: France Biotech, 169 companies, January 2022

AMOUNTS INVESTED IN R&D BY COMPANIES IN THE SAMPLE

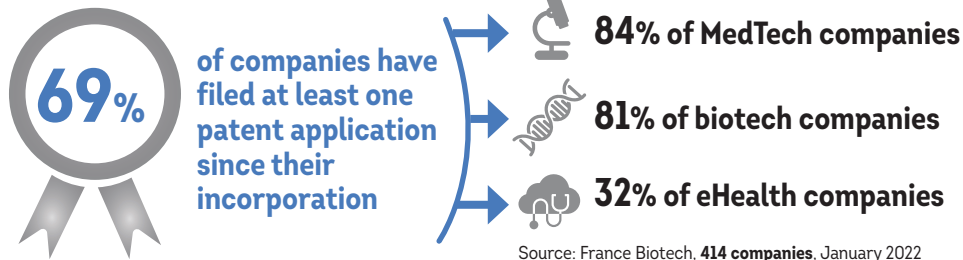


The French HealthTech companies surveyed invested over €1 Bn in R&D in 2020, which represents an average of over €3 M per company. **R&D is therefore companies' top expenditure item** (63% of their total expenditure on average) and, with clinical development, accounts for nearly half of

HealthTech companies' workforce. Despite a complex health climate, companies are continuing to invest significantly in this activity which is key to their development strategies.

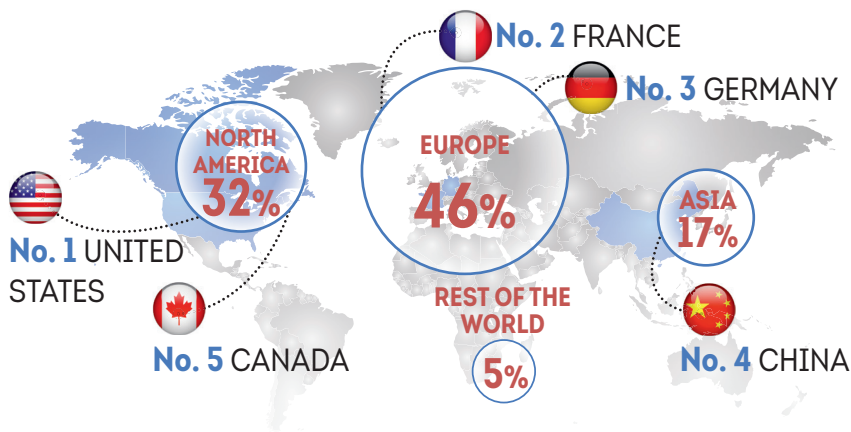
Source: France Biotech, 311 companies, January 2022

HEALTHTECH COMPANIES' PATENT APPLICATIONS



54% of companies intend to file one or more patents in future to secure their growth.

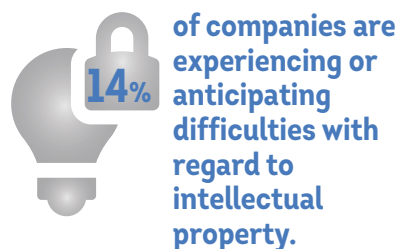
GEOGRAPHICAL DISTRIBUTION OF PATENT APPLICATIONS AND TOP 5 TARGET COUNTRIES FOR FUTURE PATENT APPLICATIONS



Intellectual property is a key challenge for innovative health companies. Almost all biotech and MedTech companies automatically file patent applications when they are set up. IP strategies are essential for companies that continue to file patent applications throughout their development, some in specific geographical areas and others at global level.

Source: France Biotech, 216 companies, January 2022

CHALLENGES, DIFFICULTIES AND SUPPORT FOR COMPANIES



TOP 5 DIFFICULTIES FOR THE PANEL OF COMPANIES

1	Financial cost
2	Counterfeiting, difficulties protecting software or algorithms
3	Contracts and licence management, particularly with public organisations
4	Need for support and finding the right service provider
5	Circumvention of patented processes and monitoring in some countries

The financial cost of patent applications is the most recurrent difficulty for companies. However, the stated difficulties vary, depending partly on company type. For instance, difficulties related to intellectual property appear most severe for certain types of companies developing algorithms, processes or software, for which patent

protection appears most problematic.

Almost all companies (86%) believe that their intellectual property strategy is sufficiently aligned with their business objectives. Moreover, two-thirds of companies believe that they are sufficiently familiar with their main competitors' patent positions and risks incurred in certain markets.

→ *In your opinion, should the public authorities take initiatives to help you with IP or support your sector?*

65% of companies would welcome initiatives from the public authorities to help them with IP.

Source: France Biotech, 327 companies, January 2022



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FRENCH HEALTHTECH COMPANIES

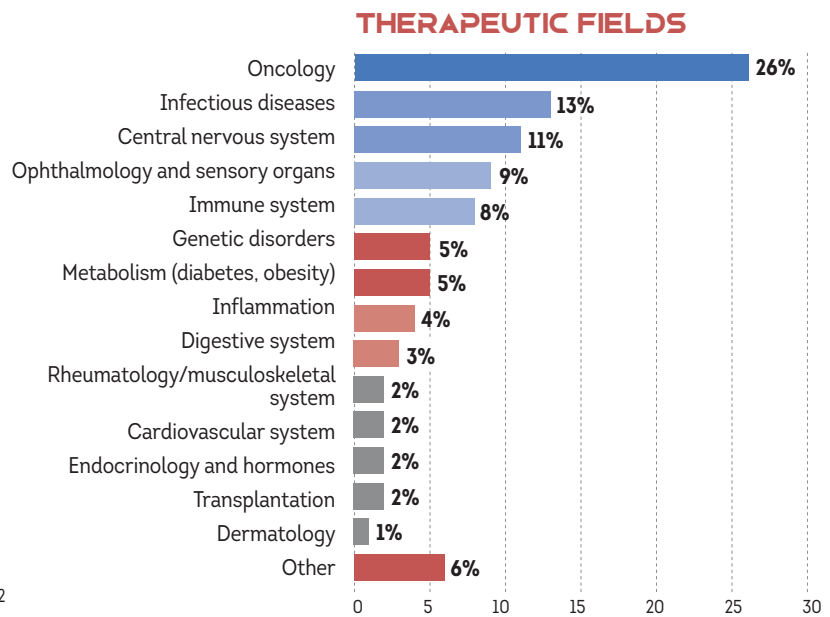
FOCUS ON BIOTECH COMPANIES

With over a quarter of products in advanced phases of clinical trials, French biotech companies have achieved a good degree of maturity. Given their purposes or designations (including orphan drug status), it is clear that the innovations being developed respond to medical needs that are, at present, largely unmet.



French biotech companies develop a wide range of products addressing all therapeutic areas. Despite this diversity, companies' R&D is focused on three key areas accounting for half of all products: **oncology** (a quarter of products in development), **infectious diseases** (13% of products) and **the central nervous system** (11%). Biotech companies' pipelines also include numerous ophthalmology products, products for sensory organs, and products targeting the immune system.

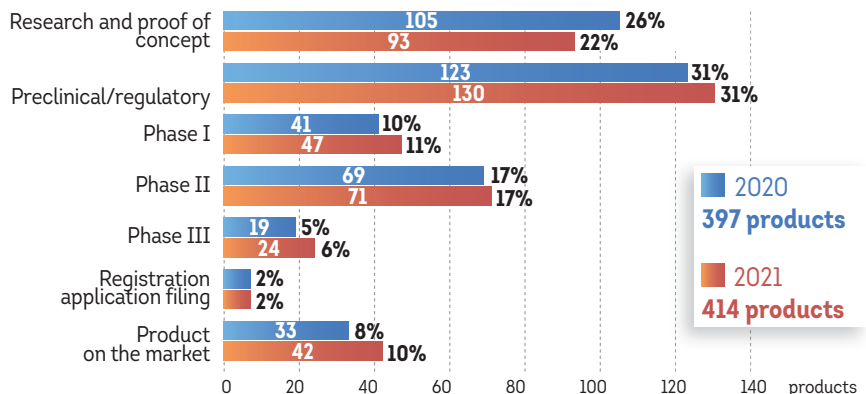
Source: France Biotech, 147 companies, January 2022



DEVELOPMENT PHASES OF PRODUCTS CREATED BY THE BIOTECH COMPANIES IN THE SAMPLE

3.3
PRODUCTS
in development on average per biotech company

Source: France Biotech, 147 companies, January 2022; Panorama France HealthTech 2020



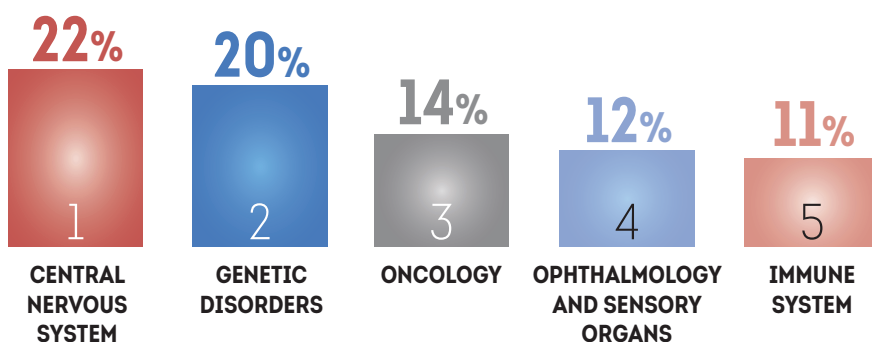
With 414 products at phases ranging from proof of concept to marketing, **companies' R&D pipelines are growing year on year**. French scientific productivity is furthermore reflected in products' increasing maturity. In 2021, 53% of development programmes representing 123 products were in their early phases (proof of concept and preclinical phases). This proportion of products in the early phases is

gradually decreasing year on year and being replaced by more mature clinical programmes (Phase II and III), while 10% of products are now on the market. It is worth noting that most products currently marketed by companies in the panel are focused on ophthalmology, the sensory organs or nutrition, or target the immune system (vaccines) or metabolism (particularly diabetes).

ORPHAN DRUG STATUS

16% of French biotech companies' products are granted **orphan drug status**

ORPHAN DRUGS: THE MOST COMMON THERAPEUTIC AREAS



A quarter of the biotech companies on the panel, i.e. 45 firms, have at least one product with orphan drug status. The three most common therapeutic areas are the central

nervous system, genetic disorders and oncology, all fields with significant unmet medical needs.

Source: France Biotech, **45 companies**, January 2022

AIMS OF INNOVATIONS DEVELOPED BY FRENCH BIOTECH COMPANIES



Source: France Biotech, **111 companies**, January 2022

Nearly all products developed by biotech companies seek to provide significant benefits in terms of patient care. **For example, over half the products in development or on the market are aimed at improving life expectancy and eradicating disease.**

disease, representing a **paradigm shift in patient treatment from a palliative to curative model.** However, biotech companies are also involved in the whole value chain, developing products whose aims include prevention and restoring patient independence and quality of life.

Over a quarter of developed products seek to eradicate a



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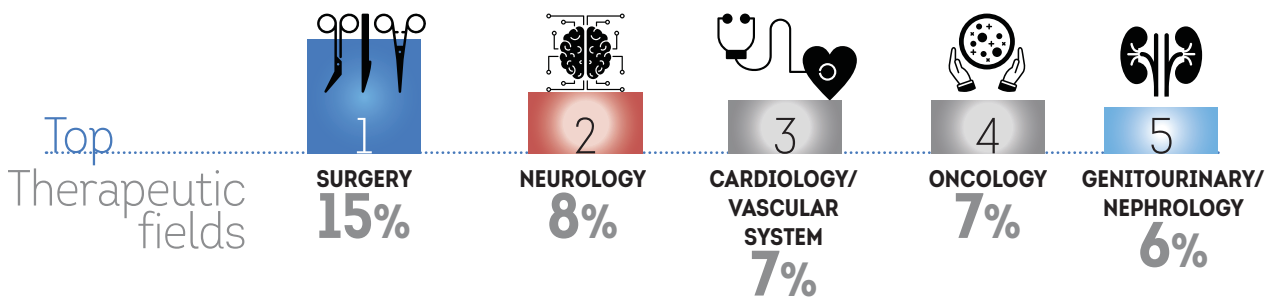
FRENCH HEALTHTECH COMPANIES



FOCUS ON MEDTECH AND DIAGNOSTIC COMPANIES

Innovative medical devices (MDs) unquestionably bring public health benefits, whether in terms of early diagnosis, restoring patient independence, or prevention.

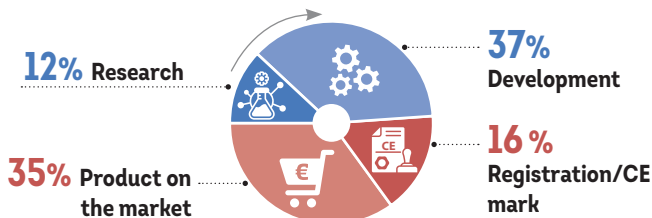
THERAPEUTIC AREAS OF THE MEDICAL DEVICES ON THE MARKET OR IN DEVELOPMENT (% OF PRODUCTS)



The 175 MedTech companies in the survey develop and market 308 products, with an average of 2 products per company. French MedTech and diagnostic companies are involved in a highly diverse range of therapeutic areas incorporating all therapeutic medical fields, with nearly

twenty disciplines represented among companies in the panel. At the top of the ranking are surgery (general, orthopaedic or reconstructive, and visceral) with 15% of products, followed by neurology, the cardiovascular system and oncology. Source: France Biotech, 161 companies, January 2022

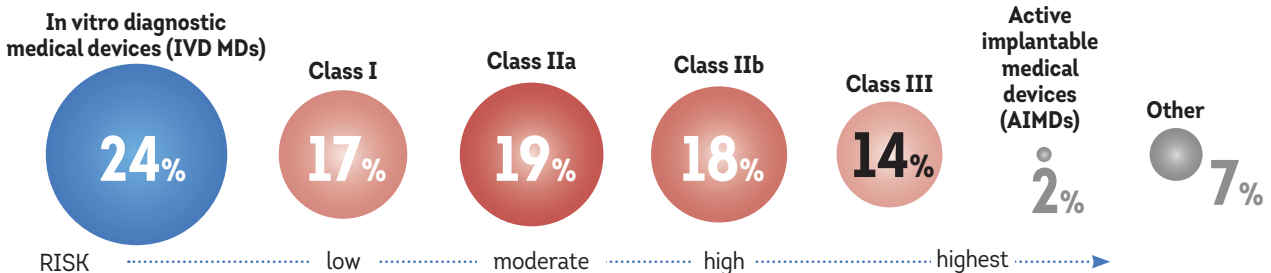
DEVELOPMENT STAGE



Source: France Biotech, 164 companies, January 2022

Of the 300 medical devices developed by companies included in the panel, over half were at advanced stages of maturity, either in the process of obtaining a CE mark (53 products) or already on the market (114 products). MedTech companies' maturity is reflected in 25% growth in the number of products on the market (91 products in 2020). Despite this, French companies reported difficulties in accessing the market and reimbursement for their innovations.

CLASSIFICATION OF MEDICAL DEVICES

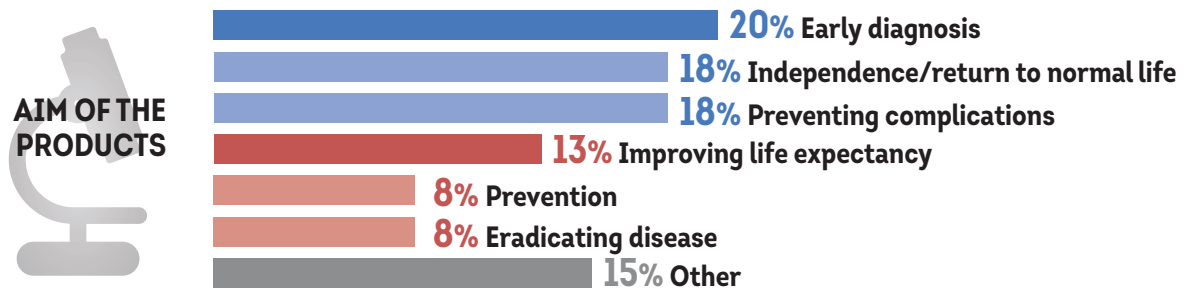


EXAMPLES OF TECHNOLOGIES:

- **IVD MDs** E.g. self-tests, tumour markers, assay reagents, etc.
- **Class I** E.g. dressings, glasses, crutches, etc.
- **Class IIa** E.g. syringes for infusion pumps.
- **Class IIb** E.g. anaesthesia or dialysis machines.
- **Class III** E.g. breast implants, stents, hip implants, etc.
- **AIMDs** E.g. pacemakers, cochlear implants.

Medical devices are regulated by a classification relating to their degree of risk and based on their specific characteristics. Among the technologies developed by companies in the survey, in vitro diagnostic medical devices (IVD MDs) represent a quarter of products, while class IIa and IIb MDs are also well represented.

AIMS OF INNOVATIONS DEVELOPED BY FRENCH MEDTECH COMPANIES



Medical devices developed by French MedTech companies pursue a variety of aims, providing **unquestionable benefits in terms of public health** and care. Over two-thirds of developed or marketed products are aimed at early diagnosis (first place), patient independence, prevention

of disease-related complications, and improved life expectancy. This reflects the fact that French MedTech companies are highly innovative.

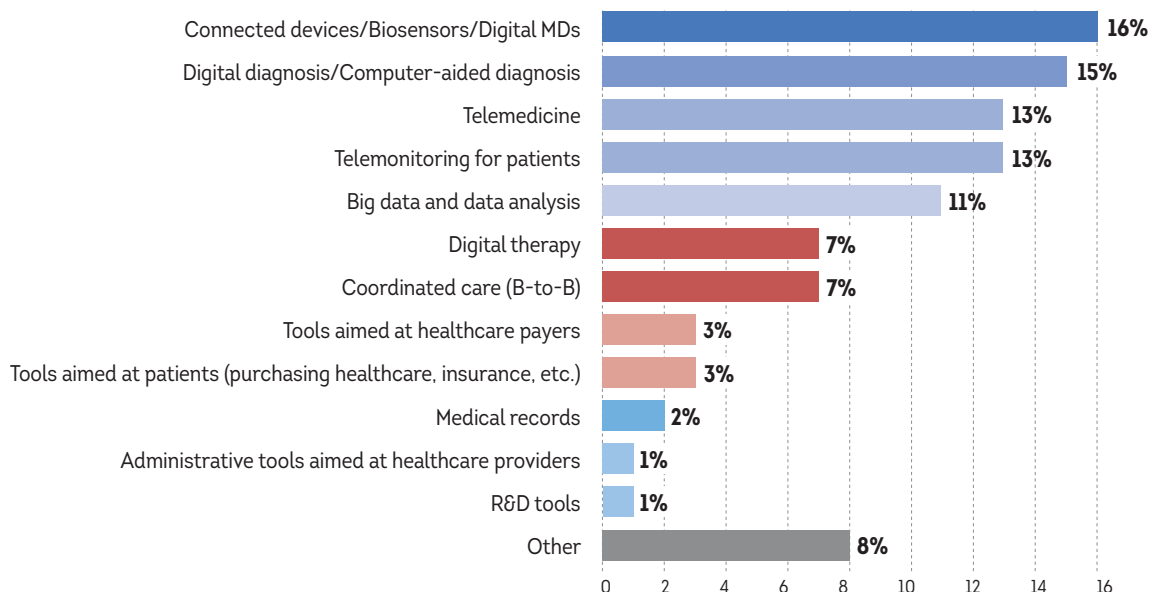
Source: France Biotech, **98 companies**, January 2022

FOCUS ON EHEALTH COMPANIES



eHealth: a booming area and a wide-ranging offering. Half of products combine medical and digital devices. However, companies' business models and market access remain key challenges.

FIELDS OF APPLICATION (% OF PRODUCTS)



Source: France Biotech, **98 companies**, January 2022

Every year, the health industry benefits from new technological advances in digital solutions. **The eHealth companies in the survey developed or marketed a total of 153 products with an average of 2 products developed per**

company. Their applications were wide-ranging and aimed at a variety of users throughout the patient care pathway: pharmaceutical companies and biotech companies, patients, healthcare professionals, hospitals and payer



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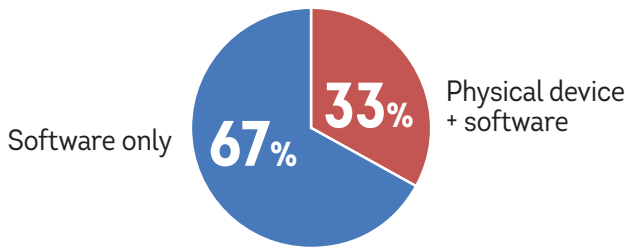
FRENCH HEALTHTECH COMPANIES

organisations. Despite this diversity, four main categories dominate the rankings, accounting for over half of products in development. In a year marked by COVID-19, the roll-out of telemedicine and telemonitoring proved a valuable means of managing the healthcare system. These applications

accounted for 26% of products (compared to 20% in 2020). Connected devices, digital MDs, digital diagnostics and big data/data analysis also featured highly among the eHealth solutions developed in France by startups.

Source: France Biotech, **98 companies**, January 2022

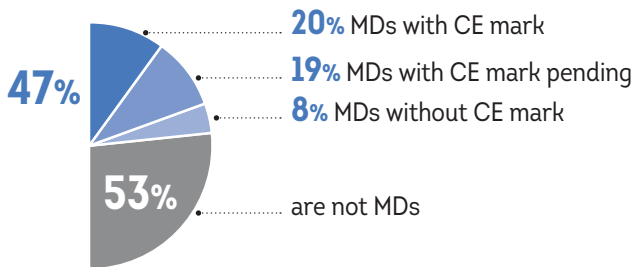
EHEALTH PRODUCT TYPE [% OF PRODUCTS]



Source: France Biotech, **60 companies**, January 2022

53%
percentage of eHealth products incorporating **artificial intelligence**

CATEGORIES AND DEVELOPMENT STAGES [% OF PRODUCTS]



Nearly half (47%) of developed or marketed eHealth solutions were medical devices, reflecting the significant overlap between MedTech and eHealth companies. The vast majority of developed MDs (82%) either bore the CE mark or CE mark approval was pending.

Source: France Biotech, **57 companies**, December 2021

CLASSIFICATION OF DIGITAL MEDICAL DEVICES

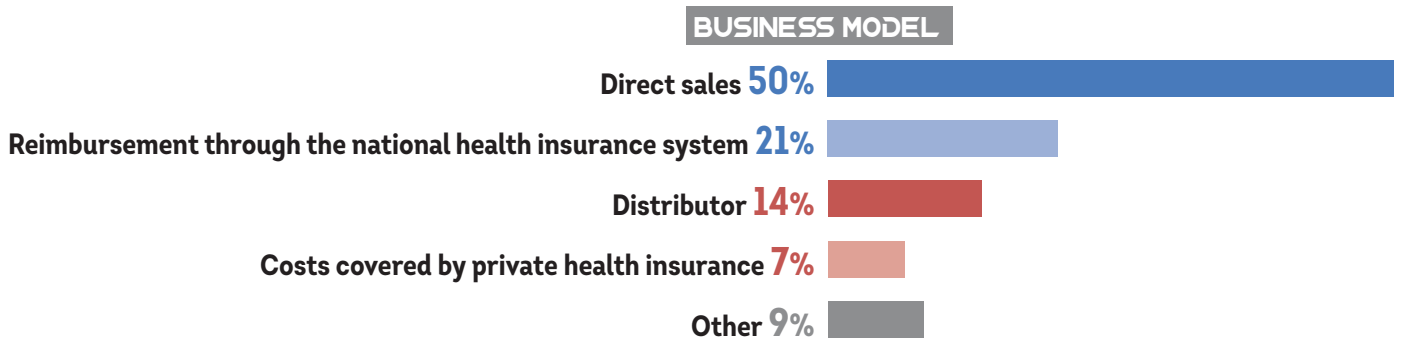


Source: France Biotech, **28 companies**, December 2021

Most of the eHealth digital medical devices produced by companies in the sample can be divided into two main classes. **Class I accounts for half of all products** and includes applications helping patients to manage their disease more effectively (particularly for chronic diseases such as asthma and diabetes) and platforms helping physicians to

diagnose and manage care for complex diseases. Class IIa (16 products) is the second most represented category. Examples include AI-based diagnostic and decision-making tools, connected telemonitoring MDs, and MDs enabling programmes to be tailored to patients.

EHEALTH COMPANIES' TARGET BUSINESS MODELS (% OF PRODUCTS)



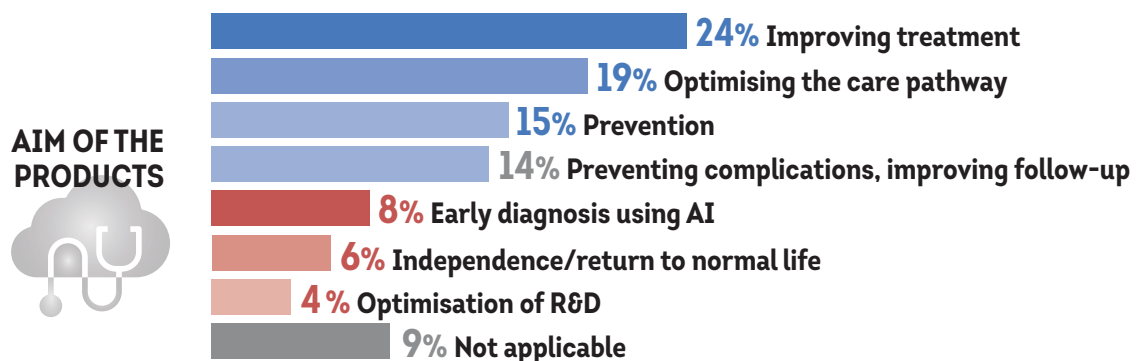
Choosing an appropriate business model is a critical issue for eHealth companies. Given the speed at which new digital solutions have emerged, existing reimbursement and cover models sometimes appear poorly suited to digital solutions. Companies are opting for different strategies, with direct sales favoured for most products, while reimbursement through the national health insurance system is a model that still attracts significant demand in France.

products have been approved for early market access schemes. In terms of schemes accessed, two companies used the Forfait Innovation scheme, one used the Article 51 scheme, and one used the ETAPES scheme. One company was able to conduct a clinical trial with POC with private health insurance companies and another company was granted early access in Switzerland and the United States.

Only 10% of respondent companies that develop eHealth

Source: France Biotech, 60 companies, January 2022

EHEALTH PRODUCT TYPE (% OF PRODUCTS)



Source: France Biotech, 59 companies, January 2022

Like their fields of application, the aims of technologies and solutions developed by eHealth companies were wide-ranging and tailored to targeted users. Most products were aimed at improving treatment. In second place, companies offered further significant progress through optimised care pathways (in hospital or private practice settings). Companies met major public health requirements through their varied models and targets. The COVID-19 pandemic

led to **faster adoption of certain technologies**, in particular those facilitating remote diagnostics, care and patient follow-up. However, further efforts are required to ensure that such technologies can be easily adopted in the long term. **There is a lack of clarity with regard to market access for certain solutions, particularly those requiring funding through the national health insurance system.**



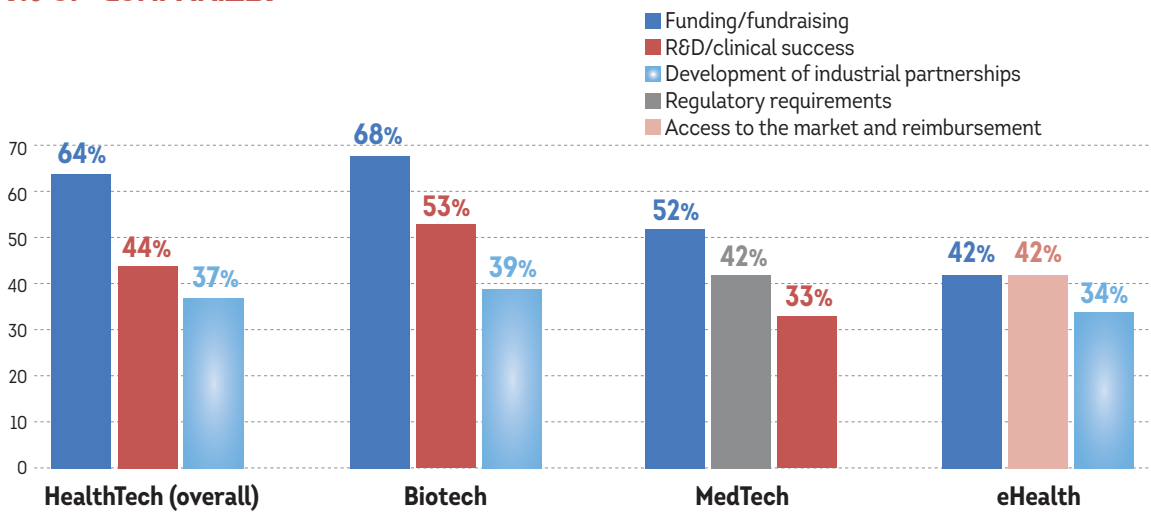
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FRENCH HEALTHTECH COMPANIES

ENTREPRENEURS' CONCERNS

Funding remains French HealthTech companies' top priority, along with successful R&D and the development of industrial partnerships. Key issues for MedTech and eHealth companies include regulatory requirements and market/reimbursement access.

TOP 3 CONCERNS FOR ENTREPRENEURS [% OF COMPANIES]



Source: France Biotech, 360 companies, January 2022

Funding is one of the main issues for HealthTech according to two-thirds of entrepreneurs in the three key sectors: biotech, MedTech and eHealth.

HealthTech companies and particularly biotech companies are typically very capital intensive and engage in high-level R&D and long development cycles, resulting in significant

and recurrent funding requirements. R&D and clinical success and the development of industrial partnerships are also critical to companies' development and growth.

MedTech companies identify regulatory requirements as a key issue, while eHealth companies are faced with complex market access and reimbursement conditions.



2

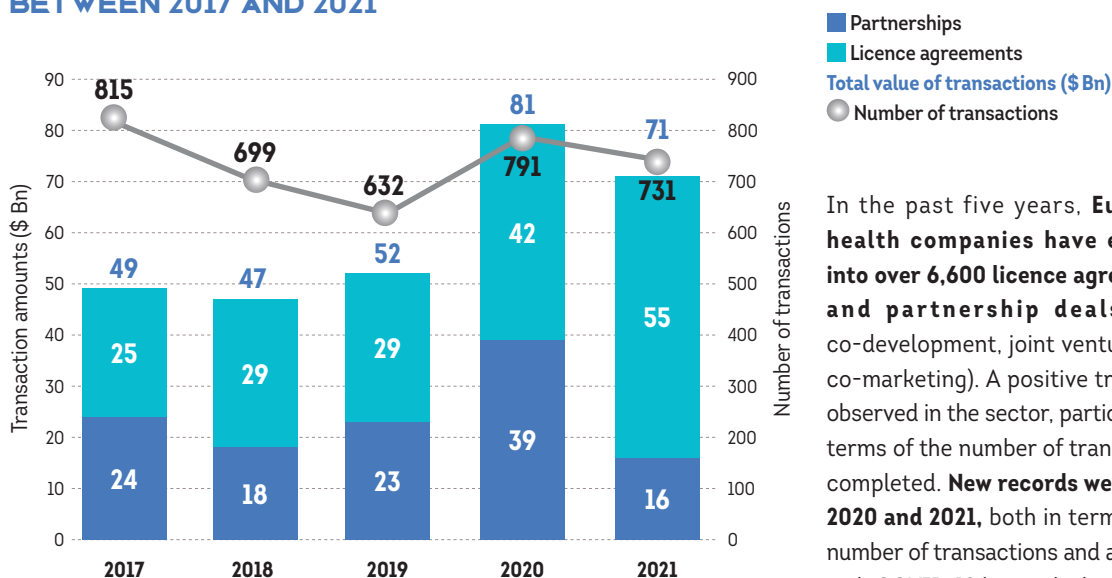
HEALTH PARTNERSHIPS

STRATEGIC HEALTHTECH ALLIANCES

European healthcare stakeholders signed over 6,000 licence and partnership agreements between 2017 and 2021. 2020 and 2021 were record years in terms of transaction numbers and amounts, while the majority of collaborations involved a wide range of biotechnology products.

1. FOCUS ON EUROPE

TREND IN HEALTH PARTNERSHIPS AND LICENCE AGREEMENTS IN EUROPE BETWEEN 2017 AND 2021



Source: France Biotech, GlobalData, January 2022, transactions announced and completed

In the past five years, **European health companies have entered into over 6,600 licence agreements and partnership deals** (R&D co-development, joint ventures and co-marketing). A positive trend was observed in the sector, particularly in terms of the number of transactions completed. **New records were set in 2020 and 2021**, both in terms of the number of transactions and amounts, with COVID-19 having little effect on transactions and even boosting them.

TREND IN THE NUMBER AND AVERAGE VALUES OF HEALTH PARTNERSHIPS AND LICENCE AGREEMENTS IN EUROPE BETWEEN 2017 AND 2021

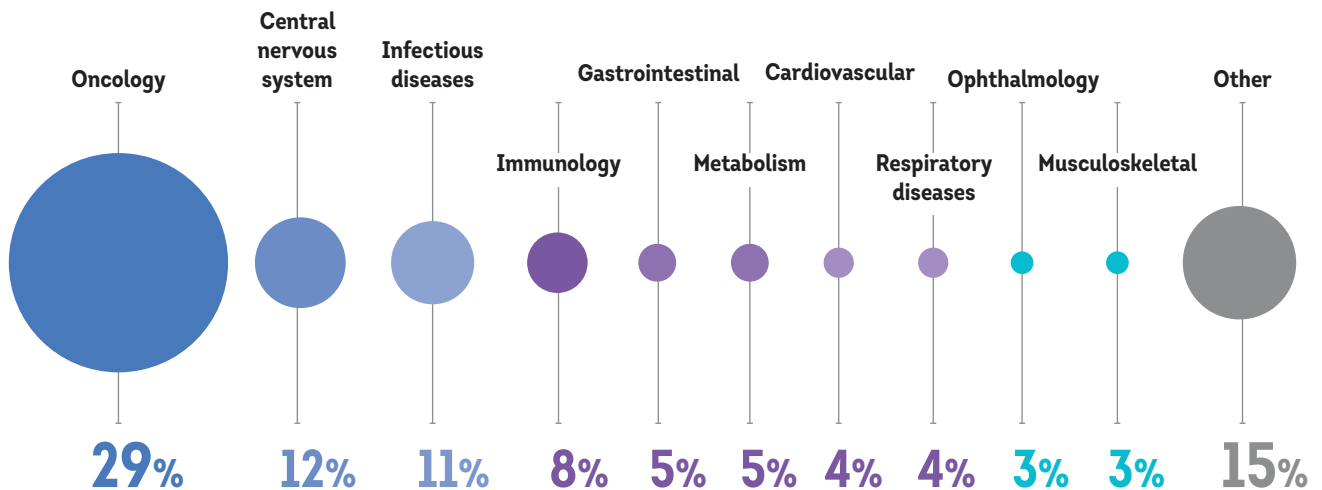
	2017	2018	2019	2020	2021
Number of transactions (amounts provided)	156	146	145	151	163
Average value per transaction	\$313 M	\$325 M	\$362 M	\$534 M	\$434 M
% change (average value)		+ 3.8%	+ 11.2%	+ 47.6%	- 18.6%

Source: France Biotech, GlobalData, January 2022, transactions announced and completed

Every year, between 600 and 800 partnership deals are completed by European biotechnology and pharmaceutical companies. On average, licence agreements account for 40% of transactions and partnerships 60%. The average

values of transactions have been on the rise since 2017, **with 2020 proving a record year averaging over \$500 M per transaction.**

DISTRIBUTION OF THE NUMBER OF PARTNERSHIPS AND LICENCE AGREEMENTS BY THERAPEUTIC AREA BETWEEN 2017 AND 2021 [% OF AGREEMENTS]

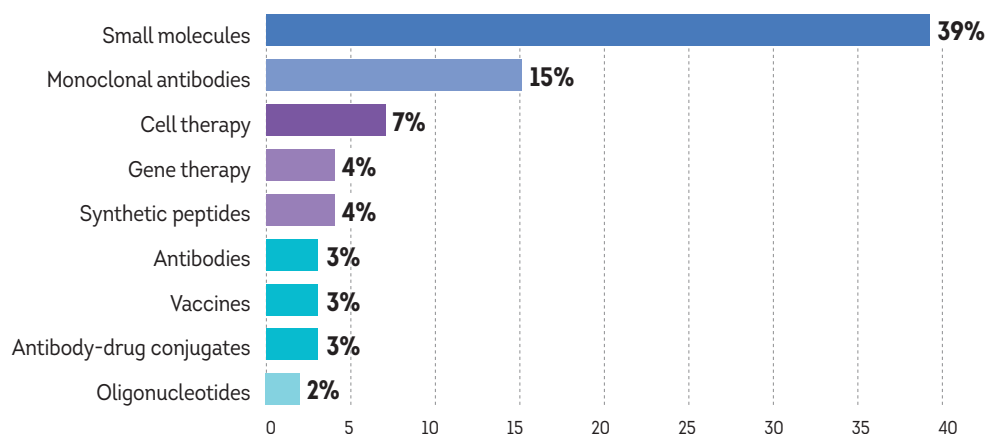


Source: France Biotech, GlobalData, January 2022

Oncology is the top therapeutic area for agreements signed in the past five years, accounting for 29% of agreements and 35% of their total value. **When combined with infectious diseases and the central nervous system, over half of all**

agreements fall within these three areas. These are also the areas that are most investigated by French biotech companies.

DISTRIBUTION OF THE NUMBER OF PARTNERSHIPS AND LICENCE AGREEMENTS BY MAIN MOLECULE TYPE BETWEEN 2017 AND 2021 [% OF AGREEMENTS]



Source: France Biotech, GlobalData, January 2022

Small molecules and monoclonal antibodies top the ranking at 39% and 15% of the number of licence agreements and partnerships respectively. **However, European health companies' technological approaches vary significantly,** with over twenty molecule categories in total. Emerging approaches including cell and gene therapies are also well

represented among the partnership and licence agreements, ranking third and fourth respectively. While small molecules represent 31% of the total value of agreements over the survey period, monoclonal antibodies also rank highly at 22% of the total value.

TOP 10 STRATEGIC ALLIANCES IN 2020 AND 2021 INVOLVING EUROPEAN BIOTECH AND PHARMACEUTICAL COMPANIES

Announcement date	Research partner/licensor	Licensor partner country	Research partner/licensee	Licensee partner country	Partnership type	Therapeutic techniques	Therapeutic area(s)	Project phase on signing date	Total potential value (\$M)*	Upfront (\$M)
12/2020	Myovant Sciences	United Kingdom	Pfizer	United States	Co-development	Small molecules	Gynaecology, oncology	Preregistration	4,200	650
06/2020	Genmab	Denmark	AbbVie	United States	Co-development	Monoclonal antibodies	Oncology	Discovery, Phase II	3,900	750
09/2021	Adaptimmune	United Kingdom	Genentech (Roche)	Switzerland	Licence	Cell/gene therapy	Oncology	Discovery	3,250	150
06/2021	Prothena Corp	Ireland	BMS	United States	Licence option	Monoclonal antibodies	Central nervous system	Phase I	2,255	NP
11/2020	Affimed	Germany	Roivant Sciences	Switzerland	Licence	Monoclonal antibodies	Oncology	Preclinical	2,091	60
06/2020	UniQure	Netherlands	CSL Behring	United States	Licence	Gene therapy	Haematology	Phase III	2,050	450
01/2020	MorphoSys	Germany	Incyte Corp	United States	Licence	Monoclonal antibodies	Oncology	Preregistration	2,000	750
02/2020	Bicycle Therapeutics	United Kingdom	Genentech (Roche)	Switzerland	Licence	Synthetic peptides	Oncology	Discovery, preclinical	1,700	30
01/2021	Merus	Netherlands	Loxo Oncology	United States	Licence	Bispecific antibodies	Oncology	Discovery	1,640	40
01/2020	Adaptimmune	United Kingdom	Universal Cells (Astellas)	United States	Co-development	Cell/gene therapy	Oncology	Preclinical	1,450	NP

*Total potential value: this amount includes the upfront payment, milestone payments and royalties where applicable. This ranking includes transactions between biotech/big pharma and biotech/biotech, but excludes big pharma/big pharma partnerships. This ranking only includes partnerships for which financial information has been provided. NP: not provided
Source: France Biotech, GlobalData, January 2022

2020 and 2021 were record years for HealthTech in Europe, not just in terms of the number of transactions completed, but also in terms of the value of agreements. For instance, the past two years saw **over twenty partnership deals signed between European biotech companies and pharmaceutical companies, worth over \$1 billion.**

The majority of the 10 largest transactions over the period (7 out of 10) were for licence agreements. However, the largest transaction was for a co-development and co-marketing agreement announced in December 2020 worth \$4.2 billion between Myovant, a British biotech company and the US pharmaceutical company Pfizer. This

agreement, with its \$650 million upfront payment, related to a small molecule developed for several indications including prostate cancer and endometriosis.

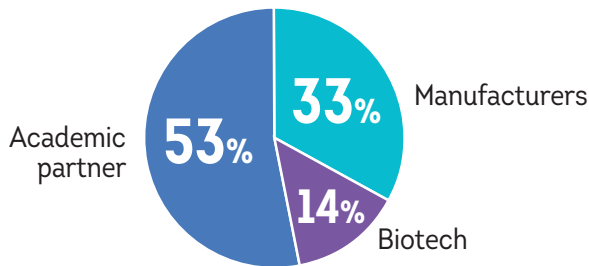
Oncology also featured highly and was involved in almost all the agreements. Apart from two agreements relating to molecules at advanced stages (preregistration and Phase III), the other collaborations were conducted at early research stages (discovery, preclinical and Phase I). Agreements on monoclonal antibodies, bispecific antibodies, cell therapies and gene therapies, all of which are biotechnology products, dominated the ranking.

Collaborative research outside Europe

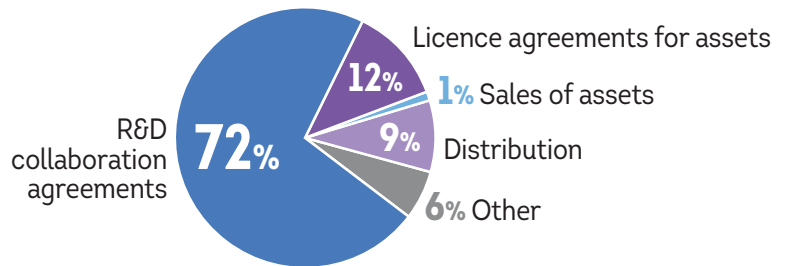
Public research stakeholders were the main partners of French HealthTech companies. A third of partnerships were conducted globally and the majority were still R&D collaborations.

2. FOCUS ON FRANCE

DISTRIBUTION BY TYPE OF PARTNER



DISTRIBUTION BY TYPE OF AGREEMENT

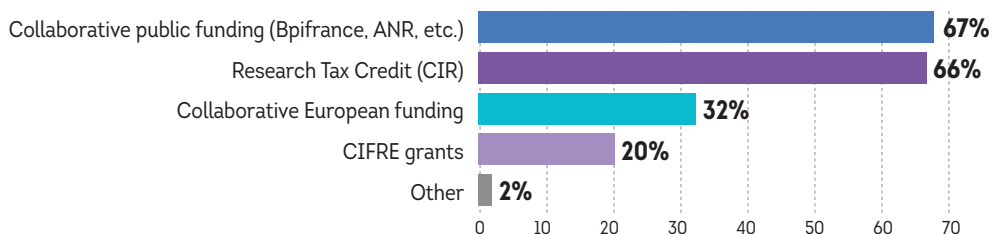


73% of companies were involved in partnerships, and therefore collaboration was a key priority for HealthTech companies. **More than half of these partnerships were with academic teams, public research teams or foundations.** Since companies' R&D mostly originates from academia, this public/private partnership continues throughout companies' development, with numerous firms continuing to collaborate with the public sector through technology

transfer (with purchasing and licensing of assets) or partnership agreements. The vast majority of agreements concluded by HealthTech companies are in the area of R&D, representing almost three-quarters of partnerships, while licensing deals for assets account for 12% of current agreements.

Source: France Biotech, **207 companies** for agreement type and **251** for partner type, January 2022

SCHEMES PERCEIVED AS BEING MOST EFFECTIVE FOR ENCOURAGING PUBLIC/PRIVATE PARTNERSHIPS



According to entrepreneurs, **two drivers appear most effective for encouraging and promoting public/private agreements: collaborative public funding and Research Tax Credit (CIR)** (each favoured by two-thirds of companies). Collaborative public funding is mainly provided by Bpifrance, the French regional authorities and the ANR (the French

National Research Agency), and includes schemes such as key competitiveness-boosting projects (PSPCs) and calls for proposals in connection with Investing in the Future programmes (PIAs). Research Tax Credit offers public research teams and companies benefits in relation to joint research projects. Consequently, the abolition of the



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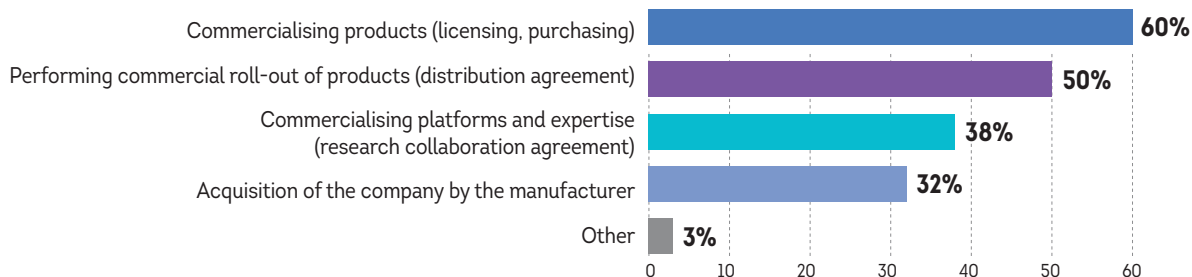
EUROPE FRANCE HEALTH PARTNERSHIPS

doubling of the Research Tax Credit (CIR) base may have the effect of impeding public/private research initiatives, which are nevertheless essential for commercialising public research and for health innovation in general. Finally, in third

position, collaborative European funding (Horizon Europe) is also one of the most effective drivers for encouraging private/public research agreements ahead of CIFRE grants.

Source: France Biotech, **317 companies**, multiple choice question, January 2022

AIMS OF INDUSTRIAL AGREEMENTS (PHARMA, MAJOR MEDTECH CORPORATION)

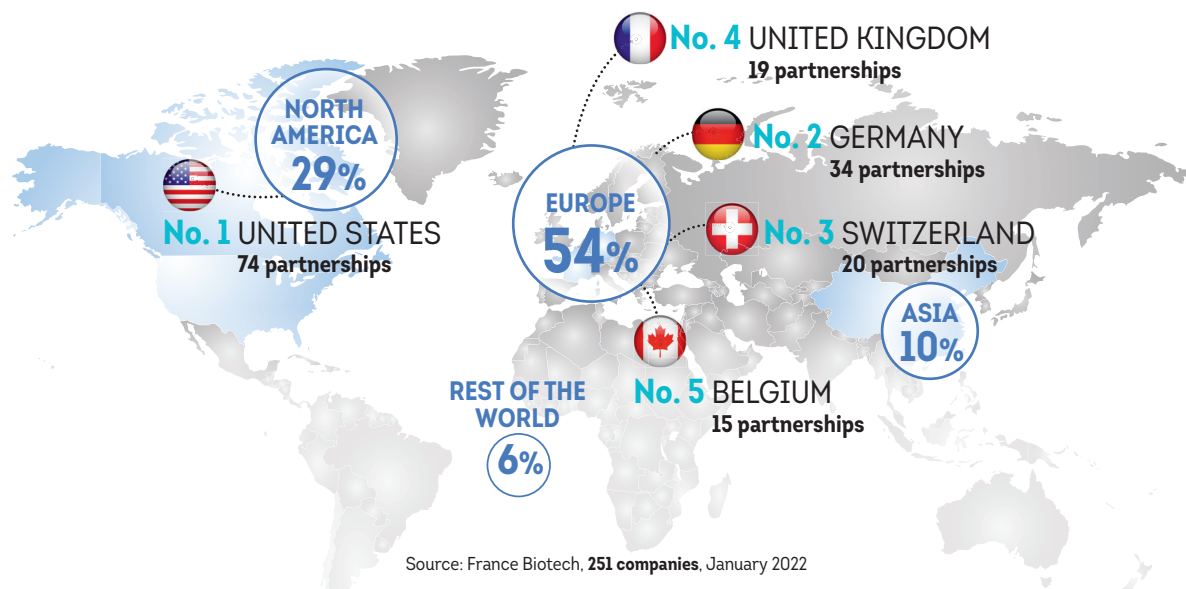


Industrial partnerships, mainly with major corporations, also feature highly and are on the rise among HealthTech companies (33% in 2021 compared to 31% in 2020). According to entrepreneurs, the key benefit of these partnerships lies in the ability to commercialise products through licences and acquisitions, as well as ensuring commercial roll-out

through distribution agreements. However, over a third of companies seek not only to commercialise their products, but also the associated expertise and their platforms through private/private or private/public partnership agreements.

Source: France Biotech, **326 companies**, multiple choice question, January 2022

GEOGRAPHICAL ORIGINS OF INTERNATIONAL PARTNERSHIPS (% OF AGREEMENTS) TOP 5 NATIONALITIES OF PARTNERS



Source: France Biotech, **251 companies**, January 2022

32% of partnerships were forged with global stakeholders. Although European research teams and companies continued to be French firms' preferred partners, the North American continent also proved its draw, accounting for just under 30% of agreements. In terms of numbers of agreements, the United States remained French HealthTech companies' main partner, followed by France's close European neighbours: Germany, Switzerland, the United

Kingdom and Belgium. The countries most represented in partnerships were also those with a strong research dynamic, whether in the university sphere, SMEs or major corporations. **Partnerships with Asia are on the rise** (10% in 2021 compared to 8% in 2020), with China and Japan topping the ranking at 12 and 11 partnerships respectively, followed by South Korea with 5 agreements.

TOP 5 STRATEGIC ALLIANCES IN 2020/2021
INVOLVING FRENCH BIOTECH COMPANIES

Announcement date	Research partner/licensor	Research partner/licensee	Licensee partner country	Partnership type	Therapeutic techniques	Therapeutic area(s)	Project phase on signing date	Total potential value (\$M)*	Upfront (\$M)
02/2021	Collectis	Cytovia Therapeutics	United States	Licence	Gene therapy (CAR-T)	Oncology	Discovery	775	15
12/2021	Genfit	Ipsen	France	Licence	Small molecules	Oncology, metabolism	Phase III	543	136
04/2021	OSE Immunotherapeutics	Veloxis Pharmaceuticals	Denmark	Licence	Monoclonal antibodies	CNS, immunology	Phase II	381	8.5
05/2021	Nanobiotix	LianBio	United States	Licence	Radiotherapy	Oncology	Phase III	240	NP
09/2021	Coave Therapeutics	Thea Open Innovation	France	Licence	Gene therapy	Ophthalmology	Phase II	89	12

*Total potential value: this amount includes the upfront payment, milestone payments and royalties where applicable.
This ranking includes transactions between biotech/big pharma and biotech/biotech, but excludes big pharma/big pharma partnerships.
This ranking only includes partnerships for which financial information has been provided.
CNS: central nervous system. NP: not provided
Source: France Biotech, GlobalData, January 2022

Of all the strategic alliances announced in the past two years involving French biotech companies, **the five highest valued partnerships occurred in 2021 and all entailed licence agreements**. All these deals related to products at advanced phases of development (Phase II or III) with the exception of the agreement between Collectis and Cytovia. This strategic R&D partnership valued at \$775 million was announced in February 2021 and concerns the development of genetically modified IPS NK and CAR NK-type cells developed using Collectis' TALEN technology. Through this agreement, Collectis has granted Cytovia a global licence

for its TALEN gene editing technology, enabling Cytovia to edit NK cells targeting several target genes for therapeutic purposes in a number of cancer indications. These agreements reveal the considerable diversity of product categories developed by companies. This top 5 includes gene therapies, immunotherapies, monoclonal antibodies and small molecules, reflecting the diversity of technological approaches taken by French biotech companies as well as pharmaceutical companies' growing interest in these types of approaches.



2

HEALTH PARTNERSHIPS



Professor Antoine Tesnière, Director of PariSanté Campus

"One ambition – to make France the global leader for digital health"

How did the PariSanté Campus project come about?

The aim of PariSanté Campus is to bring together digital health stakeholders on an iconic site to create synergies and speed up progress on all objectives related to the transformation of the digital health system. PariSanté Campus promotes a very broad vision of digital objectives for healthcare, including: objectives in terms of access to care, algorithms, company requirements, care pathways, telemedicine and data regulation, etc.

In this fertile environment, all digital health talent (researchers, physicians, teachers, entrepreneurs, institutions, hospitals) and patients will join forces to fast track innovation and make France the global leader. Having opened in late 2021, PariSanté Campus will transfer all its activities to the iconic Val-de-Grâce site, currently undergoing renovation, which will be available in 2027-2028.

What are its aims and priorities?

PariSanté Campus seeks to unite the entire digital health ecosystem and boost France's international standing to make it a global leader in digital health.

PariSanté Campus will endeavour to develop digital health based on 4 key objectives:



- Putting data at the heart of our health system: collection, storage, use, dissemination and protection of health data
- Producing future talent in the field of digital health: PariSanté Campus is a centre for education and research, and companies and institutions need access to skills to develop an active digital health sector
- Creating economic value: supporting companies, growth and job creation in a rapidly expanding sector
- Transforming and adopting health data practices: improving the health system via an approach focused on patients and health system users.

Which are PariSanté Campus' founding members?

PariSanté Campus has 5 founding

members, which are public stakeholders with a long-standing involvement in research and commercialisation of their innovations: Inserm, l'Inria, Paris Sciences & Lettres University, the Health Data Hub and the French eHealth Agency supported by 4 research institutes specialising in:

- Quantitative life sciences: Q-Bio
- Artificial intelligence: PRAIRIE
- Imaging: Institut de technologies avancées pour la santé
- Digital technology in healthcare: Institut Santé Numérique en Société (ISNS).

"THE AIM OF PARISANTÉ CAMPUS IS TO BRING TOGETHER DIGITAL HEALTH STAKEHOLDERS ON AN ICONIC SITE TO CREATE SYNERGIES AND SPEED UP PROGRESS ON ALL OBJECTIVES RELATED TO THE TRANSFORMATION OF THE DIGITAL HEALTH SYSTEM"

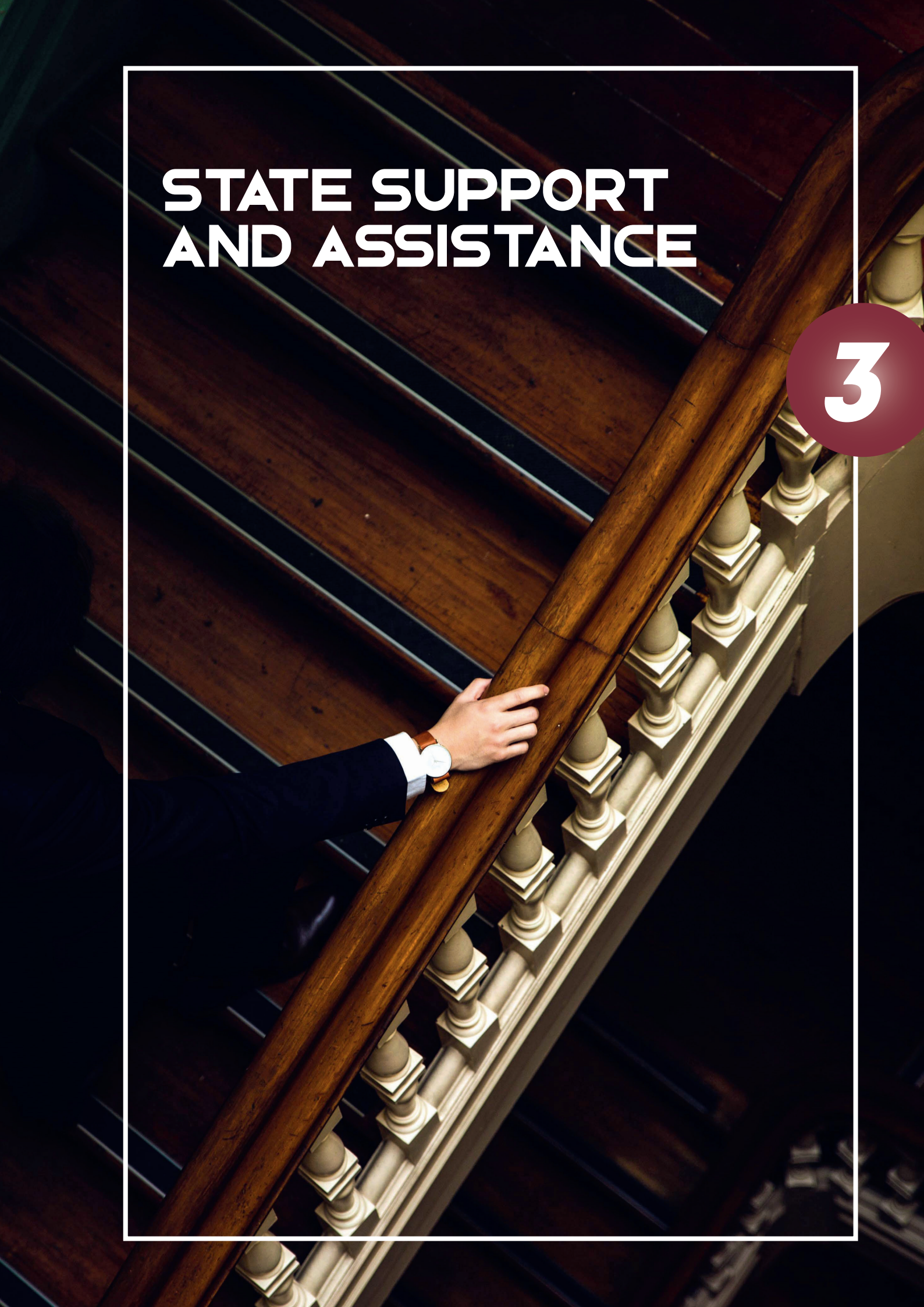
Which other stakeholders are based at PariSanté Campus?

Health and corporate sector institutions, major corporations, Dassault Systèmes, Doctolib, JOUVE, Qare, and around 30 startups have already joined PariSanté Campus (including Aqemia, Cibiltech, ResilEyes, SimforHealth, Tech2heal, Qantiq, Dr Data and Adlin). We are also very pleased to welcome France Biotech and its outstanding network to this ecosystem. ■

4 QUESTIONS FOR...

STATE SUPPORT AND ASSISTANCE

3





3

STATE SUPPORT AND ASSISTANCE



2021, a record year for supporting HealthTech companies' innovation and industrialisation

With €1.2 billion in grants and investments of €363 million in 2021, Bpifrance played a key role in developing French HealthTech companies.

CONTINUUM OF GRANTS IN 2021 FOR HEALTHTECH COMPANIES

Figures calculated for grants based on applications approved in 2021.



€1.2 Bn OF FUNDING
849 RECIPIENTS [x4 vs. 2020]

€363 M OF DIRECT AND INDIRECT INVESTMENT

R&D - Collaborative Projects

€285 M

Grant for innovation development *

- DeepTech: 122 projects → €63 M
- Innovation grants: 451 projects → €115 M

Collaborative projects

- PSPC and PSPC Region: 8 projects → €80.6 M
- Sector: 5 projects → €13 M

i-Nov competition

- Wave 6 "Mental Health": 14 projects → €6.3 M
- Wave 7 "Ultra-rapid diagnostics": 10 projects → €7 M

R&D - Priority Areas

€98 M

Biotherapies and biomanufacturing

- Acceleration strategy: 16 projects → €38.7 M
- Grand Défi: 4 projects → €5.5 M

Digital health

- Acceleration strategy: 4 projects → €5.4 M
- Grand Défi: 12 projects → €5.8 M

Emerging infectious diseases

- Acceleration strategy: 4 projects → €11.5 M
- PSPC COVID **: 1 project → €31 M

R&D - Industrialisation

€832 M

Capacity Building CEI**

- CEI 182: 62 projects → €675 M

CFP Resilience **

- 99 health projects → €123.3 M
- 7 health impact projects → €14.5 M

Territoire d'industrie* **

- 51 projects → €18.5 M

12 startups supported
[+50% vs. 2020]

Equity [+25% vs. 2020]

€158.4 M

- French Tech bridge
 - French Tech Seed
 - PSIM fund
 - Definvest fund
- €35.6 M → 12 deals

- InnoBio fund
 - Rare diseases fund
 - FABS fund
 - Patient Autonome fund
- €65.03 M → 18 deals

- Large Venture fund
- €49.7 M → 8 deals

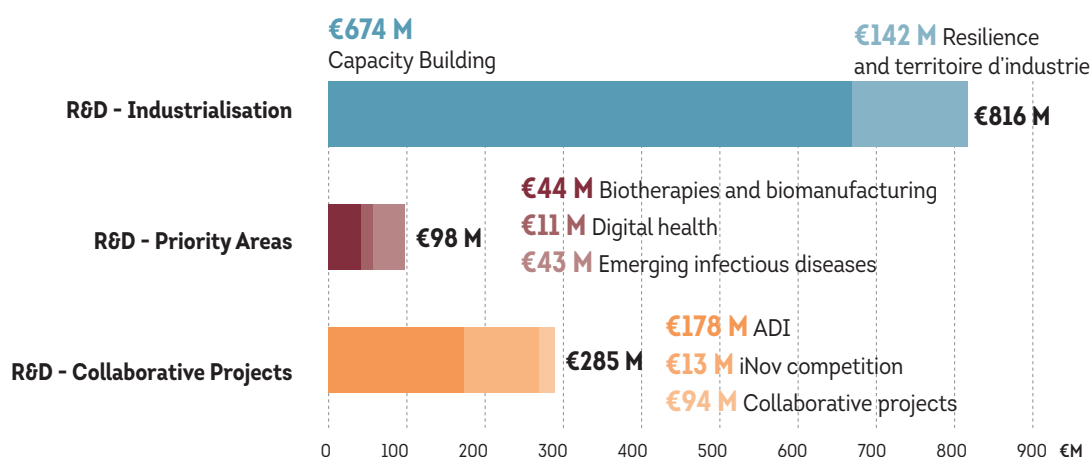
Fund of funds [vs. €140 M in 2020]

€205 M

- Seed funding
 - Venture capital
 - Growth capital
- To specialist healthcare funds

* Decision by regional authorities.
** Programmes launched due to the pandemic.

DISTRIBUTION OF INNOVATION FUNDING FOR HEALTHTECH COMPANIES IN 2021



Source: Bpifrance, January 2022.

2021 was a remarkable year for healthcare, a strategic industry both in terms of innovation and production. Over **€1.2 billion** was awarded to the industry in grants to provide over 850 projects with innovation and industrialisation support, **a fourfold increase compared to 2020**. The HealthTech share of total grants rose from 20% in 2019 to 33% of €3.7 Bn in 2021. During the pandemic, the HealthTech industry proved that it is not only a hotbed of innovation, but also has a key role to play in reindustrialising France and in European sovereignty. The government has provided the industry with significant and exceptional financial support. **Recovery Plan** programmes (CFP Resilience, CEI CAPA) launched at the beginning of the crisis in 2020 were extended in 2021, enabling the industry's production capacities in France to be expanded, modernised and relocated. In 2021, the government launched the **fourth Investing in the Future Programme**, which includes measures focused specifically on the industry as well as those described as "structural" measures. Almost €2 Bn has been ring-

fenced for acceleration strategies targeting 3 priority health industry sectors: digital health, "biotherapy and biomanufacturing" and Emerging Infectious Diseases (EIDs). These measures supplement and link to those previously initiated under the Grands Défis. Bpifrance introduced the first measures for companies through targeted CEIs and CFPs aimed at supporting these sectors with high growth potential. Further measures will be put in place in 2022 to help implement the roadmaps.

All these measures will feed into the **2030 Health Innovation Plan**, which is the result of work carried out by the Strategic Council for the Healthcare Industries (CSIS). Health is also one of the key challenges identified in the **"France 2030"** plan allocated €3 Bn. **Its aim is to "produce 20 biopharmaceuticals for cancer and chronic diseases including age-related conditions, and create the medical devices of the future"**. Measures are to be implemented from 2022 using public funding promoting innovation and industrial growth of innovative companies.



3

STATE SUPPORT AND ASSISTANCE

bpifrance

A continuum of R&D grants

Several programs are still available to support R&D phases for innovative products and services. These are tailored to the maturity, innovation level and type of projects submitted by companies and include DeepTech programmes (BFTE and ADD), national competitions such as the i-Lab and i-Nov competitions, and funding programmes for collaborative R&D projects including the PSPC (replaced by the I-Demo programme in 2021) and PSPC REGION. Bpifrance awards almost 50% of DeepTech grants to the HealthTech industry, reflecting its firm commitment to research on disruptive innovations.

Industrialisation grants

Health is one of 6 strategic industries identified by **France's Recovery Plan** for which Bpifrance has issued a call for projects aimed at supporting industrial investment projects in strategic sectors (CFP Resilience at national level) and those with a strong regional component (CFP territoire d'industriel/regional level). 158 projects have been supported with €157 M to promote investment, modernisation and relocation of the industry.

Through "Capacity Building" programmes launched in 2020 at the beginning of the pandemic, it has been possible to fund and support the research and industrialisation of health products directly linked to medical treatment of COVID-19, with 62 projects supported and €675 M awarded in grants. Half of all grants were awarded to support vaccine production capacity in France.

Targeted measures

In the health industry, acceleration strategies have been implemented for 3 priority areas within the targeted component of the **Fourth Investing in the Future Programme (PIA4)**: digital health, "biotherapy and biomanufacturing" and Emerging Infectious Diseases (EIDs). These initiatives link into the Grands Défis with compatible measures taken in related areas. In 2021, Calls for Expressions of Interest provided a national overview of projects. Applications were submitted for a total of over 400 projects.

In 2021, funding was awarded for projects to develop biotherapies and innovative biomanufacturing processes (€44 M for 38 projects) as well as for biomanufacturing integrator accreditation. These measures support the objectives of the **biotherapies and biomanufacturing plan**, which are to produce at least 5 new biopharmaceuticals, double the number of jobs in the sector, and enable the emergence of at least 1 new unicorn and 5 new biotech mid-caps in the next 5 years.

The **"Digital Health" acceleration strategy** seeks to promote the emergence of innovative digital health solutions in France alongside strong medical-economic value propositions capable of conquering an eHealth market whose global expansion is in full swing. The Grands Défis scheme awarded €6 M to 12 projects through a CFP aimed at assessing the medical and/or economic benefits of AI-based medical devices. There are plans to repeat this CFP every year to assess all types of digital medical devices. Its aim

is to justify practical use of tested devices and facilitate market access.

The aim of the **Emerging Infectious Diseases and "CBRN" threats acceleration strategy** is to enable central government to understand, prevent and monitor infectious disease emergence or reemergence phenomena. In a broader sense, it also contributes to preparations for health crises resulting from Chemical, Biological, Radiological or Nuclear (CBRN) threats.

DIRECT AND INDIRECT FUNDS

Bpifrance also continued its equity investment strategy with €158 M invested in HealthTech companies (compared to €126 M in 2020). €205 M was also invested in HealthTech funds through the fund of funds (up 50% compared to 2020), enabling additional investment capacity of €1 Bn in 2021 due to over 5-times leverage. This includes Bpifrance funds' investment in Series A funding rounds: **Egle Therapeutics**

(cell therapy, €40 M); **Emergence Therapeutics** (antibody-drug conjugates for cancer, €87 M), **Depixus** (innovative gene technology, €30.6 M) and **DNA Script** with over €140 M raised. Bpifrance has consistently funded this DeepTech startup since its incorporation in 2014 through the i-Lab and i-Nov innovation competitions, as well as the Global Innovation Competition and the Digital Innovation Competition. The life sciences startup studio Argobio was set up in 2021 after €50 M was raised. Its mission spans the incubation of highly innovative projects in their early stages of development right up to incorporation of companies and their funding through a Series A round.

SUPPORT

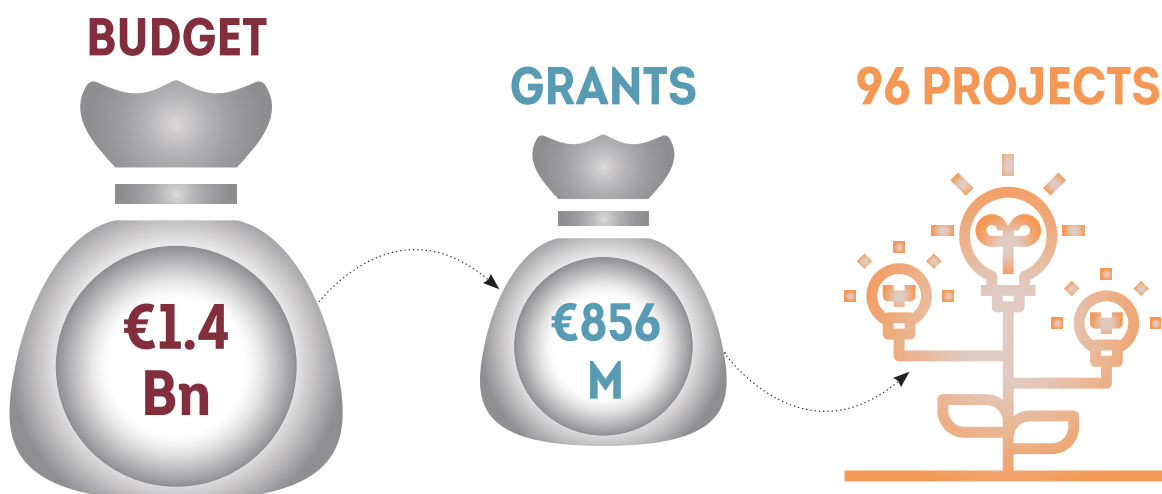
The HealthTech programme within the Hub was specifically designed to support Bpifrance investment in the health industry including biotech, MedTech and digital health startups - and help meet industry requirements and challenges: long development cycles, regulatory requirements, the scientific, technical and medical stakes involved, substantial financing needs, etc. A dedicated team provides personalised support, with the specifics of each business and its needs in mind. This service includes practical operational support, access to expert knowledge (technical advice and privileged access to major players), peer-to-peer sharing, and targeted networking. Since it was set up in 2018, the HealthTech Hub has supported 34 startups, 12 of which received support in 2021.

Tackling COVID-19

Since May 2020, over €850 M has been awarded in grants to 96 projects.

OVERVIEW OF COVID-19-RELATED PROJECTS SUPPORTED SINCE THE BEGINNING OF THE CRISIS (MAY 2020 - DECEMBER 2021)

TOTAL FOR ALL PROGRAMMES:



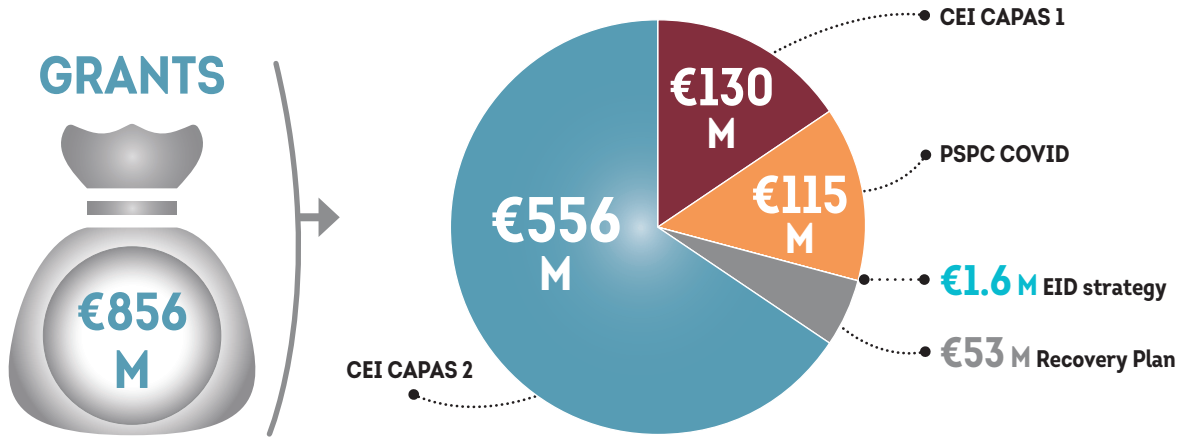


3

STATE SUPPORT AND ASSISTANCE



MEASURES TO TACKLE COVID-19



Since the outbreak of the crisis in 2020, Bpifrance has provided companies with COVID-related support for projects to develop vaccines, therapies, diagnostics and consumables; and with their R&D and production capacity ramp-up phases. **96 projects have been funded with total grants of €856 M.**

Several programmes have supported companies in their efforts to tackle COVID: the **CAPACITY BUILDING 1 and 2** calls for expressions of interest, the **PSPC COVID**, and projects under the CFP RESILIENCE and the **CEI for the acceleration strategy on Emerging Infectious Diseases (EID-CBRN)**.

Projects involving health products and equipment designed to tackle the COVID-19 pandemic and its consequences had the advantage of eligibility for grants covering up to 80% of the investment or R&D project costs (SA.57367). The government has therefore shouldered much of the risk alongside these innovative healthcare companies. In some cases, it can activate priority purchase rights for developed products. Moreover, the SA.56985 scheme was introduced to help companies and thus support the economy.

STATE SUPPORT AND ASSISTANCE

bpi france



OVERVIEW OF COVID-19-RELATED PROJECTS SUPPORTED SINCE MAY 2020

€856 M in grants

€421 M

**PREVENTIVE TREATMENTS
COVID-19 VACCINES**

Clinical development
→ €66.1 M

Biomanufacturing -
Active substance
→ €50.6 M

Excipients
→ €39.4 M

Consumables
→ €106.3 M

Filling
and packaging
→ €157.7 M



€168.5 M

**INNOVATIVE/CURATIVE
THERAPIES (EXCLUDING
VACCINES)**

Clinical development
→ €110.1 M

Scale-up and production
Biological products
→ €58.4 M



€66 M

DIAGNOSTICS

Reagent
consumables
→ €7.1 M

Consumables
→ €49.1 M

COVID-19
Diagnostic tests
→ €9.7 M



€200 M

**SYMPTOMATIC
TREATMENTS**

Production of API
intermediates
and APIs
→ €146 M

Medical devices
→ €15.4 M
Filling
and packaging
→ €37.3 M



Pascale Ribon, DeepTech Director, Bpifrance

"Along with electronics and ICT, health is one of the most dynamic DeepTech sectors"

Could you tell us the aims and missions of the DeepTech plan?

The DeepTech plan is a scheme introduced by the French government and implemented by Bpifrance since 2019. Its aim is to create 500 startups, some of which will go on to become economic champions developing research-based disruptive innovations by 2025. The DeepTech plan seeks to encourage the emergence of startups, ensure their growth and develop an ecosystem that fosters this process. DeepTech encompasses startups that share a focus on developing disruptive technology in all business sectors: health, energy, environment, process engineering, artificial intelligence and non-health biotechnologies.

The government has allocated €2.5 Bn to the scheme, with further support from France's Recovery Plan, 2030 Health Innovation Plan and New Industrial France programme. The plan includes provisions to allocate over €150 M to the DeepTech project emergence ecosystem, €80 M per year to technology transfer, €800 M to 5-year startup funding, and €1.3 Bn in direct investment and fundraising by 2023. In 2021, there was a deal flow of 250 new startups.

In 2021, Bpifrance was involved in 17 funding rounds, representing 16% of funding rounds for DeepTech startups.

What tools and services are available for companies?

We offer various tools and services to support startups at different levels of maturity:

- **Les Deeptech.fr:** a platform for launching and boosting DeepTech startups. This provides project leaders with reference tools to help first-time entrepreneurs make the right choices and access appropriate guidance.
- **The Tandem service:** this helps potential company founders, often with scientific backgrounds, to find co-founders with business backgrounds.
- **DeepTech Tour:** Bpifrance is involved in partnerships with academic stakeholders and organises a tour of



the French regions, stopping at 20 university campuses.

- **Various innovation competitions are organised** to stimulate entrepreneurial activity, including the i-PhD (prior to company incorporation), i-Lab (post-incorporation) and i-Nov (development phase) competitions.

- **Support with developing innovation campuses:** stakeholders have access to a white paper and self-assessment jointly developed with three university sites.

What types of funding are offered?

Bpifrance draws on significant financial resources to support startups through various schemes including highly subsidised financing, convertible bonds and direct investment.

- **The French Tech Emergence Grant (BFTE – for companies post-incorporation)** is a seed funding tool (offering up to €90,000). It encourages entrepreneurs to launch DeepTech companies with significant growth potential and enables them to handle initial spending once their company is incorporated, their disruptive technology protected, and their market identified.

- **The DeepTech development grant (ADD):** these subsidies or advances range from €500,000 to €2 M.

- **Tech Seed convertible bonds:** these funds are designed to boost fundraising to accelerate innovation projects currently in their post-maturation phase. They range from €50,000 to €500,000 or twice the amount raised.

Where does the HealthTech industry stand in the DeepTech plan?

The ecosystem around healthcare is something of a forerunner in this area, as it is a well-structured industry and therefore an example of what is being attempted in other fields.

Health is one of the most dynamic sectors along with electronics and Information and Communication Technologies (ICT).

Since 2019, €12 M has been injected into 139 startups through the French Tech Emergence Grant. 42% of these companies are involved in biotech and 58% in MedTech and digital health. In total, health accounts for 41% of BFTE DeepTech grants (19% biotech and 22% MedTech/digital health).

Since 2019, 65 startups have received €90 M funding through the DeepTech Development Grant. 60% of these companies are involved in biotech and

"BY ENCOURAGING THE EMERGENCE OF NEW DEEPTECH STAKEHOLDERS, BPIFRANCE HAS (...) PROVIDED THE MEANS TO CREATE FUTURE ECONOMIC CHAMPIONS OFFERING DISRUPTIVE INNOVATIONS."

40% in MedTech and digital health. In total, health accounts for 47% of ADD DeepTech grants (24% biotech and 23% MedTech/digital health).

Since 2011, the DeepTech Observatory for health has reported over 60 fundraising transactions worth €1.4 Bn. In 2021, the main health-related DeepTech investment transactions were Halio Dx (€260 M), Owkin (€159 M), DNA Script (€140 M), eCential Robotics (€100 M) and MNEMO THERAPEUTICS (€75 M).

With such a vibrant HealthTech ecosystem, 2022 looks set to be a prosperous year. By encouraging the emergence of new DeepTech stakeholders, Bpifrance has put France among the leading European countries for investment in startups and provided the means to create future economic champions offering disruptive innovations. ■



**FUNDING OF
HEALTHTECH
IN FRANCE
AND
AT GLOBAL LEVEL**

4



4.1



Would you like a little more 2021?

While 2020 saw the industry in good health despite the COVID-19 pandemic sounding the death knell for many companies, 2021 has been described more than once as a record year in financing circles. So has the HealthTech industry played its cards right this year?

In 2021, the first COVID-19 vaccines were brought to market, shining a light on the first wave of players in the vaccine race. Successive new variants then emerged, thwarting efforts to return to normal life and threatening defences that had been built thus far through testing and vaccines.

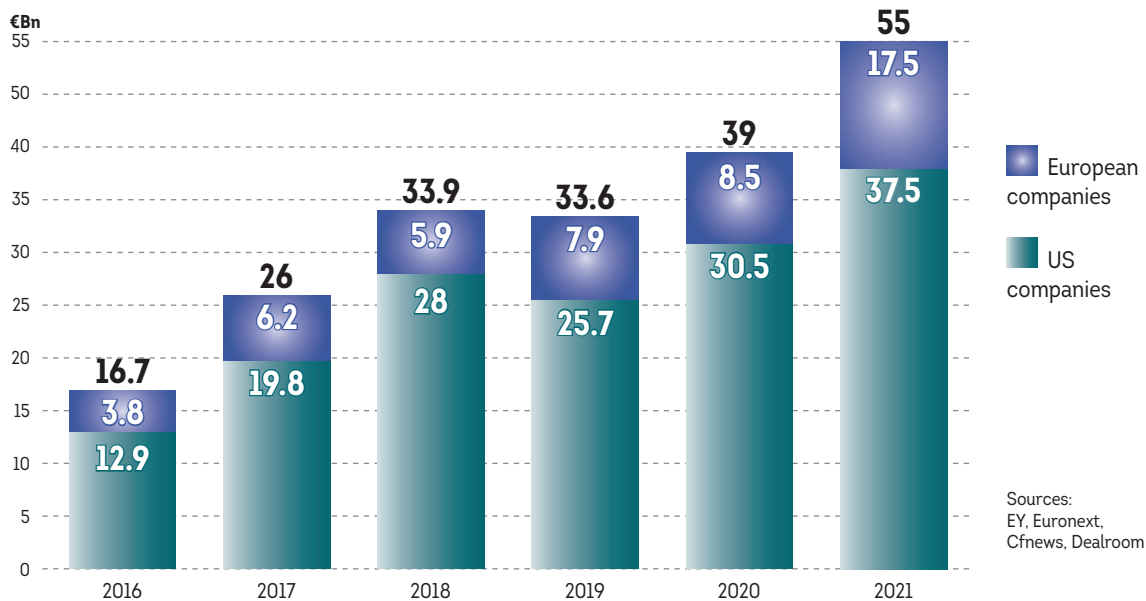
Although research continued at an unprecedented pace in this sector, all health sectors (genetic engineering, immunology, AI, oncology, etc.) pursued their innovations, clinical trials and developments, receiving substantial funding of over €55 billion.

While the effects of the pandemic persisted throughout 2021, funding continued to flow into the health sector, both through the financial markets and private funding rounds. Specialist investment funds also raised significantly higher levels of capital than in 2020, already a record year, supporting all therapeutic areas. A number of companies experienced "meteoric rises", including the US firm EQRx, which completed an initial funding round worth \$200 M in 2020 and went on to secure Series B and C funding of \$0.5 Bn and \$1.3 Bn in January and August 2021, before completing its IPO in December (through a SPAC). Oxford Nanopore Technologies followed a similar trajectory with an

IPO on the London Stock Exchange (LSE) in September (€705 M), while Janux Therapeutics proved even faster, with only 4 months between its Series A funding (\$125 M) and IPO on Nasdaq (\$223 M).

Once again, IPOs for US biotech companies raised record levels of capital in the first half, spearheaded by Sana Biotechnology (\$588 M/€483 M) and Recursion Pharmaceuticals (\$502 M/€419 M). Two companies even passed the billion dollar mark towards the end of the year: Ginkgo Bioworks (\$1.6 Bn) and EQRx (\$1.3 Bn). US biotech companies thus raised €11.9 Bn on the market (compared to €8.8 Bn in 2020, already a historic figure since the average between 2016 and 2019 was approximately €3.5 Bn).

HISTORY OF FUNDRAISING BY US AND EUROPEAN HEALTHTECH COMPANIES (IPOS AND VENTURE CAPITAL) (€BN)



European companies were not to be outdone, with an eightfold increase in sums raised on the European and US markets to €4.7 Bn, including record IPOs such as those completed by Polypeptide Group AG (€770 M), Exscientia (€440 M) and Evotec (€440 M). Sums raised through private funding rounds now exceeded €100 M per round, as in the case of British company Artios Pharma (oncology) which secured Series C funding of €130 M.

Although the level of funding had increased, the market value of biotechnology securities fell due to setbacks relating either to clinical trials (Galapagos, Polyphor – which became Spexis following its merger with the US company Enbiovix) or prices approved at the time of market authorisations (BlueBird Bio). The Next Biotech index in Europe was down 14% and Nasdaq Biotech fell 3%*. Contrasts between COVID-19 vaccine companies' results were sharper, with BioNTech, Moderna and Valneva performing well, while CureVac's share price halved following announcements of inconclusive results for their first vaccine generation in 2021.

Despite the pandemic, the medical devices sector continued

to grow in terms of revenue, market capitalisations and investment. The MedTech sector had its best year yet in terms of venture capital funding, raising \$10 Bn globally (source: Evaluate Pharma). The market capitalisation of listed companies more than doubled (+ 128%) between January 2020 and August 2021, outstripping both pharmaceutical and biotech companies (source: EY pulse report).

In the eHealth sector, marketing of COVID-19 vaccines led to faster digitisation of appointment platforms such as Kry and Doktor 24, and **growth was also observed in artificial intelligence:** Dental Monitoring was one of the year's star performers with €130 M raised through a private funding round and Sanofi made a \$180 M equity investment in the Franco-American startup Owkin. In addition to growth in the digital sector, the more "standard" sectors of diagnostics and robotics also attracted funding, with the largest funding round of \$830 M completed by the American cancer test manufacturer Caris Life Sciences, followed by Series D funding of \$600 M for the British robotic surgery group CMR Surgical. All types of funding increased in comparison to the previous year, whether in terms of venture capital or IPOs.

(*) Source: <https://investir.lesechos.fr/dossiers/huit-biotechs-proches-d-echeances-majeures/huit-biotechs-proches-d-echeances-majeures-1993197.php>. Eight biotech companies approaching major milestones - Investir - Les Echos Bourse

VENTURE CAPITAL

Despite the continuation of the pandemic into 2021, venture capital funding was in good shape, even exceeding 2018 levels. **Europe was the main driver of this growth, up more than 20% compared to the previous year, rising from €6.5 Bn to €10.3 Bn (+ 58%).**

In the US biotech sector, funds raised by Elevate Bio (\$525 M – Series C) and EQRx (\$500 M – Series B) rank among the top 10 venture capital fundraising transactions completed in the past decade. However, these transactions concern later-stage series than funds raised in 2020 and 2019, which involved major transactions for companies in their early stages of development. A total of fifteen US companies completed

transactions of \$200 M or over in 2021 (compared to eight in 2020), which were all for Series B or C funding, with the exception of Neumora Tx, Prime Medicine and G2 Bio Companies, which raised \$500 M, \$315 M and \$200 M respectively through Series A funding. In Europe, four companies finally hit the symbolic \$200 M mark, including Exscientia which raised \$225 M just months before its IPO on Nasdaq and Prague-based Sotio, which raised €280 M in Series A funding towards the end of the year. Although UK biotech companies attracted the majority of venture capital funding at €2.9 Bn, France was still in a leading position at €677 M of funded deals, taking third place behind Germany (€721 M).



4.1

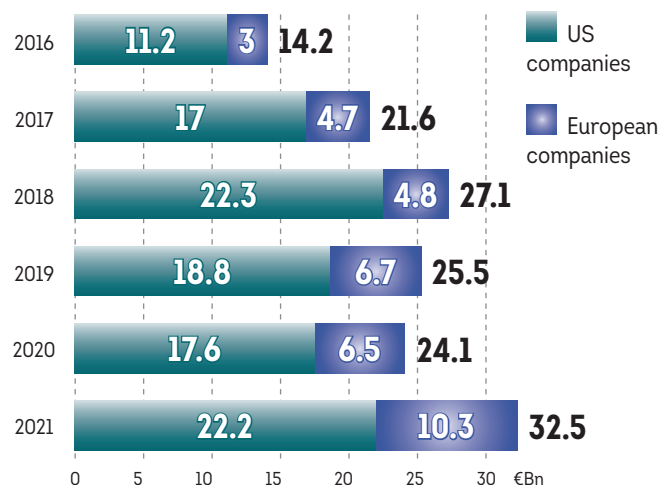
WORLD EUROPE FRANCE

HEALTHTECH FUNDING



A general increase in funding transactions was observed in the medical devices and eHealth sectors (€7.5 Bn compared to €5.7 Bn), though this still fell short of 2017's historic levels of nearly €8 Bn. However, trends differed between the United States and Europe. Volumes were slightly up in the United States compared to 2020, with venture capital transactions in the medical devices sector reaching **€5.1 Bn compared to €4.7 Bn (+8%) in 2020, driven by Caris Life Sciences' record fundraising transaction (€830 M - Series C)**. In contrast, amounts in Europe **more than doubled (+125%) while the number of transactions only increased by 10%**. The United Kingdom made by far the largest deals with 3 transactions worth over €200 M: CMR Surgical which raised €0.5 Bn, Oxford Nanopore Technologies which raised over €230 M in April with its IPO on the LSE, and Quanta Dialysis Technologies (€205 M). France also saw VC deals exceeding €100 M with DNA Script, Dental Monitoring and eCential Robotics. These large venture capital fundraising transactions continue to be an indicator worth tracking in relation to future transactions on the capital markets.

HISTORY OF VENTURE CAPITAL FUNDRAISING BY US AND EUROPEAN HEALTHTECH COMPANIES (€BN)



Sources: EY, Euronext, Cfnews, Dealroom

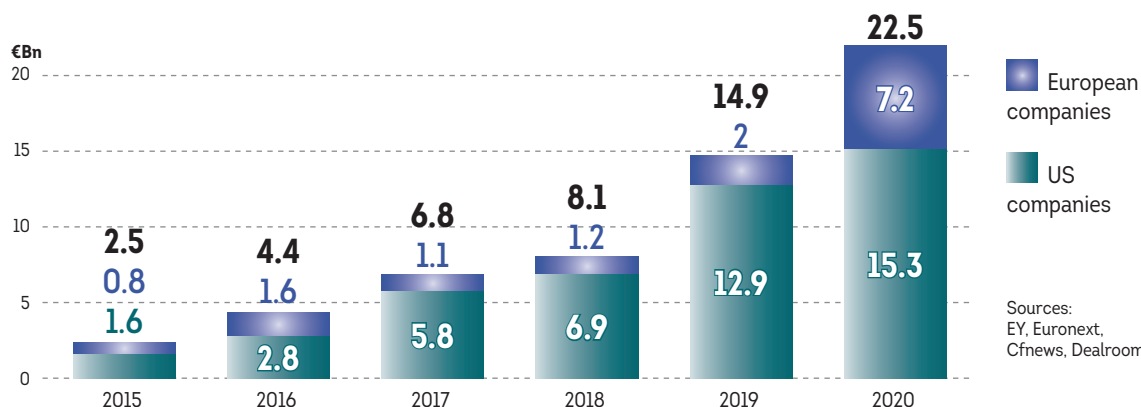
FINANCIAL MARKETS

2021 was a year of low stock market volatility in a context where the COVID-19 pandemic appeared more under control. However, the HealthTech sector saw a historic wave of new listings.

This increase in amounts raised on the markets was largely linked to the rise in the number of transactions completed by European companies: no fewer than 56 companies completed IPOs (compared to 20 in the previous year), 18 of which took place on US markets. The total amount raised increased 3.5 times. This record figure can be attributed both to the number of deals and their size, with 5 biotech transactions and

2 MedTech transactions worth over \$400 M. Although two-thirds of these large transactions are still being carried out on Nasdaq, significant transactions are also being performed on domestic markets including Oxford Nanopore Technologies' deal on the London Stock Exchange, for the medical devices sector, and Polypeptide Group AG's transaction on the Swiss market, for the biotech sector, raising €705 M and €770 M respectively, confirming European markets' increasing dynamism with sums close to those observed across the Atlantic.

HISTORY OF IPOs BY US AND EUROPEAN HEALTHTECH COMPANIES (€BN)














Sources: EY, Euronext, Cfnews, Dealroom

The market rose slightly for US companies, building on an already prolific 2020. The amount raised grew by +19% due mainly to an increase in the number of transactions (90 in 2021, up 29%). The market therefore maintained its dynamism, although growth diminished due to increased market maturity. Funding transactions on Nasdaq reached

new peaks this year, with the MedTech company Ortho Clinical Diagnostics raising nearly \$1.5 Bn in January and two other biotech companies also closing the year after raising over \$1 Bn: Ginkgo Bioworks in September and EQRx in December (these final-quarter transactions were achieved through "deSPACing").

SUMMARY OF IPOs THROUGHOUT THE WORLD BETWEEN 2011 AND 2021

MARKET	COUNTRY	NUMBER OF TRANSACTIONS	SUMS RAISED (€Bn)
Nasdaq US	 United States	607	60.9
Euronext including Euronext Paris	 Europe	114	3.2
	 France	66	1.3
Shenzen Stock Exchange (SZSE and Chinext)	 China	102	12.1
Nasdaq OMX Stockholm	 Sweden	86	1.8
Shanghai Stock Exchange (SSE and STAR)	 China	74	8.6
London Stock Exchange (AIM and LSE)	 United Kingdom	52	4.8
South Korea Stock Exchange (Kosdaq and KRX)	 South Korea	52	2.2
Hong Kong Stock Exchange (HKEK)	 China	48	12.1
Australia Stock Exchange (ASX)	 Australia	42	0.9
New York Stock Exchange (NYSE)	 United States	33	8.3

Sources: EY, Euronext, Cfnews, Dealroom

Continuing the trend from 2020, the number of SPACs (Special Purpose Acquisition Companies) rose significantly.

In December 2021, 661 SPACs were active throughout the world (i.e. stock-market-listed and seeking an operating target company) compared to 133 in October 2020 [Source: EY - Global IPO Trends]. Between 2019 and 2021, 224 SPACs completed their acquisitions, 25 of which related to the health sector (making it the fourth most targeted sector after new technologies, industry and consumer goods). Although the United States remains the most active market with over 500 active SPACs, Europe saw good levels of growth with 7 times more SPACs set up in 2021 than in 2020. Of the 42 European SPACs, 22 are listed on Euronext and 5 specifically target the Tech sector, with two focused

on healthcare (the target is often not defined in sufficient detail to clearly identify a forthcoming acquisition in the Tech sector).

In 2021, the number of business combinations with SPACs with sums exceeding \$1 Bn increased in the United States, including IPOs for EQRx (\$1.3 Bn/€1.15 Bn) and Ginkgo Bioworks (\$1.6 Bn/€1.35 Bn). Europe was not far behind with €0.9 billion raised in business combinations with SPACs split between two companies: the Swiss biotech firm Roivant Sciences (€527 M) with the vehicle Montes Archimedes Acquisition Corp. set up by Patient Square Capitaland, and the British digital health firm Babylon Health (€396 M) through the SPAC Alkuri Global Acquisition Corp.

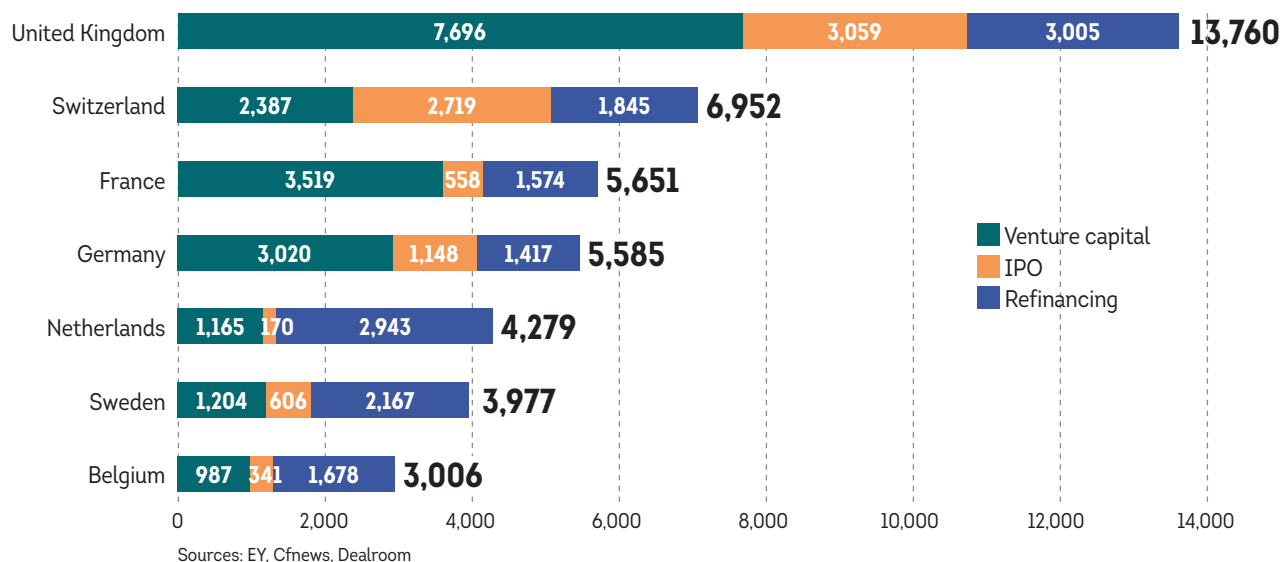
Europe: take-off

2021 confirmed the trend for dynamism already observed in 2020. While various indicators show record funds raised in all sectors, European HealthTech drove the positive figures observed at global level, particularly in terms of venture capital and IPOs, which attracted both US and Asian funds. In 2021, over €25.5 Bn of capital was raised in Europe including €21.9 Bn in the market's seven most dynamic European countries (the United Kingdom, Switzerland, France, Germany, the Netherlands, Sweden and Belgium). In particular, the average deal size almost doubled for all transaction types.

One consequence of the pandemic was to reveal the role played by these companies in terms of developing diagnostics, vaccines and pharmaceuticals, and the need to invest in innovation. European investment

funds seized on this, raising twice as much capital as in 2020 (over €9 Bn compared to €4.5 Bn [source: European Biotech Funders Cap Off Record Year for Investments (labiotech.eu)]), which was already a record year. For instance, the French fund Jeito Capital closed its first fund at over €530 M in September. One month later, Sofinnova Partners raised €472 M and in November, the Dutch fund LSP raised the highest sum in its history (€850 M) and was already investing in companies such as Egle Therapeutics (France) and Evommune (United States). **The size of the sums raised by funds proves that this is a structured and professionalised market, suggesting that 2022 will continue in the same vein.** Europe is still considered a region of attractive assets with often lower market capitalisations than comparable US firms.

TOTAL SUMS RAISED BETWEEN 2019 AND 2021 BY COUNTRY OF INCORPORATION AND BY TYPE (€M)



In terms of trends per country, the United Kingdom is the front runner and continues to increase its lead both in terms of sums raised and number of transactions completed. The Abingworth and GHO Capital funds single-handedly raised nearly €3 Bn for investment in HealthTech, and innovative companies across the Channel are attracting capital from various sources (Asia, Europe, US), completing substantial funding rounds both privately and on the financial markets.

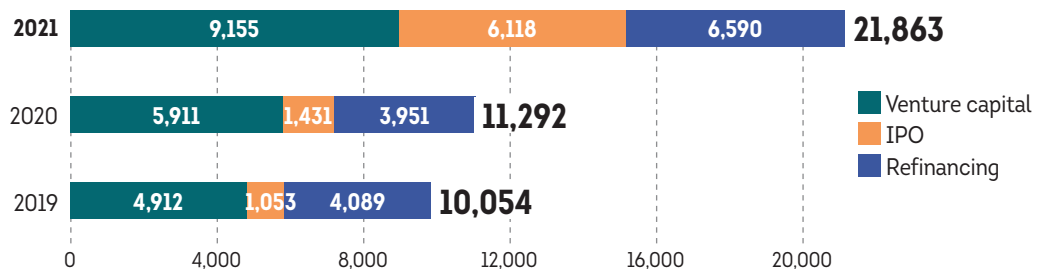
In the second pool, Switzerland, France and Germany have been playing musical chairs for the past several years. **France is back in third place at European level in terms of amounts raised between 2019 and 2021, but remains in second place for the number of transactions completed.** France had a very dynamic year in terms of IPOs, including Valneva's dual listing following its IPO on Nasdaq in May after an initial listing on Euronext, increasing its market capitalisation over the year due to positive

announcements regarding its vaccine and immediately completing a follow-on offering. Unlisted health companies' market capitalisations were significantly boosted, as revealed by the emergence of companies achieving Series A private funding rounds exceeding €40 M, including

Egle Therapeutics, Mnemo Therapeutics and Emergence Therapeutics. Emergence Therapeutics, a Franco-German immuno-oncology specialist incorporated in 2019 with support from Kurma Partners raised €87 M from investors based in English-speaking countries just before Christmas.

AMOUNTS RAISED IN 2021 BY COMPANIES FROM THE TOP 7 EUROPEAN COUNTRIES* (€M)

**United Kingdom, France, Germany, Switzerland, Belgium, Sweden, Netherlands*



Sources: EY, Cfnews, Dealroom

Switzerland, which ranks second in Europe in terms of amounts raised, maintained a very different profile to France, echoing the German and Dutch markets. Transactions were more concentrated and higher in value here, with three Swiss companies, PolyPeptide Group AG, Idorsia Ltd. and Roivant Sciences, featuring among the top ten fundraising transactions in 2021 completed by the top 7 European countries for all funding types. They alone raised €1.9 Bn, which is 45% of the total capital raised in 2021 by

Swiss companies (€4.2 Bn). The same trend was observed in the Netherlands, where the largest fundraising transaction in 2021, worth €1 Bn, was completed through refinancing by Argenx SE, a Euronext and Nasdaq-listed company, accounting for 52% of total funding in 2021 received by Dutch companies. The firm also received FDA approval in December to market its treatment Vyvgart for a rare autoimmune disease, generalised myasthenia gravis.

VENTURE CAPITAL ONWARDS AND UPWARDS FOR EUROPE

2019 was an outstanding year for venture capital in Europe, surpassed by 2020 despite the crisis, while 2021 smashed all records for venture capital funding raised.

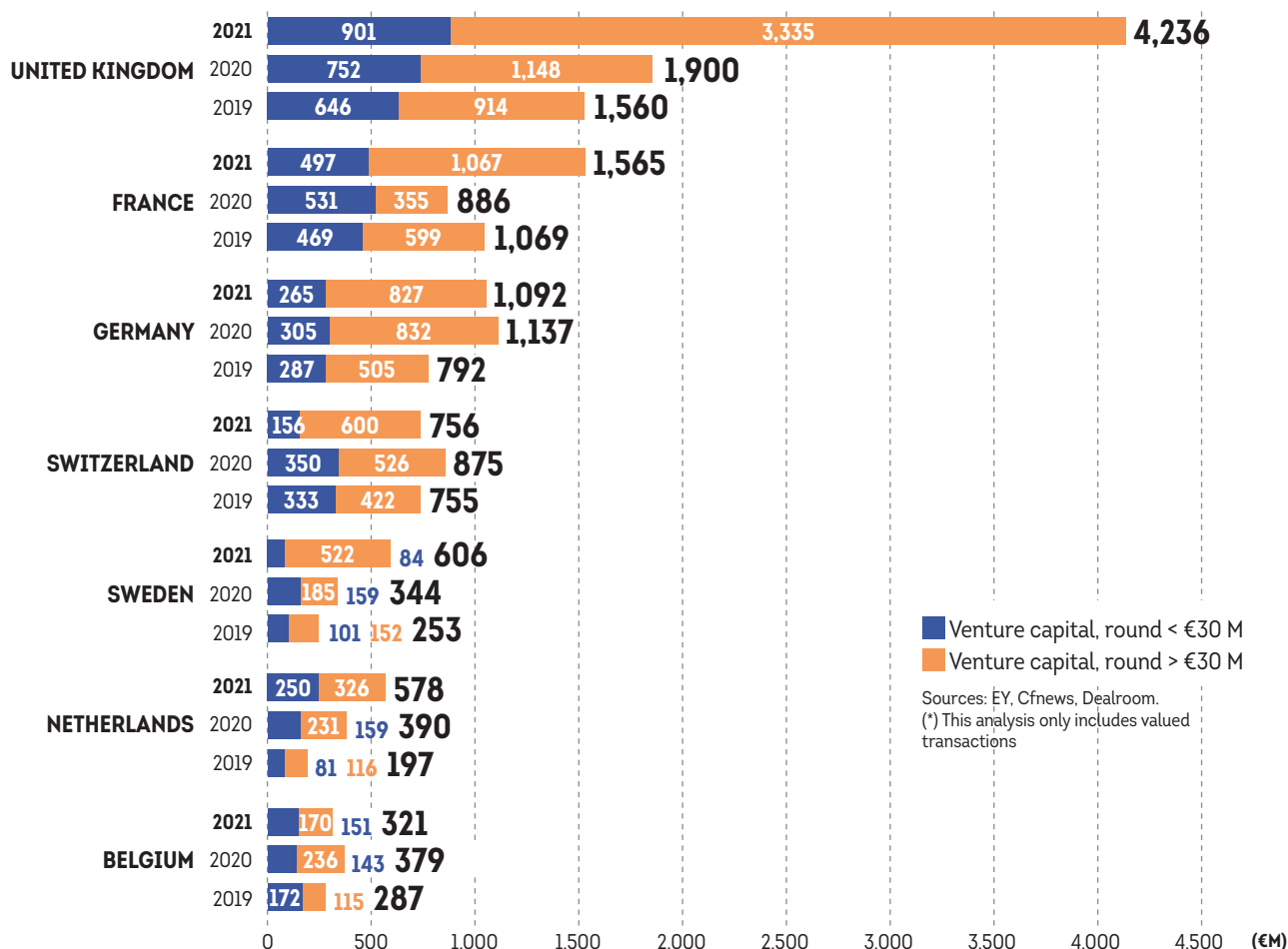
France rose to second place in Europe in terms of venture capital funding raised in 2021, enjoying a significant increase in investments exceeding €30 M (201% growth in this segment).

While 2021 continued to benefit companies working on COVID-19 related topics, MedTech companies also did well. The largest sums were raised by CMR Surgical (€504 M) which develops connected robots for surgery, Kry (formerly Livi) (€262 M) a competitor of Doctolib, and Oxford Nanopore Technologies (€233 M) which develops diagnostic testing and sequencing products.

This fundraising was largely prompted by a desire to develop markets in Europe or at international level.

2021 also saw growth in venture capital deal sizes for eHealth companies. France ranked top in this field with 38% of eHealth funding in 2021. Specialist European funds' interest in Series A and B funding continued to grow in 2021. In France, Jeito Capital invested in Quell Therapeutics' Series B round (€135 M) and also in Pulmocide (€75 M), two biotech companies developing treatments for pulmonary diseases. 2021 saw an upturn in later-stage series, key examples of which included the Series C round for British oncology company Artios Pharma, raising €130 M and French manufacturer DNA Script, raising €142 M.

VENTURE CAPITAL TRANSACTIONS* PER COUNTRY BETWEEN 2019 AND 2021 (€M)



COMPANIES FINANCED* AND AVERAGE DEAL SIZE PER COUNTRY IN 2021 (€M)

UNITED KINGDOM



FRANCE



GERMANY



SWITZERLAND



NETHERLANDS



SWEDEN



BELGIUM



Sources: EY, Cfnews, Dealroom. (*) This analysis only includes valued transactions











As in 2020, European companies' ability to complete major transactions increased. **In the United Kingdom, France, Sweden and the Netherlands, the average deal size increased by over 50%**, peaking at +86% for France and +119% for the United Kingdom. **Moreover, 17 companies raised over €100 M in 2021, which is twice as many as in 2020.** Among the recipients were ten British companies, once again confirming their dominance in this market, three French firms and two Swedish companies, highlighting strong French and Nordic activity within the field of venture capital.

Venture capital continued to be more accessible in France than in Switzerland, Germany or Belgium, with France remaining in second place in terms of the number of transactions, compensating for often smaller average deal sizes than those of its neighbours. **The average deal**

size in France increased, largely due to MedTech companies including the French manufacturer DNA Script which featured in the top 10. This company was financed by US funds including Coatue Management and Catalio Capital Management, with further investment from the French Bpifrance Large Venture Fund, the next level of funding after Bpifrance seed funds.

In contrast, only 25 transactions took place in Sweden, where Kry's fundraising transaction worth €262 M inflated the average deal size bringing it to €24 M compared to €14 M without this transaction (which was also the level in 2020). Since the number of transactions involving Swedish companies remained unchanged, it was fortunate that telemedicine pioneer Kry (formerly Livi) was able to perform so well.

TOP 10 VENTURE CAPITAL TRANSACTIONS IN 2021 COMPLETED BY THE TOP 7 EUROPEAN COUNTRIES

RANKING	COMPANY	COUNTRY	AMOUNT RAISED (€M)	YEAR	SECTOR	INVESTORS' COUNTRY OF ORIGIN
1	CMR Surgical	 United Kingdom	504	2021	MedTech	Japan, Hong Kong
2	Kry (formerly Livi)	 Sweden	262	2021	eHealth	United States
3	Oxford Nanopore Technologies	 United Kingdom	233	2021	MedTech	Singapore, USA, UK, Japan
4	Centessa Pharmaceuticals	 United Kingdom	206	2021	Biotech	United States
5	Quanta Dialysis Technologies	 United Kingdom	205	2021	MedTech	USA, Denmark
6	Exscientia	 United Kingdom	186	2021	Biotech	Japan, Denmark, UAE, Hong Kong
7	DNA SCRIPT	 France	142	2021	MedTech	USA
8	Vaccitech	 United Kingdom	139	2021	Biotech	UK, China, USA, Monaco
9	Quell Therapeutics	 United Kingdom	136	2021	Biotech	Europe, USA, UK
10	NewAmsterdam Pharma	 Netherlands	132	2021	Biotech	Europe, USA

Sources: EY, Cfnews

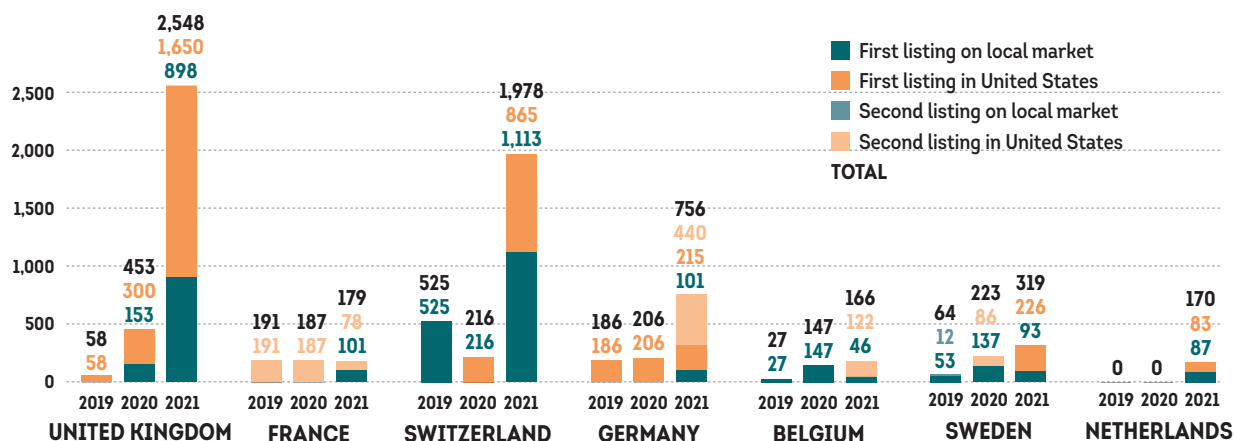
IPOS: EUROPE THRIVING BOTH IN TERMS OF NUMBER OF TRANSACTIONS AND AMOUNTS

In Europe, amounts raised through Initial Public Offerings (IPOs) **tripled and the number of transactions followed the same trend.** While the number of listings on the US market almost doubled between 2020 and 2021 (8 in 2020 compared to 18 in 2021 including 4 dual listings), the local markets' performance was particularly remarkable with 38 transactions (compared to 8 in 2020). The United Kingdom and Switzerland saw very substantial transactions in 2021, while the number of transactions exceeding €30 M has considerably increased in recent years for all countries.

However, significant contrasts in market behaviour persist among European countries. **The Swiss market was notable in terms of amounts raised, largely due to the year's most substantial IPO for PolyPeptide Group AG (€770 M),** a Swiss company developing and

manufacturing peptides which completed its IPO on the Swiss Stock Exchange. Sweden reported numerous yet smaller transactions on its domestic market, i.e. 14 IPOs with an average deal size of €4 M. The only Swedish company to complete an IPO on Nasdaq was the MedTech firm Olink Holding AB, raising €226 M. **On Euronext, while 2020 placed the emphasis firmly on revaluing the sector, 2021 brought a historic wave of new listings, with 17 worth €417 M breaking records set in 2017.** Euronext remained French companies' preferred market since 7 of the year's 9 listings took place on Euronext, and the other 2 were dual IPOs on Nasdaq of companies already listed on Euronext. Finally, following two consecutive years without IPOs for the Netherlands, two Dutch companies successfully achieved listing in 2021: Lava Therapeutics (€83 M) on Nasdaq and Onward Medical (€87 M) on Euronext.

IPOS IN THE TOP 7 EUROPEAN COUNTRIES* BETWEEN 2019 AND 2021 (€M)



Sources: EY, Euronext, Cfnews, Dealroom. *The top 7 includes the Netherlands, which reported no IPOs between 2018 and 2020

Although the number of IPOs on US markets only accounts for a third of the number of transactions, these markets remain dominant in terms of the size of sums raised, with a total of €4.2 Bn representing 59% of funds raised through IPOs. Swiss companies seized this opportunity, completing 5 of their 8 IPOs directly on US markets, including Roivant (€527 M), Pharvaris (€157 M) and VectivBio (€123 M). Similarly, a third of UK IPOs were completed on the US market, representing two-thirds of the amounts raised. However, the British MedTech company Oxford Nanopore Technologies, which completed its IPO on the London Stock Exchange in October raising €705 M, held its own against its

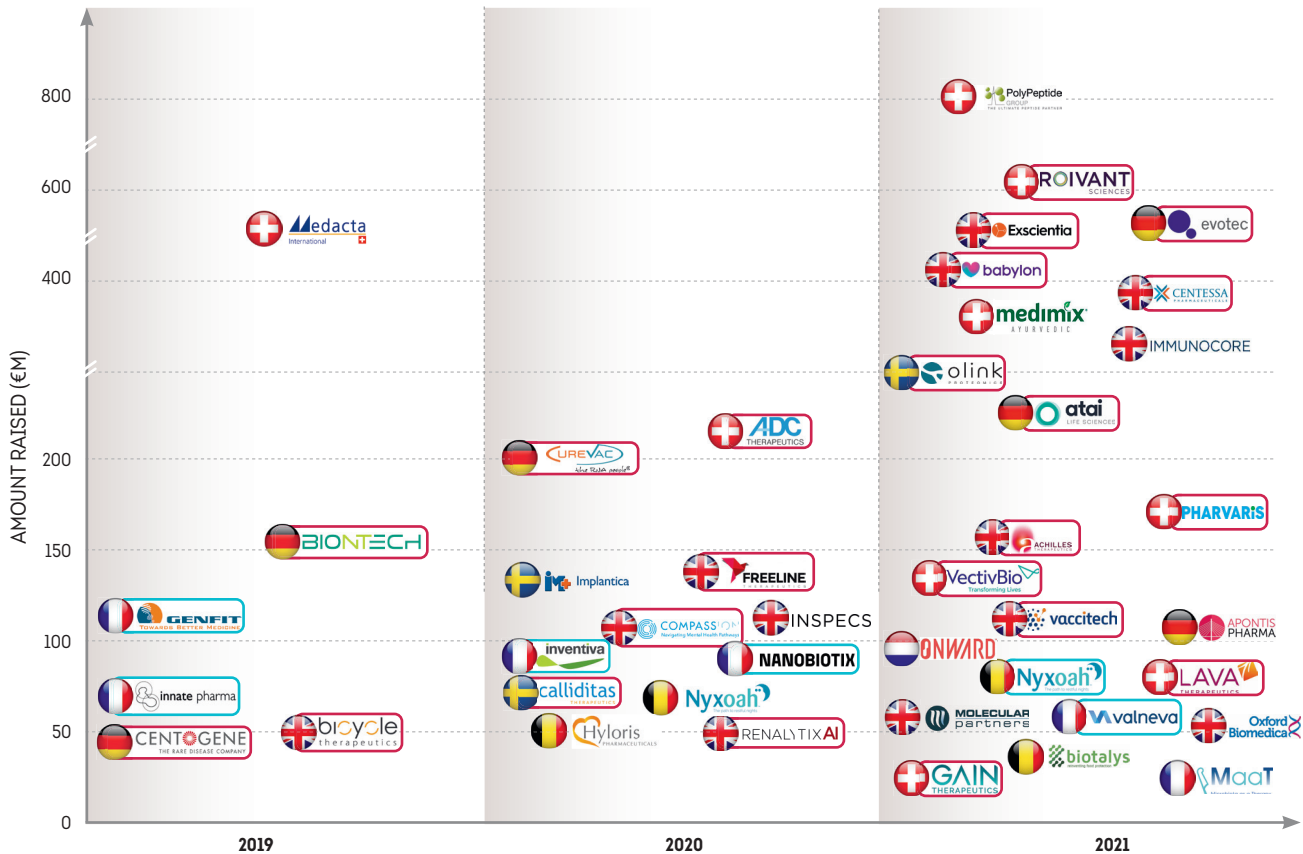
Nasdaq-listed compatriots in 2021, as this was the highest sum raised through an IPO by a British company this year. The system of business combinations with SPACs continued to emerge as an appealing alternative, enabling European companies to access US listing venues, with €0.9 Bn raised in 2021 by European companies through this process. Its appeal continues to lie mainly in the visibility gained with US funds and the potential for subsequent refinancing. However, for the least structured innovative companies, the financial and particularly operational cost of compliance with US market reporting requirements remains a significant barrier.

TOP 5 IPOs FOR EUROPEAN COMPANIES IN 2020 AND 2021

RANKING	COMPANY	COUNTRY	AMOUNT RAISED (€M)	YEAR	SECTOR	STOCK MARKET
1	PolyPeptide Group AG	Switzerland	770	2021	Biotech	SIX (Zurich)
2	Oxford Nanopore Technologies	United Kingdom	705	2021	MedTech	LSE (London)
3	Roivant Sciences	Switzerland	527	2021	Biotech	Nasdaq (New York)
4	Evotec SE	Germany	440	2021	Biotech	Nasdaq (New York)
5	Exscientia Holdings Limited (NasdaqGS:EXAI)	United Kingdom	440	2021	Biotech	Nasdaq (New York)

Sources: EY, Euronext, Cfnews, Dealroom

IPOs EXCEEDING €30 M COMPLETED BY EUROPEAN COMPANIES



UNITED KINGDOM BELGIUM GERMANY FRANCE SWITZERLAND SWEDEN

IPO on Nasdaq US and NYSE (direct listing)
 Dual listing: IPO on Nasdaq and post-listing on Euronext

Sources: EY, Euronext, Cfnews, Dealroom

The number of IPOs exceeding €30 M increased fivefold between 2019 and 2021, confirming the positive trend initiated in 2020 and the fact that companies

are completing their IPOs at a more mature stage of development. Over a third of IPOs were completed on the European markets.

REFINANCING IN EUROPE: EUROPEAN MARKETS ON THE UP

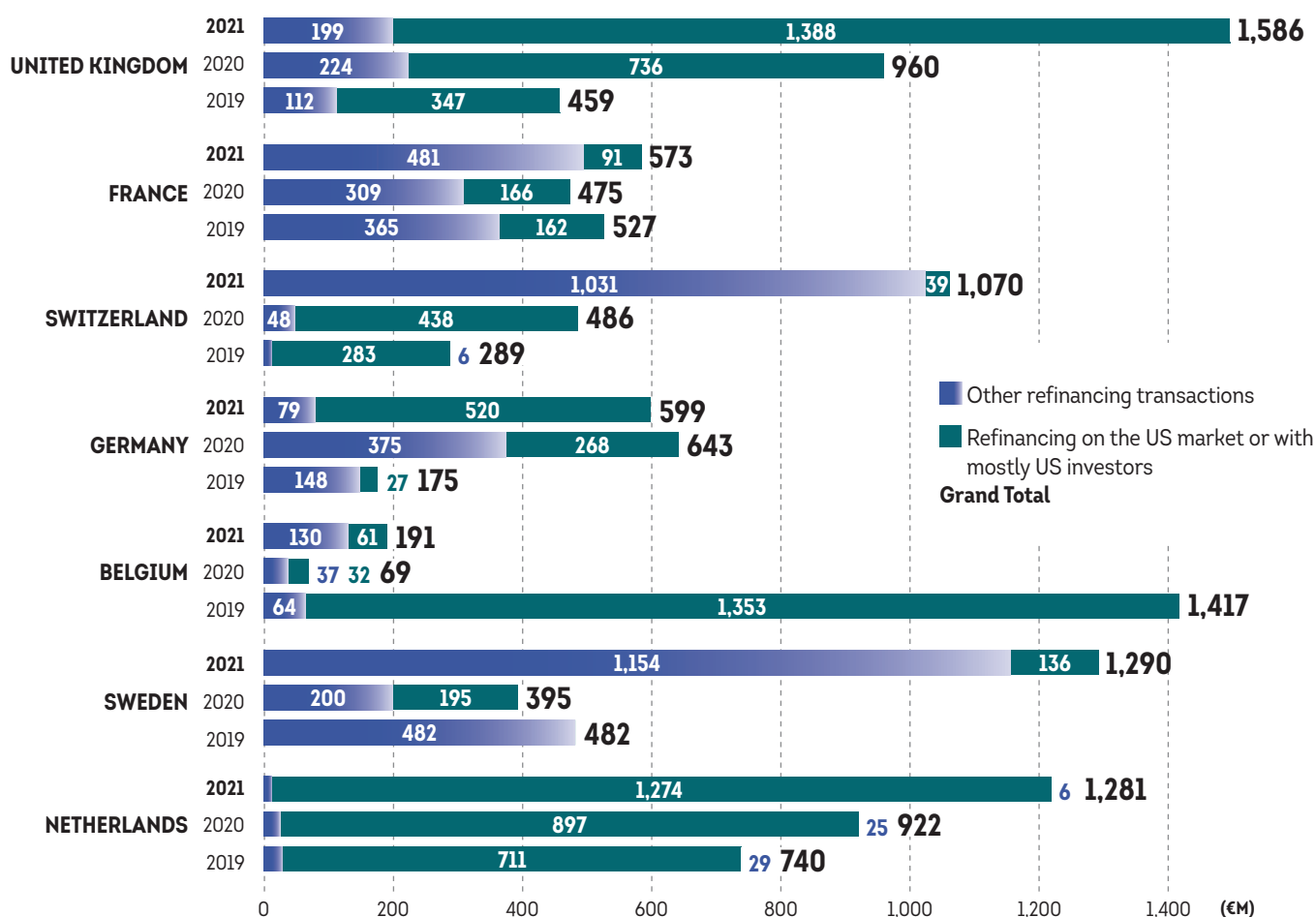
In 2021, fifteen companies raised over €100 M through refinancing totalling €4.6 Bn, which is 58% of the €7.9 Bn raised through refinancing transactions. Nine transactions by this "top 15" were completed on the US market or mainly with US investors.

After reaching a certain level of maturity, a significant number of European HealthTech companies opt for an additional listing in the United States in the form of an American Depository Receipt (ADR), mainly on Nasdaq US. They then naturally refinance across the Atlantic with US funds. Euronext also featured prominently in these pan-European refinancing transactions, with over €2 Bn raised in secondary transactions in 2021.

The dominant role played by US markets or US

investors in refinancing was mainly seen in instances where local markets were less dynamic, for example in Germany or the Netherlands. The top transaction was completed by Dutch biotech company ArgenX, which continued its meteoric rise by raising €952 M in February 2021 (representing 74% of refinancing sums for the Netherlands) having raised €729 M the previous year. It closed the year in style by announcing FDA approval for its generalised myasthenia gravis treatment in December 2021. The second largest transaction was completed by dual-listed German company CureVac, which raised over €425 M on the US markets (with a total of €599 M raised through refinancing).

REFINANCING TRANSACTIONS (€M) BETWEEN 2019 AND 2021

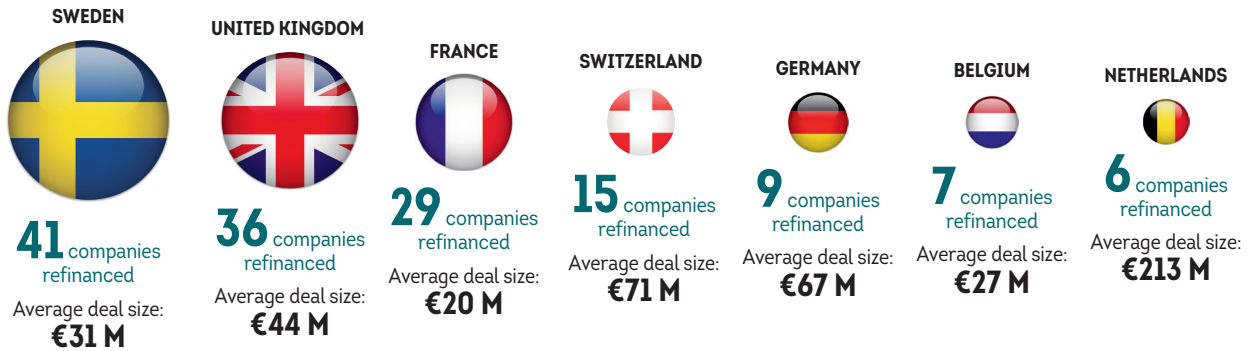


Sources: EY, Euronext, Cfnews, Dealroom

The top 3 countries for companies accessing refinancing through the markets include the Netherlands due to the ArgenX transaction, with the other two podium places filled by the more dynamic UK and Swedish markets. Sweden's dynamic local market allows listed Swedish companies to refinance, raising sums of over €200 M as in the case of Vitrolife AB (€349 M) or Surgical Sciences Sweden AB (€265 M). Due to its historic ties with the ecosystem of US investors, the United Kingdom continued to attract the majority of refinancing transactions with these investors.

In contrast, Switzerland has seen a reversal in this trend since 2019, with the refinancing of Tecan Group Ltd. (€330 M) on the Six Swiss Exchange in 2021 conducted mainly with European stakeholders and representing over half the capital raised by Swiss companies. Belgium has seen a return to significantly lower levels since Galapagos BV's fundraising transaction in 2019, which accounted for almost all of the capital raised (€1.4 Bn), and the country has focused primarily on European investors.

REFINANCED COMPANIES AND AVERAGE DEAL SIZE PER COUNTRY IN 2021



Sources: EY, Euronext, Cfnews, Dealroom

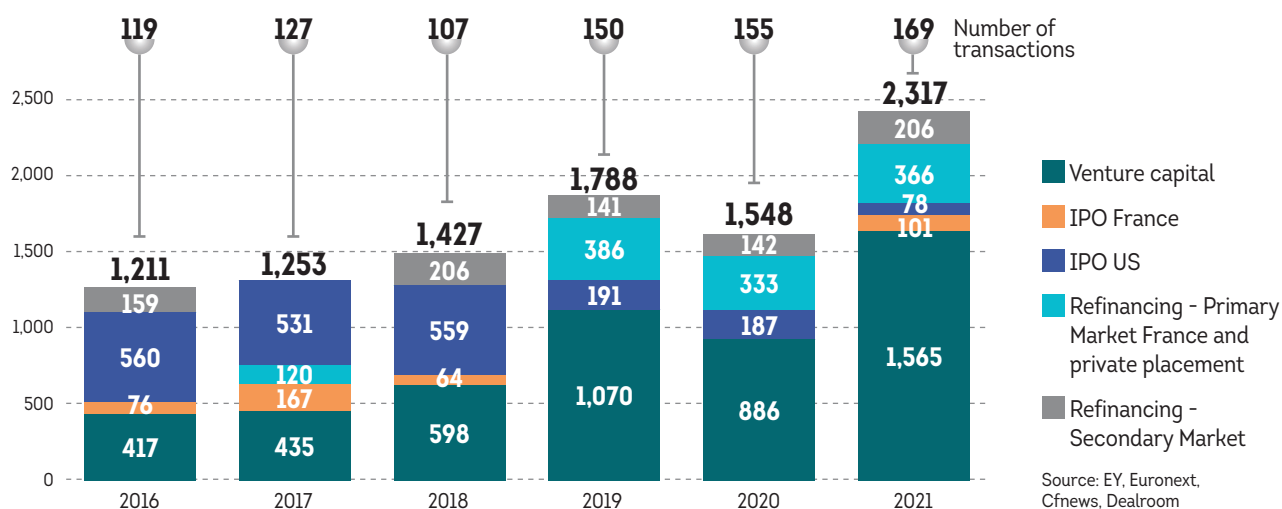
HEALTHTECH FUNDING IN FRANCE

In 2021, French HealthTech companies attracted record levels of investment (€2.3 Bn of funding) driven by the economic recovery and the gradual reopening of the country post-COVID. The persistence of the pandemic and, in particular, the emergence of new variants helped increase awareness of biotech companies' key role in our society.

Once again, venture capital funding proved highly successful due to the increased size of private investment funds. Private funding rounds exceeding €30 M have become increasingly common. €841 M was raised through the top 10 venture capital transactions in 2021, almost equalling the total raised in 2020 through

venture capital (€886 M through over 100 transactions). While the number of deals made has only increased 10% compared to 2020, the average deal size has increased by 45% to €13 M (compared to €9 M in 2020). According to Euronext, in just one year, the market capitalisation of French HealthTech companies increased from €12.9 Bn to €16.2 Bn (despite disappointing clinical results from several leading companies). With dual listing on Nasdaq since 11 May 2021, Valneva significantly raised hopes with its COVID-19 vaccine technology. The French biotech company achieved market capitalisation of €2.7 Bn in late December 2021.

FUNDING TRENDS FOR THE FRENCH HEALTHTECH SECTOR (€M)

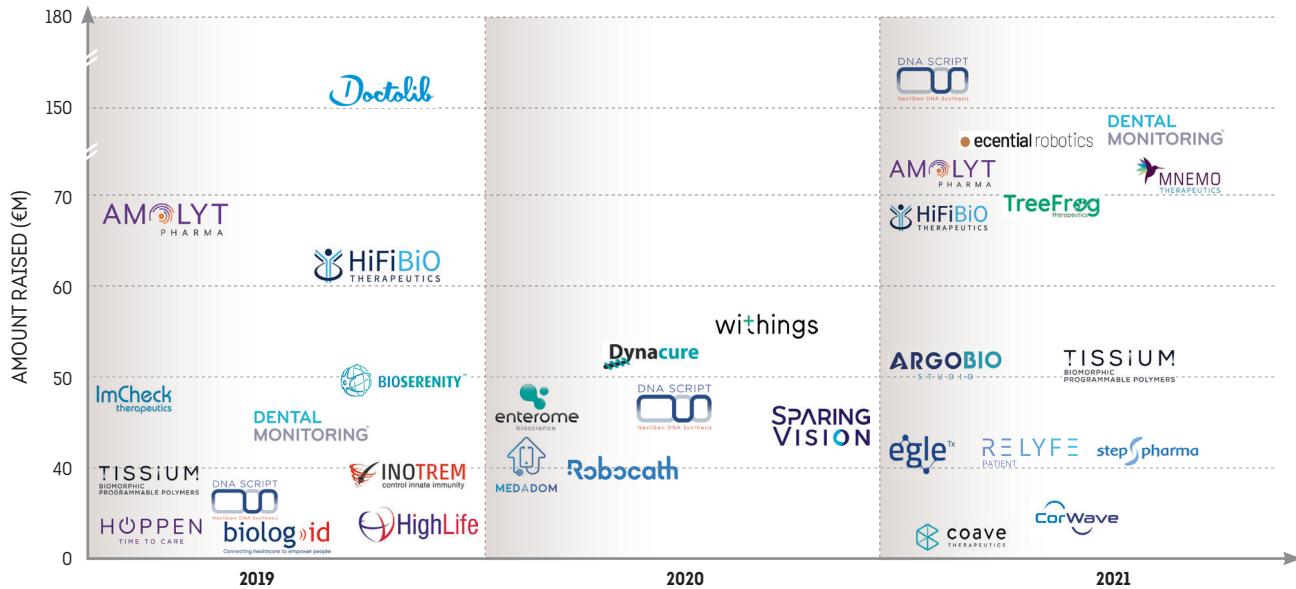


VENTURE CAPITAL IN FRANCE: INCREASING NUMBERS OF SUBSTANTIAL FUNDRAISING TRANSACTIONS

Following a lacklustre 2020, **venture capital regained its appeal for French HealthTech companies in 2021**. In 2021, the substantial sum of €1,565 M was raised compared to €886 M in 2020. This 76% rise was due to average deal sizes doubling those seen in previous years and record fundraising,

with 3 MedTech companies raising over €100 M: DNA Script, Dental Monitoring and eCentral Robotics. In 2020, the front runners struggled to raise over €50 M per entity, while in 2021, 7 French HealthTech companies exceeded this level.

VENTURE CAPITAL RAISED BY FRENCH COMPANIES EXCEEDING €30 M



Source: EY, Euronext, Cfnews, Dealroom

In particular, the French HealthTech sector was bolstered by funding of eHealth companies.

- In October 2021, Dental Monitoring raised €129 M in its Series B funding round. This latest venture capital fundraising transaction increased the dental and orthodontic platform's market capitalisation to over €1 Bn, making it a French health sector unicorn alongside Doctolib.
 - eCential Robotics: €100 M raised to fund a robotised medical device designed to assist with surgical procedures. One of the year's major transactions, achieved not through venture capital but through Sanofi's \$180 M equity investment in the Franco-American company Owkin, shows that the development of artificial intelligence also has its place in the French health landscape. The Owkin platform's patient data and learning models should boost the French pharmaceutical group's oncology portfolio.
- Companies developing medical devices continued to

appeal to investors. Three key venture capital fundraising transactions in 2021 attracted foreign investment: DNA Script, Tissium and Corwave all completed their third funding round in 2021 with support from US, Asian and European investors (the European Commission made its first direct investment in Corwave). French biotech companies also completed highly lucrative private funding rounds, with some achieving success from the first rounds. The remarkable Series A rounds achieved by two biotech companies, Egle Therapeutics and Mnemo Therapeutics, from the Institut Curie's incubator raised €40 M and €75 M respectively, a sign of investors' recognition. Capital was provided by French and also increasingly international investors: Bpifrance, LSP and Takeda Venture invested in Egle, while Sofinnova Partners and the New York firm Casdin Capital led the round completed by Mnemo.

TOP 3 VENTURE CAPITAL FUNDRAISING TRANSACTIONS IN 2020 AND 2021

	COMPANY	DATE	AMOUNT RAISED (€M)	SECTOR	ORIGIN OF MAIN INVESTORS
1	DNA Script	October 2021	142	MedTech	United States
2	Dental Monitoring	October 2021	129	eHealth	United Kingdom, France
3	eCential Robotics	January 2021	100	eHealth	France
1	Withings	July 2020	53	eHealth	France, Netherlands, Germany
2	Dynacure	April 2020	50	Biotechnology	United States, Netherlands
3	DNA Script	July 2020	45	Biotechnology	United States, France, Israel

Sources: EY, Euronext, Cfnews, Dealroom, VentureSource

A LOOK BACK AT FUNDING THROUGH THE MARKETS

In 2020, the only IPOs were dual listings on the US market. **2021 marked a major return of French health companies to the Paris market.**

Of the 9 IPOs completed by French companies in 2021, two were double listings, as in 2020, this time for biotech companies Valneva and Biophytis totalling €78 M, and there were no fewer than **7 IPOs on Euronext totalling €101 M raised on this market. This has been the best year in terms of the value and number of transactions since 2017.**

However, the sums raised through IPOs were still

lower than those raised through venture capital, and only Valneva was able to raise over €50 M by going to the US market.

In 2021, no fewer than 7 IPOs were completed by French HealthTech companies on the Euronext Paris market:

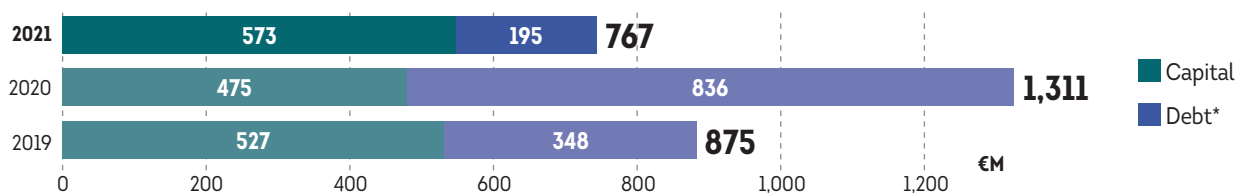
REFINANCING OF LISTED COMPANIES: UPTURN IN REFINANCING THROUGH THE MARKETS

French companies experienced a return to form in relation to refinancing on the markets and the market was significantly more dynamic, aided by lower stock market volatility in a climate where the COVID-19 pandemic appeared more under control. **Although refinancing levels fell short of 2018 (over €750 M), they were still higher than in 2020 (€573 M compared to €475 M) with substantial deal sizes.** Several transactions are worth highlighting this year, with 3 even exceeding €50 M. This year it was MedTech company Biosynex that set the tone by raising €15 M on Euronext Growth. However the highest value raised through refinancing was achieved

by Valneva in the winter of 2021 immediately after its IPO on Nasdaq and just before the announcement of the European Commission's purchasing agreement concerning its COVID-19 vaccine.

Another emerging trend was listed companies' significantly reduced recourse to debt, a sign that the health crisis that shook 2020 was reaching its end. In terms of loans taken out, the situation appeared to be returning to normal in 2021, with €195 M of funding through debt (including €35 M in state-guaranteed loans) compared to €836 M in 2020 (including €430 M in state-guaranteed loans).

FUNDING SOURCE OF FRENCH LISTED COMPANIES (€M)



(*) Debt: bond issues and loans granted in the financial year. Convertible loans are included in debts, and the conversion premium is recognised as capital. Sources: EY and listed companies' websites (press releases and financial reports)

TOP 3 REFINANCING TRANSACTIONS IN 2020 AND 2021

	COMPANY	DATE	AMOUNT RAISED (€M)	SECTOR	TRANSACTION DESCRIPTION
1	Valneva	November 2021	76	Biotech	Issues of ADS (Nasdaq) and ordinary shares (Euronext)
2	Abivax	July 2021	60	Biotech	Offering limited to specialist investors
3	Carmat	March 2021	56	MedTech	Ordinary share issue (Euronext)
1	DBV Technologies	February 2020	136	Biotech	Issues of ADS (Nasdaq) and ordinary shares (Euronext)
2	Lumibird	June 2020	44	MedTech	Euronext public offering
3	Sensorion	September 2020	30	Biotech	Private placement with European and US investors

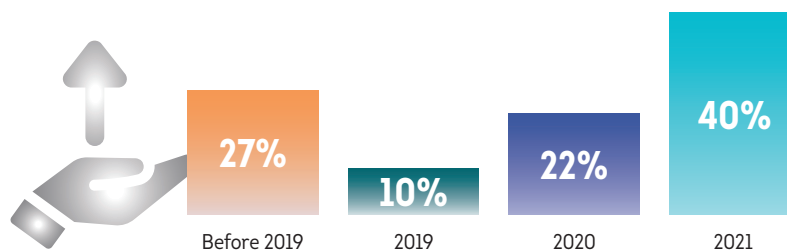
Sources: EY, Euronext, Cnews, Dealroom

KEY DATA ON FUNDING OF FRENCH HEALTHTECH COMPANIES

Significant and recurrent funding needs. In total, HealthTech companies have raised nearly €5.23 Bn since their incorporation with an average of €15 M raised per company (median value of €1.2 M) through an average of two funding rounds.

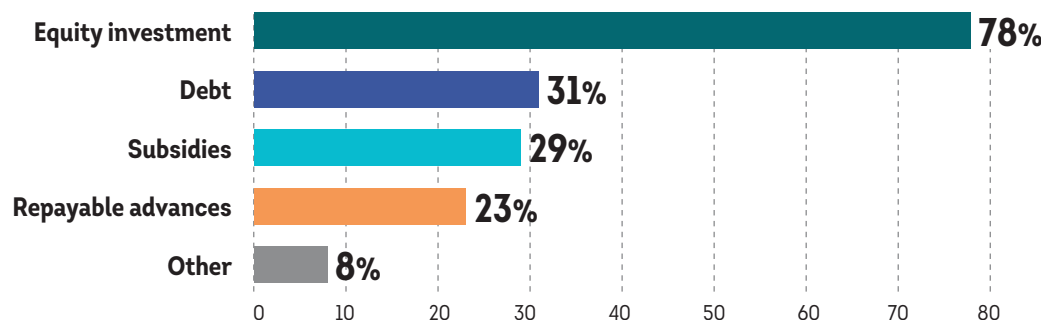
When did you last raise funds? (% of companies)

Due to the business and nature of HealthTech companies, they need recurrent funding to develop their products and meet their cash flow requirements. **Consequently, almost two-thirds of companies have raised capital over the past two years** and 40% in 2021.



Source: France Biotech, 386 companies, January 2022

What type(s) of funding did you access in your latest funding round? (% of companies)



Source: France Biotech, 262 companies, January 2022

Since HealthTech companies' development cycles are long, particularly for biotech companies (approximately 10 to 15 years), they require regular funding of various different types. Younger companies tend to rely on subsidies and revolving credit early in their development, with 29% and 23% of companies respectively opting for these types of funding. When products move to the clinical phase or companies enter their growth phases, the nature and value of funding changes, with companies turning mainly

to private venture capital funds for their Series A and B rounds, which traditionally involve equity investment. These equity investments also include capital increases for listed companies during their refinancing phases. In total, three-quarters of HealthTech companies use these types of funding. Due to the COVID-19 pandemic, the past two years have seen greater recourse to debt in the form of state-guaranteed loans, bank loans and bonds.



4.3

WORLD EUROPE FRANCE

HEALTHTECH FUNDING

4 QUESTIONS FOR...

Philippe Tibi, economist and professor of strategy and finance at École Polytechnique

"France is the European Union's top centre for growth venture capital: our funds manage over €12 billion in this asset class"



Philippe Tibi is currently leading an initiative on behalf of the French Ministry of the Economy and Finance aimed at funding future French technology leaders. He is the vice-chair of the French Pension Reserve Fund supervisory board and a Suez board member. He joined UBS in 1986 as Technology Director and held various posts in London and Paris before becoming its CEO for France between 2004 and 2012. He founded Pergamon Campus. Among other roles, he has served as Chairman of the French Financial Markets Association (AMAFI) (2007-14). Philippe teaches strategy and finance at École Polytechnique, Shanghai Jiao Tong University and AUEB Athens. <https://tinyurl.com/Rapport-Tibi>

What prompted the initiative?

The scheme was set up to address a market failing concerning finance for the final stages of the funding cycle for scale-ups. This had been severely impeding their growth. Companies whose growth phase was in full swing, with a product, market and clients all in place, were struggling to find late-stage funding to become European or global leaders in their sector. The key limiting factor was the availability of funding or lack thereof.

What have you put in place?

We have persuaded 21 long-term investors (insurers, pension funds and EDF) to invest up to €6 billion in two asset classes: late-stage/growth venture funds and global tech listed shares. They made this pledge to Bruno Lemaire, Minister of the Economy and Finance and Cédric O, Secretary of State for the Digital Transition and Electronic Communications in January 2020.

It has now been honoured, since these investors have collectively approved approximately 50 late-stage venture funds which have already raised over €12 billion and around 20 stock market funds which have also raised approximately €12 billion.

We have exceeded our target, which was to raise €20 billion over three years. The ministers have set us the target of €30 billion by the end of 2022 for this asset class.

Around 12 of these funds manage capital exceeding €500 million, with the largest managing €1.6 billion. Based on its current number of funds and managed assets, France

is now the European Union's top country for investment. HealthTech accounts for approximately 20% of funds.

What is the situation with regard to specialist HealthTech funds?

There are around ten specialist HealthTech funds with the arrival of newcomers such as Jeito I and Lauxera I and management companies that have offered new funds or successor funds such as Andera BioDiscovery 6, Kurma Growth Opportunities, LBO France Digital Health II, Seventure Health for Life Capital II, Sofinnova Crossover, Techlife Capital I and Truffle Capital Medeor.

"WE HAVE STRENGTHENED FUNDS THAT FINANCE AMBITIOUS STARTUPS THROUGH THE COMMITMENT OF LONG-TERM FRENCH INVESTORS"

However, there is room for improvement, since on a like-for-like basis in terms of track record, health funds raise less funds than their digital counterparts. To date, the biggest health fund to have closed its fundraising is Jeito at €540 M.

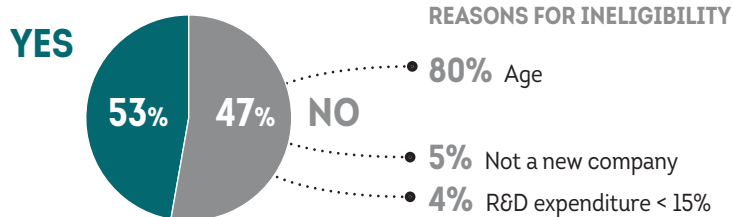
What are the next steps for expanding the HealthTech offering?

We must increase our efforts to boost the number of specialist HealthTech funds. The next steps will involve familiarising insurance funds with the HealthTech industry. We are actually in the process of setting up special training with France Biotech for end investors. ■

INNOVATIVE YOUNG COMPANY (JEI) STATUS AND RESEARCH TAX CREDIT: ESSENTIAL SCHEMES FOR HEALTHTECH COMPANIES

Innovative Young Company (JEI) status

ELIGIBILITY FOR JEI STATUS



Innovative Young Company (JEI) status is widely used by innovative SMEs in the health sector, with over half of companies awarded the status in 2021. The most important benefits of this status for HealthTech companies include **cost optimisation, recruitment of new staff, and increased credibility for companies' innovation strategies.**

Source: France Biotech, **394 companies**, January 2022



EXTENSION OF THE ELIGIBILITY PERIOD

JEI status is an important factor boosting France's appeal as it allows innovative health start-ups to optimise their costs. For the past several years, the 8-year eligibility period has been considered inconsistent with development cycles for HealthTech and particularly

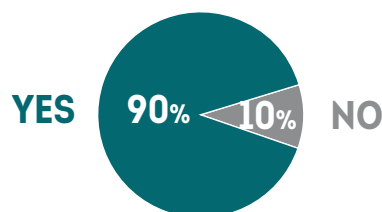
biotech and MedTech companies. Consequently, 71% of the surveyed companies proposed extending the status award period as their first recommendation and 24% suggested an increase in the cap for eligible expenses.

The 2022 Finance Act, which came

into force on 1 January 2022, has sent a strong and very positive signal to all young, innovative health companies. This new measure extends the eligibility period by 3 years, enabling companies aged under 11 years to be granted JEI status (compared to 8 years previously).

Research Tax Credit (CIR)

CIR SYSTEM USED?



Source: France Biotech, **392 companies**, January 2022

Almost all French HealthTech companies (90%) use the Research Tax Credit scheme. Companies view Research Tax Credit as an important tool encouraging public/private partnerships. Companies in the panel report that an average of **22% of their R&D expenditure incurred through academic partnerships is eligible for Research Tax Credit.** As of 1 January 2022, R&D expenditure outsourced to public organisations will no longer be doubled under the Research Tax Credit scheme. This benefit previously enabled many public laboratories to collaborate with HealthTech companies. The introduction of **Research**

FOCUS ON RESEARCH TAX CREDIT FOR 2020

89% of companies stated that they experienced no difficulties accessing their Research Tax Credit for 2020.

However, over half (57%) of companies experiencing difficulties mentioned speed of reimbursement and greater clarity regarding payment dates.

Collaboration Tax Credit (CiCo) was adopted in the 2022 Finance Bill. This allows companies using public research organisations to access tax credit on the basis of invoices related to their partnership agreements. **CiCo is one of a raft of new measures aimed at supporting research programs in France,** including the fourth Investing in the Future programme and the France 2030 plan. With a tax credit rate of 50% for SMEs and 40% for other companies (capped at €2 M and non-combinable with CIR), this scheme could maintain the special relationship between public laboratories and HealthTech companies.

STOCK MARKET FUNDING OF BIOTECH COMPANIES

Why opt for stock market funding?

Biotech firms may be more inclined than any other innovative companies to consider the merits of an IPO to fund their research programmes and increase their capacity to forge industrial and commercial partnerships.

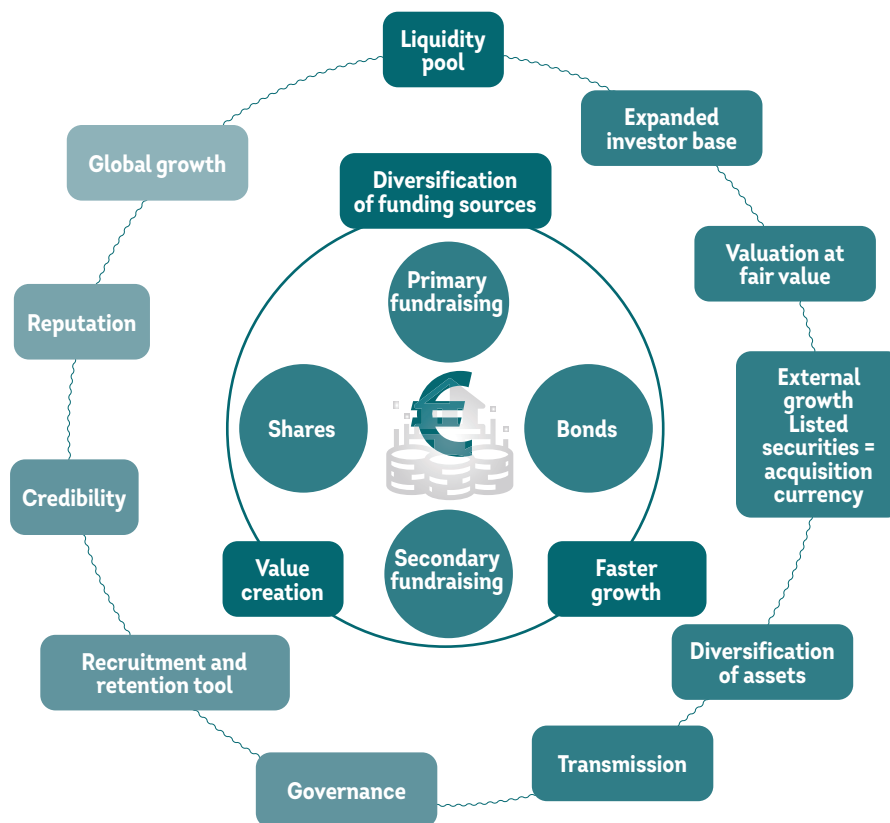
In a sector that involves long cycles, it is often necessary to replenish and expand the shareholder base to access sufficient funding and ensure long-term continuity of operations.

In addition to initial funding acquired during the IPO, listing provides access to a diverse pool of international investors and long-term funding sources that are regularly available and enable requirements for the company's various growth phases to be met.

IPOs significantly speed up biotech companies' growth, providing more than just access to new financial resources. They also boost visibility and credibility in the eyes of stakeholders including clients, financial partners and major pharmaceutical companies. Moreover, listing helps attract and retain talent through value sharing mechanisms and enhanced reputation. In order to meet listing requirements, companies must also improve their structure and implement best governance and transparency practices.

Finally, **by offering continuous access to investors, listing enables companies to gradually fund their research and market access for their entire scientific pipeline.**

REASONS TO COMPLETE AN IPO



Source: Euronext



At what stage should an IPO be considered?

The merits of an IPO should be considered once a company achieves a certain degree of maturity, often after several private fundraising rounds. Biotech companies use subsidies and public funds supplemented by funding from venture capital funds to complete their preclinical and Phase I stages. Most complete an IPO in Phase II or even III. These phases are particularly capital-

intensive with the launch of expensive large-scale, often transnational clinical trials.

Beyond the clinical trial phase, other key factors for considering an IPO include the company's capital requirements and market capitalisation. In addition to pipeline diversity, various factors should be examined in detail, including the therapeutic field, target population and market size for the most advanced indication.

STAGE OF RESEARCH AT THE TIME OF IPO

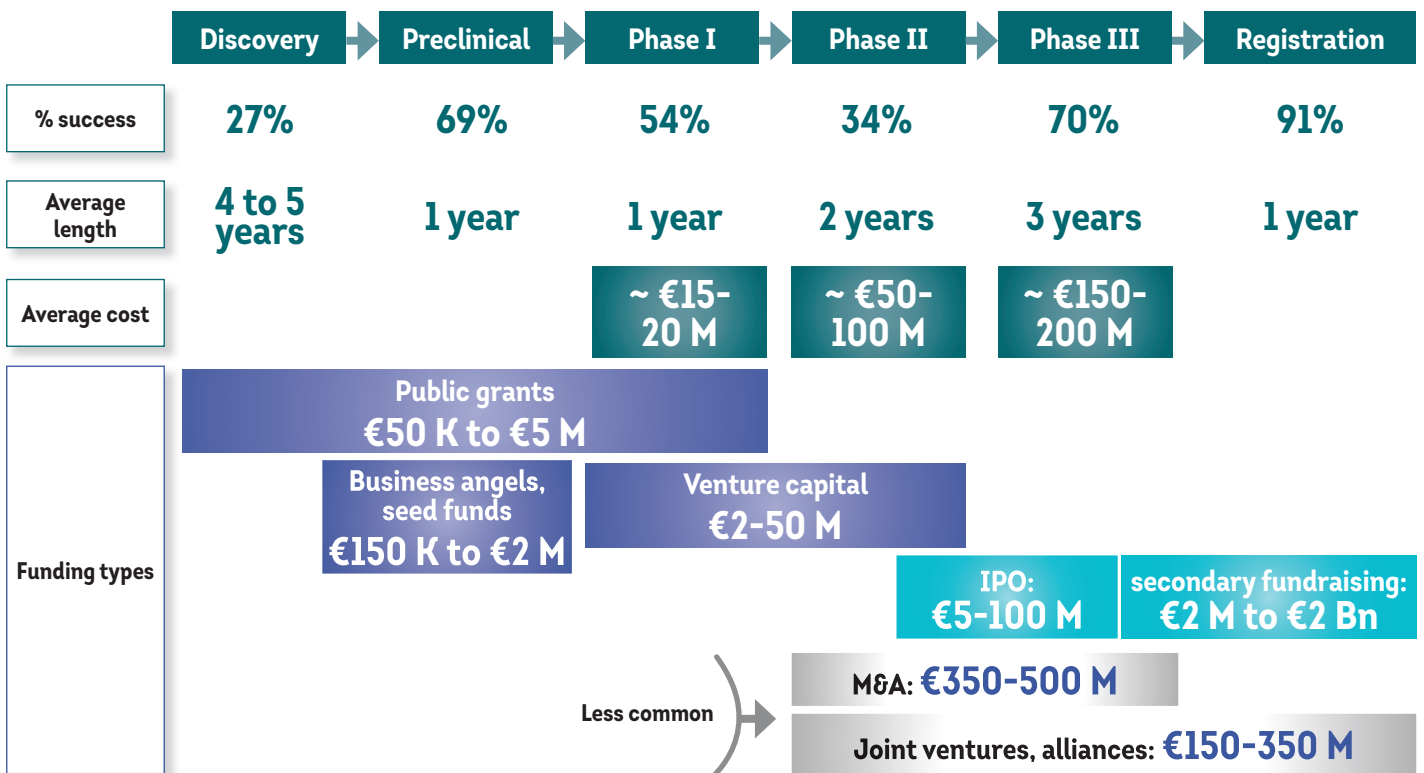


In terms of the funding stage, most IPOs are currently used to attract private investors during a Series B round or later to replace a Series C round. As the French and European venture capital funding chain develops, biotech companies are reaching more advanced stages of maturity when they

come to complete their IPO. Finally, stock-market investors overwhelmingly favour proprietary platforms enabling them to develop a diversified portfolio rather than primarily funding a single molecule.

Source: Euronext

HEALTHTECH COMPANIES' FUNDING PATHWAY



Source: Euronext, France Biotech, European Investment Bank

KEY FACTORS FOR A SUCCESSFUL IPO

Although MedTech and biotech companies are well represented among the ranks of French and European listed firms, best practices must still be implemented to ensure a successful IPO due to intense competition for capital. The main aims of these best practices are to ensure that companies are transparently managed and present investors with an optimal risk profile.

1. Quality and potential for historic shareholders to reinvest are key factors for ensuring a successful process. Specialist health venture capital funds and funds able to submit subscription undertakings* prior to the transaction can boost the attractiveness of the deal for other classes of investors.

These scientific opinion leaders are ideally placed to persuade generalist stock-market investors or private shareholders to subscribe to the transaction.

2. The quality of the board of directors and scientific board will also be subject to particularly closely scrutiny

by investors.

3. The team's scientific and business experience is crucial to convincing investors. Since the development of new drug candidates is a complex process, a good track record and solid academic background are essential for establishing the team's credibility. This requires:

- a recognised scientific board composed of first-class global specialists and experts in the target therapeutic fields (experience, scientific publications, etc.);
- a high-quality and mature scientific pipeline. Although the main product is often in Phase II when a company completes its IPO, the number of other products in the pipeline and the level of scientific progress made with them are also key indicators for investors of an optimal risk profile.

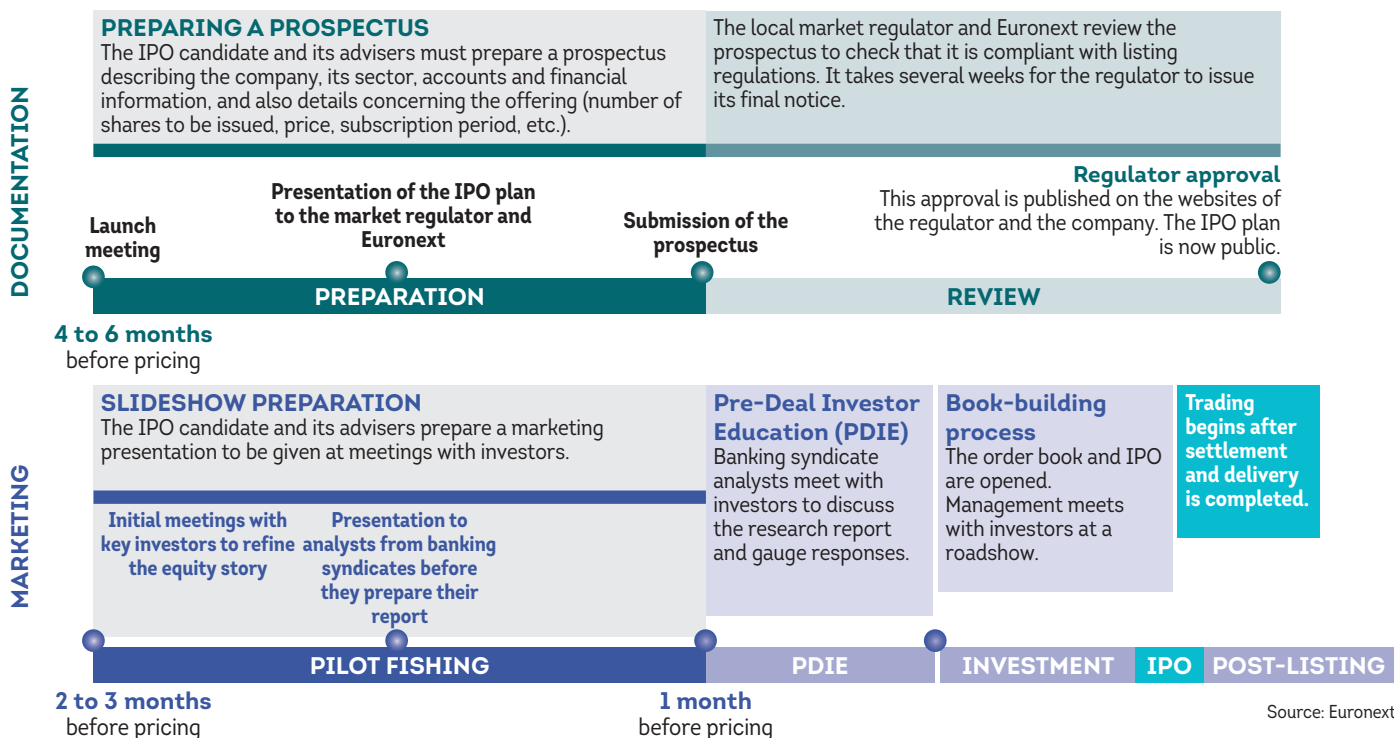
*Subscription undertakings reflect a will to guarantee coverage of some of the capital raising requirements for an IPO. The anticipated percentage can vary between 20% and 50% depending on a number of criteria relating both to the company and the market.

How to prepare an IPO

Completing an IPO on the financial markets is a closely supervised process for which quality internal and external teams must be formed.

They should be involved in both preparatory phases for the IPO – the documentation and marketing phases.

PREPARING AN IPO

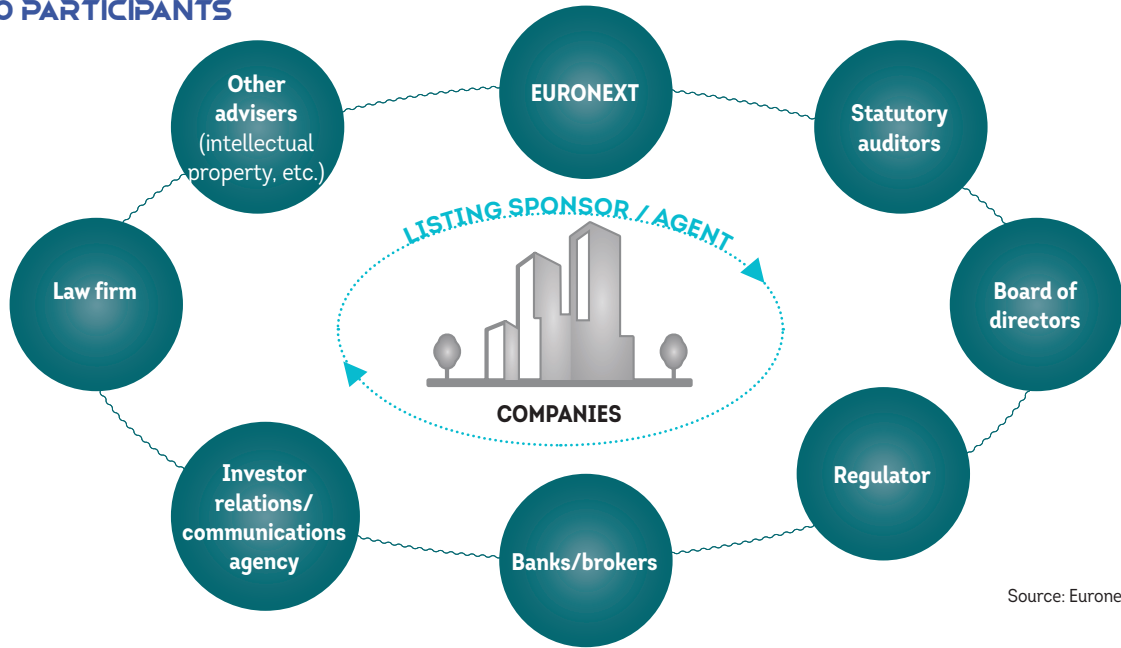




To ensure this work is carried out effectively, the company should draw on external resources including bankers specialising in IPOs and advisers to help it prepare the documentation (to be submitted to Euronext and/or the AMF) and the equity story (used for attracting investors).

The banking syndicate manages the overall schedule and structure of the transaction, and also provides an initial valuation. Other advisers should also be included in the company's working group (communications agency, legal advisers, statutory auditors, etc.).

IPO PARTICIPANTS



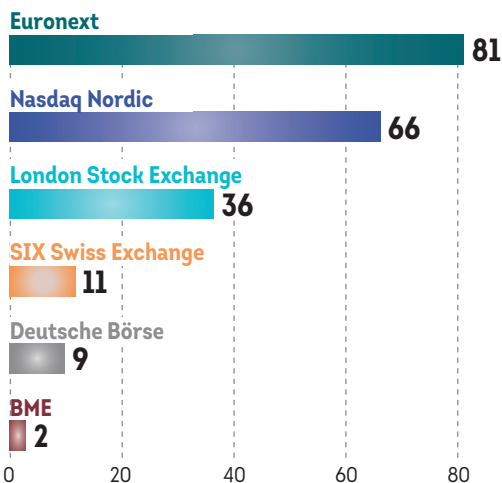
Source: Euronext

→ *How to choose a venue for your IPO*

Almost all French biotech/MedTech companies are listed in Paris or Europe. This is a logical choice due to the proximity of the investor

pool, partners and clients, employees, etc. **Euronext is Europe's top venue for life science listings and the world's second-ranking market.**

NUMBER OF BIOTECH COMPANIES LISTED ON EUROPEAN MARKETS











Source: Euronext

Of all the major global venues, Euronext offers access to the broadest and most diverse pool of investors. While Europe and the world's top area for savings, the Eurozone, are well represented, global investors including those from English-speaking countries are also very active and account for a significant portion of sums invested in Europe and particularly in Paris.

By completing an IPO in Europe, biotech companies can gain access both to a local savings pool and global investors, particularly those from English-speaking countries. In late 2021, the pool of life sciences investors on Euronext included 746 institutional investors from 36 countries including the United States (37%) and the United Kingdom (17%).

TOP 8 ACTIVE INSTITUTIONAL INVESTORS IN HEALTHTECH COMPANIES LISTED ON A EURONEXT MARKET

RANKING	INSTITUTION	VALUE (€M)	INVESTOR TYPE	COUNTRY
1	The Vanguard Group, Inc.	745	Insurance & Pensions	 United States
2	Norges Bank Investment Management	617	Sovereign	 Norway
3	Baillie Gifford & Co.	406	Asset Management	 United Kingdom
4	BlackRock Fund Advisors	405	Asset Management	 United States
5	Wellington Management Co. LLP	399	Insurance & Pensions	 United States
6	Federated Global Investment Management	387	Asset Management	 United States
7	RTW Investments LP	342	Hedge Fund	 United States
8	Bellevue Asset Management AG	244	Asset Management	 Switzerland

Source: Euronext

In recent years, European HealthTech companies have proved that they are capable of raising significant sums in Europe to support their development. They have achieved this by accessing a wide-ranging and diversified pool of investors both in Europe and across the Atlantic.

Moreover, there have been significant increases in European funds' resources. In 2021, they raised over €10 Bn with a total of €88 Bn under management. Those specialising in biotech raised €745 M with a total of €11 Bn under management.

REASONS AND PROCESS FOR DUAL LISTING

Some biotech companies opt for dual listing if the primary target market for their products is the United States and their pipeline is sufficiently mature. Such companies include Nanobiotix, Inventiva and Erytech Pharma which completed IPOs on Euronext Paris then in the United States. Sums raised prior to dual listing are increasing in size.

By completing initial IPOs in Europe, these companies are opting to be listed close to their geographical roots, gaining experience of the IPO process and laying the foundations for their stock market activities through secondary fundraising. They subsequently consider dual listing across the Atlantic to secure global visibility with a strong presence in

Europe and the United States. In terms of shareholding, the prerequisite for dual listing is to create a pool of US investors with equity in the company. This consolidation is one of the key objectives of capital increases performed in Europe following an IPO on Euronext.

Other variables including time-to-market, admission fees and eligibility requirements should also guide this decision. The scope of regulatory requirements concerning financial reporting should also be considered. These may vary by market type (regulated market or multilateral trading facility) and also by listing venue due to local regulatory requirements. The cost of listing must also be taken into account.

Gilles Avenard, Chief Executive Officer and Co-Founder
of Acticor Biotech

"Acticor Biotech raised €15.5 M following its IPO on Euronext Growth on 1 November 2021"



acticor-biotech.com

Gilles Avenard is a current board member, CEO and co-founder of Acticor Biotech, as well as an adviser to several biotech companies. Gilles is an M.D. and co-founded BioAlliance Pharma SA - ONXEO (NYSE EURONEXT), serving as COO until 2010.

He was involved in the development of several innovative drugs up to their official registration for Europe and North America. Previously, he worked as a project director for Hoechst Marion Roussel (Sanofi) and was also a medical director for Bio-Transfusion (LFB).

ACTICOR BIOTECH

Incorporated in 2013, **Acticor Biotech** is a clinical-stage biotech company specialising in the development of drugs for treating cardiovascular emergencies. In particular, it is currently developing glenzocimab, a first-in-class stroke treatment, for which two Phase II clinical trials have already been completed.

Why did you opt for an IPO?

Having completed a highly successful Series C funding round between 2018 and 2021, we needed resources to fund Phase II/III trials for our stroke treatment. An IPO seemed a sensible option. Moreover, we believed the timing was right and we had sufficient maturity to present our plan to stock market investors. No innovative treatments for the acute phase of strokes have emerged in the last 20 years, largely due to the risk of brain haemorrhage. The medical stakes are therefore extremely high. Having demonstrated the safety of our drug, a fundamental stage in our development, we had everything we needed to present the plan to non-specialist investors.

How did you find the IPO process?

It's a marathon – you have to go the distance and tick all the boxes. Some members of my team and I already had experience of IPOs. We decided to initiate the process in the first half of 2021 and were listed by 1 November 2021, which is very quick. We were able to test market appetite for our plan. For instance, we took part in the Euronext IPO Days where we received positive feedback from banks.

Due to a lack of major successes in our field over the past 20 years, specialist investors and listed comparables have become increasingly scarce on the market. We also had to do a lot of educational work with "generalist" investors, particularly since Acticor Biotech is a single-product company. Private investors also responded very positively to us, contributing €2 M to the transaction.

How did you choose a listing venue and market?

We were torn between Paris and Brussels, as one of our cornerstone investors, Newton Biocapital, has a strong presence in Belgium. However, given our roots and funding history, Paris seemed a logical choice of venue. At that stage, we hadn't considered going to the United States, although our company was already recognised in Europe. In terms of the listing market, although we prepared for a potential IPO on the highly regulated Euronext market, we eventually opted for Euronext Growth, which is open to innovation-focused mutual funds (FCPIs) and imposes less stringent requirements.

"SUPPORT FROM HISTORIC AND SPECIALIST INVESTORS IS CRUCIAL FOR CREATING A RIPPLE EFFECT"

What advice would you give to entrepreneurs who are considering an IPO?

Firstly, you need a certain level of maturity as listed companies have a responsibility to their investors. You need a credible message and business model for non-specialist investors. Support from historic and specialist investors is crucial for creating a ripple effect.

Once the company is listed, a news flow is required within 6 to 12 months of the IPO to bolster the transaction. And of course, the company must be structured to meet transparency requirements and financial reporting obligations. ■

An aerial photograph of three rowers on a rowing machine. The rowers are positioned vertically in the frame, from top to bottom. They are all wearing dark athletic gear and are captured in the middle of a rowing stroke, with their arms extended forward holding the blue oarlocks. The machine's structure, including the white frame and the oarlocks, is visible. The background is dark, making the white and blue elements of the machine stand out.

**STEERING COMMITTEE
PARTNERS
CONTRIBUTORS
CORPORATE SURVEY
PARTICIPANTS**

5

STEERING COMMITTEE



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France Biotech



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The authors would also like to thank **Louis Faure-Geors**, an intern at France Biotech, for his valuable contribution to the report.

FRANCE BIOTECH IN ACTION

France Biotech is actively working with the public authorities to promote the development of the innovative HealthTech sector, with policy proposals relating notably to taxation and financing of startups, partnerships between academic research and industry, market access, and easing of regulatory requirements and their burden on innovative health companies.

France Biotech spearheads proposals emanating from its **7 committees and 4 working groups** that serve as a think tank for innovative ideas.

- Biotherapies Committee (Biomanufacturing and Advanced Therapeutic Medicinal Products (ATMPs))
- Business Development Committee
- Legal Committee
- Corporate Finance Committee
- eHealth Committee
- MedTech & Diagnostics Committee
- Human Resources Committee
- Clinical Trials Working Group
- Market Access Working Group
- Patient, Carer, Family, Healthcare Professional Working Group
- Technology Transfer Working Group

France Biotech is both a **national observatory** for monitoring the innovative health technology sector in France and a **platform for sharing best practices** among all ecosystem stakeholders.

- Publication of surveys, white papers and bulletins (Health Innovation Plan, Health Technology Transfer Observatory, survey on pay in the sector, etc.)
- Organisation of workshops and conferences
- Organisation of major annual events: HealthTech Awards, Panorama France HealthTech
- Production of video content (webinars, France Biotech – Le Talk, Les Pépites HealthTech, etc.)
- Contribution to numerous French and international events related to health innovation

France Biotech's aim is to **put the spotlight on the HealthTech companies that are embracing innovation** through its role in a number of private and quasi-public organisations, including:

- The European associations EuropaBio and EUCOPE
- The International Council of Biotechnology Associations (ICBA)
- The French Pharmaceutical Trade Association (LEEM)
- The Strategic Committee for Health Industries (CSIS)
- The Strategic Industry Committee (CSF)
- The Health Industry Alliance for Research And Innovation (ARIIS)
- The health Competitiveness Clusters network
- The French Care initiative (French Tech)

PANORAMA FRANCE HEALTHTECH

Every year since 2002, France Biotech has published Panorama France HealthTech (formerly Panorama of the French Life Sciences Industry®), a unique French analytical review of developments in the innovative HealthTech sector over the previous year both nationwide and globally. The findings of the France Biotech review provide an insight into the situation of companies and serve to inform policy proposals for improvements to give the industry its rightful recognition.

PARTNERS



France Biotech was founded in 1997 as an independent association, uniting the country's leading innovative health companies and their expert partners. As a leader in health innovation working in close cooperation with public authorities in France and across Europe, France Biotech is ideally positioned to address the challenges facing the HealthTech sector, notably corporate financing, taxation on innovation and regulatory and market access-related issues. Its committees and working groups strive to identify viable solutions to create the necessary conditions for a competitive and attractive industry. Its mission is to support HealthTech startups and SMEs in their quest for international expansion and give them the capability to rapidly design and develop new innovations and get them to the point of care. Since September 2019, France Biotech has been chaired by Theranexus CEO Franck Mouthon. The association currently has 430 members.

www.france-biotech.fr



Bpifrance equity investments are made by Bpifrance Investissement. Bpifrance funds companies at each stage of their development through loans, guarantees and equity investments. Bpifrance supports them with their innovative projects at global level. Bpifrance insures their export business through a wide range of products. It also offers companies advice, training, networking and an accelerator programme for startups, SMEs and mid-caps. Bpifrance and its 50 regional offices provide entrepreneurs with an effective, local one-stop shop to help them face their challenges.



Euronext is the leading pan-European market infrastructure operator, connecting European economies to global capital markets, to accelerate innovation and sustainable growth. It operates in Belgium, France, Ireland, Italy, Norway, the Netherlands and Portugal. With nearly 2,000 issuers and total market capitalisation of just under €6,900 billion represented at the end of December 2021, it offers an unrivalled franchise of first-class indexes and a strong wide-ranging national and international client base. Euronext operates regulated and transparent spot and derivatives markets and is the world's largest bond and fund listing venue. In addition to its main regulated market, Euronext operates growth markets, simplifying access to listing for small- and mid-caps. Euronext is Europe's biggest marketplace for life sciences.



EY's corporate purpose is to help build a fairer world by creating long-term value for our clients, our employees and our communities, and by instilling greater trust and confidence in capital markets. EY's teams are expert in data processing and new technologies, operating in over 150 countries and striving to create conditions to foster trust in the economy and address the challenges associated with growing, transforming and managing our clients' business. With expertise in auditing, consulting, law, strategy, tax and transactions, the EY teams are well-equipped to navigate the complexities of today's world, ask the right questions and provide relevant answers. You can find more information about our organisation at www.ey.com

CONTRIBUTORS

France Biotech would like to thank the following organisations that contributed to the Panorama France HealthTech 2021 report.



HEALTH COMPETITIVENESS CLUSTERS



Atlanpole Biotherapies is the health competitiveness cluster for western France accredited by the French Ministry of Industry. Since its inception in 2005, it has served as a framework for an innovative interregional sector covering the three regions Centre-Val de Loire, Pays de la Loire and Brittany.

Its aim is to develop the medicine of the future, by harnessing skills from laboratories and companies throughout the biopharmaceuticals value chain, from the discovery of therapeutic targets to clinical trials. The work of Atlanpole Biotherapies is based around three broad strategic fields – immunotherapy, radiopharmaceuticals and regenerative medicine, and it has also branched out to three new areas, namely digital technologies for innovative therapies, clinical nutrition/microbiota, and animal health.

It continues to experience strong growth, with more

KEY FIGURES

- ◆ More than 230 members
 - ◆ More than 65,000 jobs, including 6,000 private R&D jobs, representing more than 25% of jobs nationally in the biotech-health sector
 - ◆ 823 approved projects with a total worth of more than €920 M since inception
 - ◆ 30 innovative products in the health sector brought to market since inception
 - ◆ 4 publicly traded companies
- contact@atlanpolebiotherapies.com

than 230 members and 65,000 jobs, including 6,000 private R&D jobs over the entire area. The COVID-19 crisis has provided an opportunity for member companies including NG Biotech, OSE Immunotherapeutics, Valneva and Xenothera to demonstrate their responsiveness and adaptability.

The competitiveness cluster offers its members a comprehensive, custom-designed package to develop their business. They receive tailored

support for any collaborative innovation projects, together with access to the European networks to which the cluster belongs and access to specific grants aimed at companies seeking to reach international markets. They can also broaden their networks and identify key partners by taking part in the many events organised by the cluster, or boost their visibility with the communication tools provided.



BioValley France operates throughout eastern France. Its aim is to serve as a leader for the health sector, providing a framework and bringing together all relevant stakeholders, including companies of all sizes, research laboratories and health and training companies, to build a strong, united community.

Four major topics

BioValley France provides expertise and tailored support in four areas:

- Drugs and innovative therapies;
- Diagnostics;
- Medical technologies;
- Digital health.

Dedicated services to boost your health innovation projects

- Business strategy: guidance on strategy, regulatory issues, intellectual

property (legal and financial aspects), market access, innovation marketing;

- Innovative projects: identifying funding schemes, project set-up support, expertise and accreditation, targeted networking, navigating the startup landscape;
- International relations: partnerships with

international clusters, international missions and delegations, organisation and support for major trade fairs;

- Visibility and influence: events organisation, guidance on communications strategy, press relations, publication of news and vacancies for members, directory of members.

Further information: biovalley-france.com

KEY FIGURES

- ◆ More than 240 members
- ◆ More than 550 R&D projects supported and/or approved
- ◆ More than €250 M in public funds raised by members
- ◆ More than €620 M in funds invested in supported projects
- ◆ 7 international partnerships: Belgium, Canada, Germany, Israel, Japan, Switzerland and the United States
- ◆ 9 out of 10 members renew their membership each year



Eurobiomed is the health cluster for the Sud Provence-Alpes-Côte d'Azur region and the Occitanie/Pyrénées-Méditerranée region. The aim of Eurobiomed is to promote the growth of companies in the health industry, to develop and lead one of Europe's major networks of health stakeholders, and to generate a new dynamic that will consolidate France's position as a global leader in health innovation.

Eurobiomed offers resources and dedicated solutions for companies and research organisations in the health industry to encourage innovation and development and help them secure funding. The ultimate aim of the members' strategic and business goals is to improve treatment and quality of life for patients.

With more than 14 years of expertise, Eurobiomed supports the development of innovations that tackle the challenges facing the future of medicine by providing comprehensive assistance to help its members develop their innovations and bring them to market. Since 2006, 336 projects supported by Eurobiomed have been

funded through various calls for proposals at European, national and regional level, representing more than €1.2 billion in investment, including €461 million in public grants.

Since 2014, Eurobiomed has developed a comprehensive support package for companies to support them in their growth. Each year we offer guidance to more than a hundred companies in the areas of strategic positioning, regulatory compliance, asset protection, boosting equity capital, market access and developing contacts with potential clients.

Eurobiomed represents its companies and is committed to developing an ongoing dialogue with public authorities to provide the sector with an environment that is conducive to its development, in particular by working in partnership with France Biotech.

Eurobiomed has its registered office in Marseille; it currently has more than 400 members, including 336 companies, and 16 staff members.

<https://www.eurobiomed.org/>



Lyonbiopôle Auvergne-Rhône-Alpes is a specialist health competitiveness cluster with an international dimension. Since its inception in 2005, it has united and led the Auvergne-Rhône-Alpes region's innovative health ecosystem. It represents and promotes this regional network of scientific, technological and medical innovation stakeholders at local, national and international level. Its aim is to help these stakeholders build the medicine of the future and provide patients with tomorrow's health innovations, whether in terms of technologies, products or services.

Besides providing access to an outstanding industrial, academic and clinical network, Lyonbiopôle Auvergne-Rhône-Alpes offers its members a range of services in 3 key areas:

- **Innovation:** support for R&D projects: emergence, partnership set-up, structuring, funding, etc. at regional, national and European level.
- **Development:** growth support for companies from strategic to operational aspects, including funding, HR

LYONBIOPÔLE IN NUMBERS

- ◆ 277 members
- ◆ 195 supported projects
- ◆ 42 funded projects with a total budget of €126.8 M and €49.1 M of public funding
- ◆ €369 M of capital raised by Lyonbiopôle Auvergne-Rhône-Alpes members
- ◆ 95 jointly organised events

and a hosting service.

• **Promotion:** representation of members and the regional health network in France and at global level.

Lyonbiopôle Auvergne-Rhône-Alpes now brings together, advises and supports over 275 members from the corporate, academic and hospital sectors. It includes a group of 6 founder

members composed of 4 major manufacturers (Sanofi Pasteur, bioMérieux, Boehringer Ingelheim Animal Health and Becton Dickinson), the French Alternative Energies and Atomic Energy Commission (CEA) and the Mérieux Foundation, 15 subsidiaries of major corporations and mid-caps, 230 innovative SMEs (biotech, MedTech, etc.), 17 centres of competence (teaching hospitals, universities, foundations, etc.) and 4 associate members. It was awarded the European Cluster Excellence Initiative Gold Label and is a stakeholder in various European initiatives including bioXclusters, MAGIA2MARKET, S3MartMed and EIT Health.

Further information: www.lyonbiopole.com



Medicen is the health competitiveness cluster for the Greater Paris Region. Its unique network comprises more than 510 players in health innovation, including 420 SMEs in HealthTech, health industry manufacturers, major national research institutes and healthcare institutions. This regional network helps identify clinical and academic needs, paving the way for future solutions and providing support for the development of innovative diagnostic and therapeutic solutions.

The Medicen cluster leads and supports the ecosystems of the three HealthTech strands: MedTech, biotech and eHealth. The cluster encourages interdisciplinary collaboration to overcome specific diagnostic and therapeutic challenges and address unmet medical needs, with a growing focus on governance and the use of health data.

As a competitiveness cluster, Medicen aims to transform scientific innovation into therapeutic value for patients, as well as economic value, industrial processes and

jobs. To support its members and help them grow their projects, Medicen has three key areas of action:

- Promoting the emergence of research and innovation projects,
- Encouraging the growth of startups and SMEs in France and at international level,
- Guiding project leaders to relevant sources of funding, whether public (calls for proposals at regional, national and European level) or private (relations with investors and manufacturers).

Medicen facilitates encounters between partners, offers project set-up guidance and boosts the visibility of its members to provide them with the keys to success, in France and worldwide.

Since 2005, 1,950 projects have been assessed and 470 projects have been supported by Medicen, receiving a total of €2.3 billion in funding, half of which was publicly funded, resulting in more than 200 products, prototypes, services and processes being brought to market.



Clubster NSL, a network of professionals in industry, academia and healthcare involved in innovation in the area of nutrition, health and longevity in Hauts-de-France.

Clubster NSL – Nutrition, Health, Longevity in Hauts-de-France – is a **competitiveness cluster at the convergence of nutrition and health, bringing together stakeholders in the fields of agronutrition, biotech and pharma, MedTech and hospital tech, eHealth and the silver economy.** It promotes dialogue and cooperation between academia and industry and supports innovative projects that are eligible for regional, national and European funding. It works to facilitate the emergence of innovative projects between private and public stakeholders with the aim of advancing and promoting the nutrition and health sector.

Clubster NSL is currently composed of **350 member structures with wide-ranging profiles:** startups, companies, healthcare establishments and research and training organisations. Clubster NSL provides its

CLUBSTER NSL IN NUMBERS

- ◆ 350 members
- ◆ 280 approved projects
- ◆ 135 funded projects
- ◆ €215 M funding received
- ◆ 120 events each year

members with the support of a dynamic team and the resources and partners they need to **innovate together, fund their projects and develop their business.**

The cluster is based in the Hauts-de-France region. It is France's third leading cluster of excellence in nutrition and health. **The region has some 1,100 companies, with 32,000 employees, operating in the areas of nutrition and health, and more specifically in the sectors of biotech and pharma, MedTech and hospital tech, eHealth, agronutrition and the silver economy.**

Each year, Clubster NSL joins forces with Eurasanté to organise four European business conventions designed to foster innovations for the future in the field of nutrition, health and longevity: BioFIT: biofit-event.com, MedFIT: medfit-event.com, NutrEvent: nutrevent.com and AgeingFit: ageingfit-event.fr.

- Follow our news: www.clubster-nsl.com
- Twitter: @ClubsterNSL
- For any queries, email: contact@clubster-nsl.com

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3M Purification
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SiVIEW
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Spineguard*
Spineway*
Spot-To-Lab
Stimul'in
Surgimab
Swallis Medical
SynapCell SAS
Synaxys
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T

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