



French health tech

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France Biotech

Created in 1997, France Biotech is a French non-for-profit organization that brings together the country's leading innovative health companies and their expert partners. France Biotech's primary mission is to support the development of this industry in France, by improving the tax, legal, regulatory and managerial environment in which these companies operate and by advocating for their recognition as a leading-edge industry. France Biotech also aims to turn French innovative health technologies into world leaders. The organization, which championed the creation of the French Young Innovative Company (JEI) status in 2004, develops a wide range of actions intended to set the innovative health sector on an independent and high-performance course. France Biotech is chaired by Maryvonne Hiance and has more than 200 members. For more information, please visit www.france-biotech.fr

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French health tech

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Summary

Health Tech: a major revolution in the next decade

The health care sector will experience a major transformation in the years to come: a new wave of technological innovations will soon make it possible to treat incurable diseases, improve the daily life of patients affected with disabling pathologies, and increase life expectancy.

This health tech revolution is fed by multiple disruptive innovations coming from biotech, medtech, and digital tech. In France, and all over the world, thousands of companies are exploring new therapies that relying on technological breakthroughs in the biology sector (immunotherapy, cellular therapy, DNA sequencing and editing), advances in terms of medical equipment (surgical robots, medical imaging, diagnostic tools, nanotechnologies), and multiple digital innovations (Big Data, the Internet of Things, 3D printing).

These health tech innovations will help address the global health care challenges of the next decade. Cancer, which already accounts for one in six deaths worldwide, will reach 233 million new cases by 2030. Over the same period, the two-year increase in life expectancy in developed countries will reinforce the importance of a healthy lifestyle. Furthermore, 7,000 orphan diseases remain, for which there are yet no – or too few – appropriate treatments.

Health techs will facilitate the advent of a personalized, preventive, and predictive medicine, and will play a major role in improving the health care pathway and access to treatment. Last, but not least, more efficient therapies will enable us to better control health care costs by decreasing hospitalization durations and side effects.

France: the next global health tech hub?

Today, France has exceptional dynamics in terms of health tech, with more than 600 companies well positioned in the health care innovation sector. The top 20 among them are developing promising products that could eventually affect 250 million patients worldwide (11 million in France).

Economic consequences will be substantial: French health techs could generate an annual turnover of €40 billion and 130,000 additional jobs by 2030. Hence, 1.7% of the labor force could work in the health care sector by 2030 – and meet the needs of a significant global market, with strong demand in the long term outlook.

France has many of the assets required to become a health tech leader

France has many of the assets required to emerge as a European and global epicenter of health tech.

The country has an excellent reputation for scientific research. France is fourth in the global ranking of nations for Nobel Prizes, and second for Fields Medals (mathematics). Its research institutes are already renowned: France is the only country other than the United States that is ranked in the global top 10 for health care research centers, with two institutions: INSERM and AP-HP.

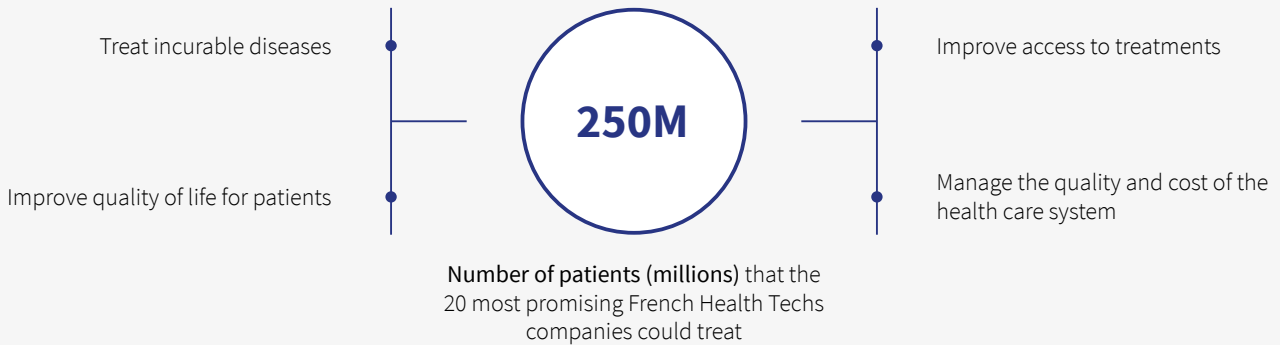
France also benefits from one of the best health care systems in the world, and from public hospitals open to innovation. By integrating research, teaching, and treatments within academic hospitals, France has built a quality national network. This is a real asset for health techs from the perspective of clinical research or market access.

Finally, another of France's advantages is the numerous public funding systems for innovative companies. With tax credits for research (CIR), participation from the public investment bank Bpifrance, benefits from the Young Innovative Company status (JEI), and availability of public investment programs (PIA), France has the most generous aid programs for innovative startups in the world.

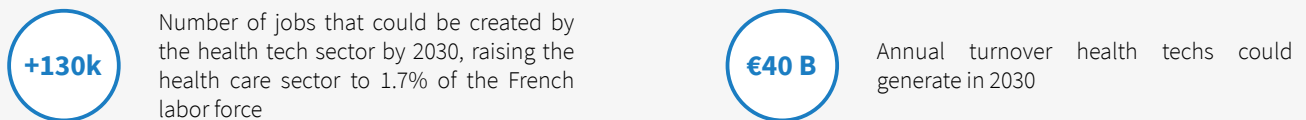
In light of its scientific and clinical excellence, its public support for innovation in health tech, and its exceptional entrepreneurial dynamics and promising pipeline, France definitely has a place on the next global hub for health tech – one that has the potential to deliver paradigm-shifting treatments to patients, as well as strong economic impact in the years to come.

THE FRENCH HEALTH TECH, A SIGNIFICANT SOCIETAL & ECONOMICAL POTENTIAL

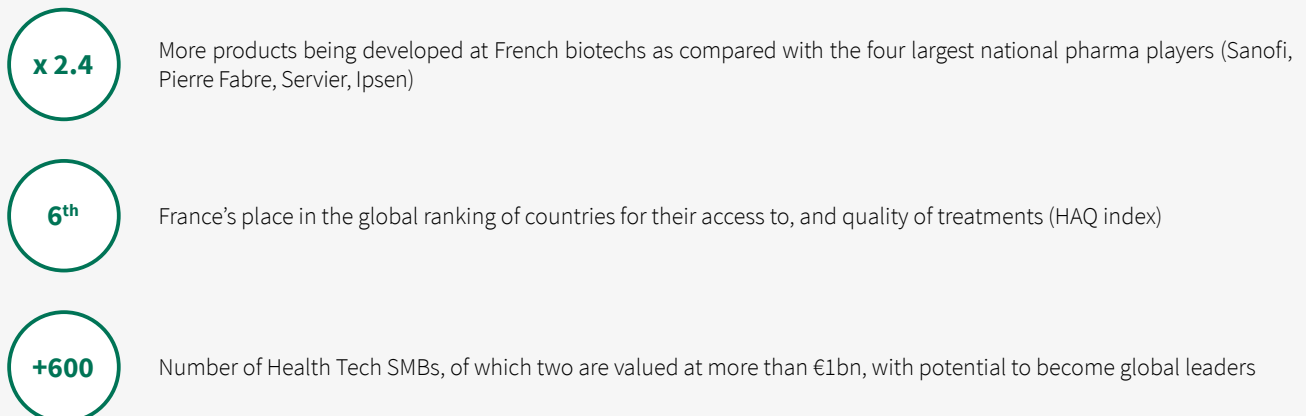
A MAJOR CONTRIBUTION TO GLOBAL PUBLIC HEALTH CHALLENGES



A PROMISE TO DELIVER STRONG ECONOMIC IMPACT



3 REASONS TO BE OPTIMISTIC FOR THE FUTURE



Introduction

The convergence of the latest scientific breakthroughs in biology (genome sequencing and editing, cellular therapy, synthetic biology, monoclonal antibodies, etc.) with engineering technologies and information technologies has the potential to revolutionize medicine. A third of the *Deep Tech* startups, focused on artificial intelligence, Big Data, robotics, and nanotechnologies, address human health issues, from prevention to innovative equipment and treatments, through health care system management. It's a new world.

For some years now, French companies have been engaged in an innovation race, with exceptional creativity in hundreds of technological directions, and with the support of public authorities. Today, the “French tech” brand is recognized worldwide, and the industry has raised almost €5 billion in five years (about \$6.1 billion) – an ever-growing figure.

Moreover, in the past, France has been able to create favorable conditions for the development of its health care industry, representing €67 billion of turnover in 2016¹ (about \$82 billion). This field thus remains robust, despite relative stagnation since the early 2010's.

In this general context, France has the potential to become one of the world's next hubs for health tech, thanks to its entrepreneurial, industrial, medical, and scientific dynamics. The country has several assets – including DBV Technologies, Cellectis, and Genfit, which could grow exponentially in the next decade. On October 30, 2017, the Swiss pharma group Novartis acquired the French rising star AAA² for €3.3 billion, validating France's potential in terms of health care innovation.

This report intends to demonstrate the potential and attractiveness of the French health tech stage, by:

1. Showcasing how the health tech revolution will be able to address global health challenges
2. Estimating the medical and economic potential of the French health tech hub
3. Outlining the main scientific, clinical, financial, and entrepreneurial assets of the French environment

We are convinced that France will be one of the next global health tech hubs – and we hope that many entrepreneurs, scientists, doctors, analysts, and engineers will join us on this journey to address the challenges of health care.



¹ LEEM, L'économie du médicament, 05/09/2017; BMI Research, France Medical Devices Report, Q4 2017

² Advanced Accelerator Applications

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Health Tech: a major revolution in the next decade

1.1 A TECHNOLOGICAL REVOLUTION AT THE CROSSROADS OF DIGITAL TECH, BIOTECH, AND MEDTECH

The ongoing digital revolution affects all sectors. Data processing through algorithms (Artificial Intelligence, Big Data, predictive analysis), new materials and 3D printing, robotics (robots, nanotechnologies), and the advent of a connected and virtual world (augmented reality, Internet of Things, sensors) are at the heart of the transformation of production methods and lifestyles. While these technologies find applications in all industries, some industries have benefited from greater industrial and public awareness, which accelerated their implementation. The success of the French tech initiative and the related industrial successes such as Blablacar, OVH, and Criteo are good examples. Many companies have integrated real-time customization and marketing technologies to improve user experience.

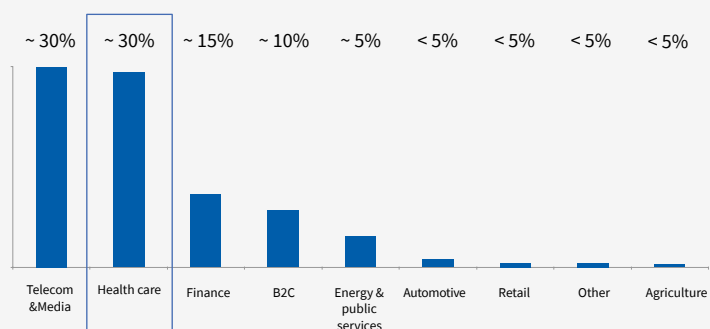
Health care represents a significant share of this new world: a third of the startup companies based on these disruptive technologies focus on health care. Moreover, they have captured 50% of the capital raised in 2016 in the sector³.

HEALTH CARE: A THIRD OF THE 'NEW WORLD'

Disruptive technologies

- Artificial Intelligence, Machine Learning and Big Data
- Robotics and Drones
- Virtual reality and IoT
- 3D Printing

Number of start-ups using disruptive technologies per industry, in 2016, worldwide

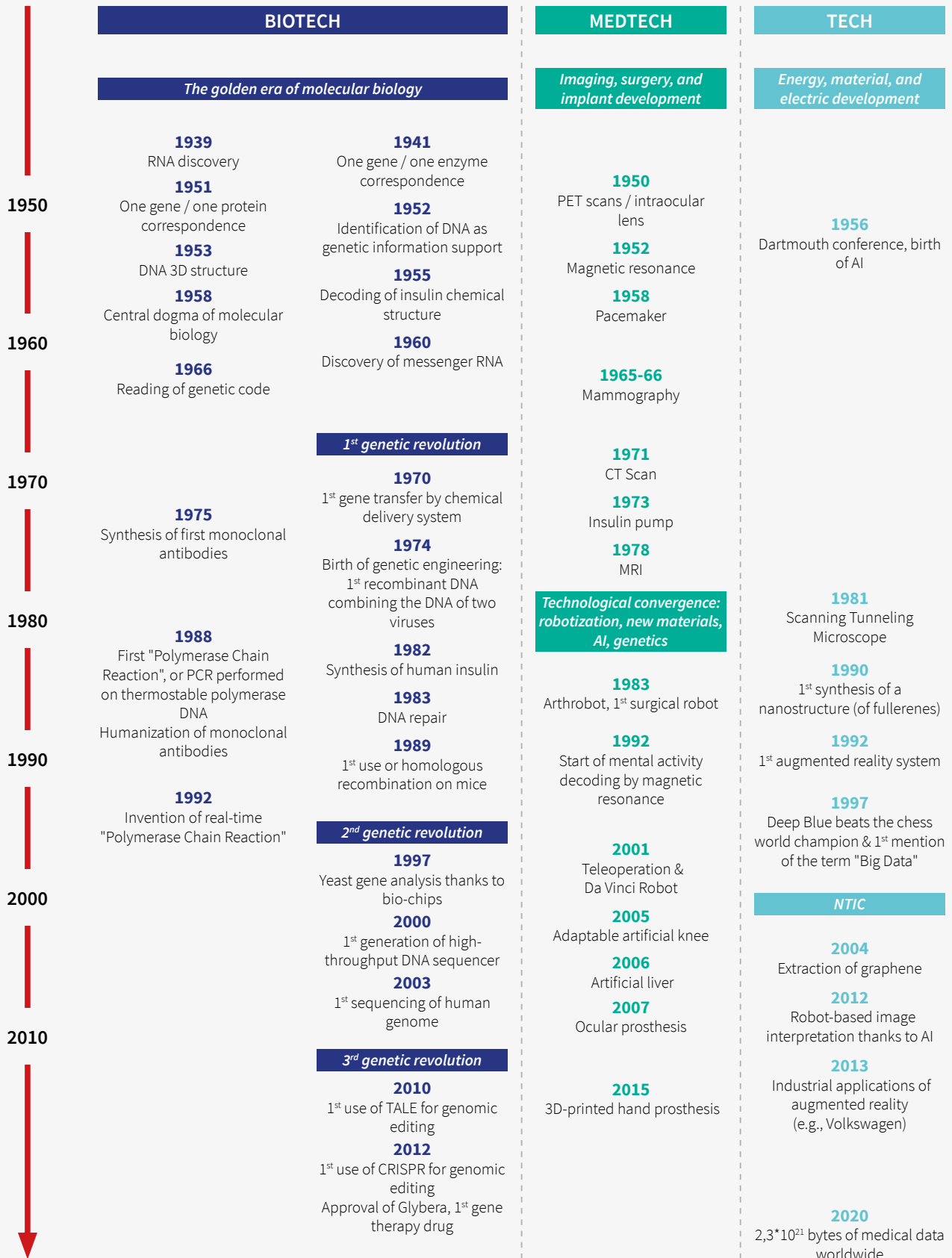


Source: Pitchbook, BCG Analysis

ILLUSTRATION 1

³ Pitchbook. Data extracted on 9/21/2017. Worldwide data, in 2016.

TIMELINE OF BIOTECH, MEDTECH, AND DIGITAL TECHNOLOGY EVOLUTION



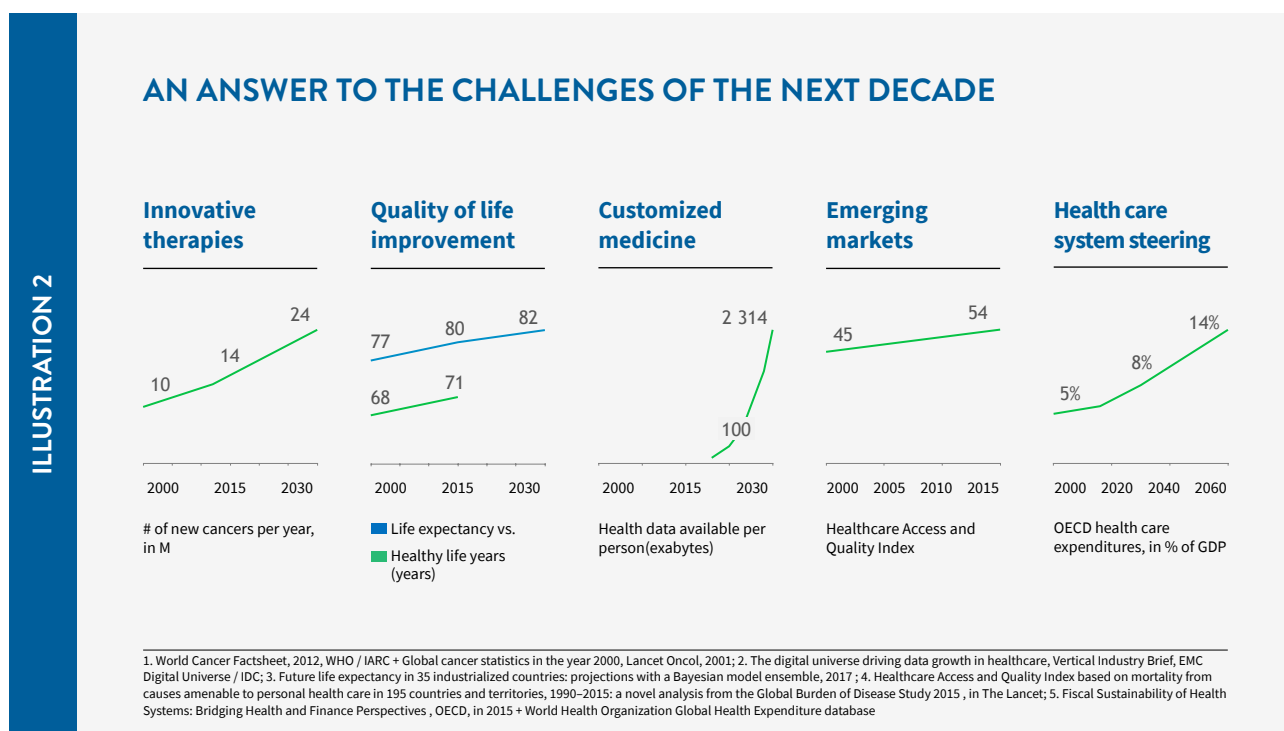
"WE HAVE COME TO A PHASE OF TECHNOLOGY CONVERGENCE"

NAWAL OUZREN,
SENSORION

The meeting of digital with the deep evolution of medical technologies in medtech and biotech offers the opportunity to push the boundaries of current medicine. DNA sequencing, genome editing, cellular therapy, immunotherapy, microbiome⁴, synthetic biology, proteomics⁵, non-invasive surgery, and diagnosis imaging are opening new therapeutic pathways for patients.

1.2 A SOLUTION TO GLOBAL HEALTH CHALLENGES

The revolutions engendered by health tech should help address the present global health challenges: treating incurable diseases, upgrading quality of life with chronic diseases, customizing health care pathways, making new treatments widely accessible, and steering the quality and costs of health care systems.



Medical stakes in innovative therapies and personalized medicine

Biotechs and medtechs are on the front line of innovative therapy development. The stakes are high: cancer, already responsible today for one death in every six worldwide, will represent 233 million new cases by 2030⁶. The 7,000 orphan diseases identified are highly disabling and affect 300 million people on the planet. Over 95% of them do not have

⁴ Definition: All the microorganisms of an individual. Source: « HUMAN MICROBIOME », Encyclopædia Universalis

⁵ Definition: Proteomics consists in studying all the proteins in an organism, a biological fluid, an organ, a cell, or even a cellular compartment. Source: Jérôme Garin. (2013). *Dossier d'information*. INSERM

⁶ WHO (2016), *Cancer Factsheet*, February 2016

**"IN ORDER TO
GIVE PATIENTS THE
BEST OF CARE, THE
TREATMENT SHOULD
BE MANAGED
HOLISTICALLY, FROM
PREVENTION TO
REMISSION"**

MICHEL FINANCE,
THERADIAG

curative treatments^{7,8}. Currently, 175,000 patients are on waiting lists for organ donations in the US and the European Union, and transplant shortages are commonplace⁹.

Along with the development of new treatments, personalized medicine also improves the whole treatment pathway through the collection and analysis of health care data. It is estimated that 1,000 terabytes of data are amassed throughout a patient's life. This includes classical clinical data, but also DNA sequencing and data from connected applications¹⁰. Prevention and medical monitoring will thus be defined by each patient's health data; and, in the future, the most efficient treatments will be identified using diagnostic and genome analysis tools.

These innovations should extend life expectancy by curing life-threatening or incapacitating diseases and improving chances and durations of survival. By 2030, the life expectancy for 35 industrialized countries will have increased by two years to 82 years¹¹.

This increase in life expectancy should also come with an increase in the number of years of good health – as is it currently lower than life expectancy by eight years on average, and increases at a slower pace than life expectancy¹². Medical progress made by health techs should meet this major challenge for our society through less invasive, more proactive treatments that have fewer side effects.

Access to treatments

Access to treatments, mainly in emerging countries, remains an essential issue at the global level. According to the Healthcare Access and Quality Index, health care systems worldwide only reach 54% of their maximum capacity in terms of accessibility and quality of the treatments delivered¹³. Here health tech is again a source of progress, notably in telemedicine, which is useful for reaching populations poorly covered by health care systems.

Steering of the health care system and patient pathway

The capacity to ensure health care spending sustainability will certainly also be a challenge for the sector in the next decades: public health care expenditures should represent 14% of OECD countries' GDP in 2060, versus 6% today if the current pace continues¹⁴. The capacity of biotech and medtech to develop a more preventive and predictive medicine which consider the whole treatment pathway should limit cost increases. Indeed, many services made possible by the digital revolution should facilitate the coordination of treatment pathways between hospitals and private professionals. By improving the quality and security of treatments and decreasing hospitalization durations, medical costs should be better controlled.

In addition, the development of new treatments to cure currently chronic diseases will relieve health care systems from some recurring charges.

⁷ Parliamentary office for evaluating scientific and technological choices. (2017). *Les enjeux économiques, environnementaux, sanitaires et éthiques des Biotechnologies à la lumière des nouvelles pistes de recherches*

⁸ Global Genes Project. *Who we are*. Consulted on 10/1/2017

⁹ European Commission. (2015). Computer graphics « *ORGANS, BLOOD, TISSUES & CELLS IN THE EU* »

¹⁰ IBM Watson Health. (2016). *The Age of Big Data and the Power of Watson*

¹¹ Vasilis Kontis et al. (2017). "Future life expectancy in 35 industrialized countries: projections with a Bayesian model ensemble", *The Lancet* (02/21/2017)

¹² WHO (2016). *Statistiques sanitaires mondiales*

¹³ GBD 2015 Healthcare Access and Quality Collaborators. (2017). "Healthcare Access and Quality Index based on mortality from causes amenable to personal health care in 195 countries and territories, 1990–2015: a novel analysis from the Global Burden of Disease Study 2015", *The Lancet* (07/15/2017)

¹⁴ OECD. (2015). *Fiscal Sustainability of Health Systems: Bridging Health and Finance Perspectives*; World Health Organization Global Health Expenditure database

France: one of the next global health tech hubs

2.1 EXISTING HEALTH TECHS IN FRANCE ALONE HAVE SIGNIFICANT MEDICAL POTENTIAL, AFFECTING UP TO 250 MILLION PATIENTS WORLDWIDE

"WE HAVE THE POTENTIAL TO TRANSFORM CANCER INTO A CHRONIC, NON-LETHAL DISEASE BY 2030-35"

LAURENT ALEXANDRE,
DNA VISION

"DATA SHARING IN HEALTH TECH IS OPENING AN UNPRECEDENTED ERA OF KNOWLEDGE AND PROGRESS"

PATRICK GUÉRIN,
OPEN HEALTH

In 2017, the potential of new treatments stemming from French biotech/medtech innovations was already exceptional. New products and services are likely to provide, if they come to maturity, an answer to some of the most pressing health challenges of the decade.

Hemato-oncology, metabolic, cardiovascular, or neuro-ophthalmic diseases; medical imaging; and diagnosis: these are some of the French areas of excellence that will achieve a particularly significant impact (see opposite). Innovations in the pipeline of French biotechs/medtechs in these domains could affect up to 250 million patients worldwide by 2030, and 11 million for the French territory alone.

Improvement in life expectancy and quality

Some treatments proposed by French companies bring an improvement in life expectancy. In France, Collectis and Innate Pharma in hemato-oncology, Genfit with metabolic diseases, and Carmat with cardiovascular diseases, are developing truly disruptive treatments.

The therapeutic innovations considered will also improve the patients' quality of life, be they affected by chronic diseases for which treatments are still rigorous and painful, or by non-lethal, disabling diseases. Among the French leaders are DBV Technologies in food allergies; Nicox, Gensight, and Pixium Vision in neuro-ophthalmic diseases; and Theraclion in oncology.

The internationalization of these companies will be essential for them to fulfill their potential in terms of public health. Being limited to the French market would mean abandoning, on average, 96% of patients potentially treatable by these therapies.

Beyond the new therapies, French biotechs/medtechs should be able to improve patient care through the advent of personalized, preventive, and more efficient medicine, mainly due to new diagnosis and monitoring technologies. There are many initiatives in this domain, including some linked to patient pathway optimization.

Another field relates to patient data use in order to monitor treatment quality and security, foster pathology comparisons and segmentations, and introduce the medical-economic dimension of treatments.

The existence of a centralized health insurance database in France may be a decisive advantage for building tools to identify the best care, circulate them, and adjust patient pathways accordingly.

THERAPEUTIC POTENTIAL OF SOME INNOVATIONS IN THE PIPELINE OF FRENCH BIOTECHS / MEDTECHS

Therapeutic area Potential # patients	Company	Pathologies	Creation date	Capitalization (€M)
ONCOLOGY WORLD - 39M FRANCE - 0,6M	Transgene	Non-small cell lung cancer	1979	184
	Collectis	Acute leukemia, multiple myeloma	1999	828
	Innate pharma	Leukemia, lymphoma, multiple myeloma	1999	590
	Nanobiotix	Cancer (radiotherapies)	2003	320
	Erytech Pharma	Leukemia, pancreas cancer	2004	359
NEURO-OPHTHALMIC DISEASES WORLD - 73M FRANCE - 3,1M	Nicox	Glaucoma	1996	272
	AB Sciences	Alzheimer	2001	371
	Gensight	AMD, glaucoma	2012	115
METABOLIC DISEASES WORLD - 49M FRANCE - 3,8M	Genfit	NASH	1999	778
	Adocia	Diabetes	2005	105
	Poxel	Diabetes	2009	132
	Inventiva	NASH	2012	117
CARDIOVASCULAR DISEASES WORLD - 40M FRANCE - 1,9M	Carmat	Heart failure	2008	142
MEDICAL IMAGING AND DIAGNOSIS	EOS imaging	Imaging systems for orthopedics surgery	1989	98
	Advanced Accelerator Applications	Injectable solution preparation kits	2002	2120
VACCINES	Valneva	Vaccines	2013	230
	Abivax	Vaccines and anti-viral therapies	2013	118
OTHER WORLD - 44M FRANCE - 2M	Amplitude Surgical	Orthopedics surgery material	1997	230
	DBV Technologies	Food allergies	2002	1790
	Vexim	Traumatic spinal pathologies	2006	214

Note: Selection based on most important market capitalization as of Q3 2017

**"HEALTH TECHS,
GIVEN THEIR
INTERNATIONAL
SCOPE, ARE A
HUGE POOL OF
OPPORTUNITIES FOR
FRANCE"**

BERNARD GILLY,
IBIONEXT

Medical contribution to treatment quality and health care cost control

The topic of the cost of some new treatments is obviously a complex one that deserves innovative and long-term approaches, while not ignoring economic and ethical questions raised by very costly treatments. Several points deserve attention.

- Some new approaches, such as those which target specific patient sub-populations (for instance, cancer), improve treatment quality and potentially deliver savings. Innovations may give patients an improved quality of life, avoiding costly daily allowances (for instance in psychiatry) or complex surgeries. In order to assess them, a "full-cost" approach is required, of course complementing the "treatment" quality approach.

- All innovations improving prevention, diagnosis, or care pathway optimization also avoid costs. Many startups are being created to provide a healthy life, or to help connect the various stakeholders in a treatment pathway. Early diagnosis and monitoring to avoid relapses also deserve an economic approach. If we focus on prevention, a greater use of clinical preventive services in the US would result in a \$3.7 billion savings while preventing the loss of more than 2 million life-years annually¹⁵.

- Part of innovation focuses on health care data use, which is likely to enable better care, process optimization, or benchmarks to facilitate hospital reorganizations and help articulate stakeholders' work.

Innovative drugs curing chronic diseases often have high upfront costs. However, they mostly result in considerable savings if we consider total treatment costs. For example, curing a sickle-cell disease patient would avoid yearly transfusion costs of about \$300,000 per year over an average treatment period of 30 years, amounting to some \$9 billion overall¹⁶. Collectis, CRISPR Therapeutics, and BlueBird Bio are using different technological platforms (TALEN, CRISPR-cas9, LentiGlobin BB305) to try to develop such a cure^{17 18}.

Many governments around the world are trying to address the issue of deficits in public health insurance. In France alone, the government aims to reduce the social security deficit from €3 billion to €2.2 billion in 2018 (\$2.7 billion)--versus a baseline of €200 billion (\$245 billion) that is expected to be spent on social security--and save €1.6 billion (\$2.0 billion) in hospital costs over five years. As part of this plan, innovative therapies will contribute to eliminating 30% of non-relevant expenditures, as will an increase in outpatient surgeries¹⁹.

Even taking into account the cost of innovations, it is important to realize that many of them will result in major savings, often accompanied by improvements in patients' quality of life.

2.2 AN ECONOMIC POTENTIAL ESTIMATED AT €40 BILLION (\$49 BILLION) OF TURNOVER AND 130,000 ADDITIONAL JOBS

The French biotechs/medtechs' success is expected to translate into significant economic benefits. In order to estimate the potential, it is worth noting that the current French situation may be compared with that of Boston in the mid-1990's, a few years before the spectacular boom of its biotech/medtech industry: scientific excellence, a dense fabric of highly innovative SMBs, increasingly late-stage pipelines.

¹⁵ Michael V. Maciosek & others (2010). « Greater Use Of Preventive Services In U.S. Health Care Could Save Lives At Little Or No Cost

¹⁶ Estimations of M. Rodger Novak, founder of CRISPR Therapeutics, in the 2017 report of the French Office parlementaire d'évaluation des choix scientifiques et technologiques, on « The economic, environmental, sanitary and ethical stakes of biotechnologies given new research progresses »

¹⁷ Sun N. et al. (2012). Optimized TAL effector nucleases (TALENs) for use in treatment of sickle cell disease. *Molecular BioSystems* (04/2012)

¹⁸ Sandrine Cabut. (2017). « Drépanocytose : succès d'une thérapie génique chez le premier patient traité ». *Le Monde* (10/3/2017)

¹⁹ Eric Dessons. (2017). « L'épreuve de feu d'Agnès Buzyn, atout social du président », *Le journal du dimanche*, (10/22/2017)

Boston, Massachusetts, had at that time 50,000 direct and indirect jobs in biotechs/medtechs--as many as France in 2016; for a market size of \$9 billion versus €10 billion for SMBs and middle-market companies in France²⁰.

A potential of €40 billion (\$49 billion) of turnover by 2030

Since then, Boston has become the main global hub for biotechs/medtechs. The state is expected to grow by about 10% per year until 2030, and build a market of about €40 billion. This is what France could achieve if it succeeds in fostering a similar dynamic²¹. This explosion was made possible by the success of several blockbusters--innovative, patent-protected therapies without international competition, that generated significant revenues for the companies that developed them.

This growth perspective should be compared with OECD forecasts of +2.5% for French GDP by 2030²².

The biotech/medtech industry should also re-energize the health care industry, representing 330,000 direct and indirect jobs and €67 billion (\$82 billion) of turnover in 2016^{23,24}. Yet biotechs/medtechs are an essential innovation source for large industrials. The French biotechs alone have 2.4 times more products under development than the four largest French pharma players (Sanofi, Pierre Fabre, Servier, and Ipsen)²⁵.

Expected creation of 130,000 direct and indirect jobs in France

The emergence of a French biotech/medtech sector would of course generate employment opportunities. As the French leaders in the field establish themselves and new therapies are launched in the market, additional jobs in R&D, production, marketing, sales, and support will be created as well.

Following Massachusetts's dynamic, French biotechs/medtechs could represent 180,000 direct and indirect jobs by 2030, or 130,000 additional French jobs as compared with today²⁶. Health care could thus represent 1.7% of the French labor force in 2030, including the jobs currently existing in the rest of the pharma industry²⁷.

A competitive and innovative industry is a driver of attractiveness in international competition for the best talent, be it scientific (researchers, PhD students, engineers), managerial (project leaders, business developers), or financial (analysts, investors). It contributes to the overall wealth of the French knowledge economy. The caliber of talent attracted is an additional asset as companies benefit from the skills and increase their potential.

Moreover, therapeutic and medical innovations require numerous clinical trials which retain the best scientists in public hospitals and protect the hospitals' outstanding quality while enabling patients to have priority access to the most innovative treatments.

An opportunity to bolster biomanufacturing capabilities

The development of biotechs/medtechs would also contribute to reinforcing French industrial production of biopharmaceuticals, as biotechs/medtechs require numerous specialized subcontractors for the bioproduction of their innovative therapies.

²⁰ MBC and BCG. (2001). MassBiotech 2010, *ACHIEVING GLOBAL LEADERSHIP IN THE LIFE-SCIENCES ECONOMY*; EY. (2017, 2010, 2009, 2006, 2003). *Biotechnology Report: Beyond borders*; Evaluate Ltd – Extraction on 08/30/2017; Société.com – Extraction on 09/07/2017; BCG Analysis; France Biotech. (2016). *Panorama 2015 de l'industrie des sciences de la vie en France*

²¹ MBC and BCG. (2001). MassBiotech 2010, *ACHIEVING GLOBAL LEADERSHIP IN THE LIFE-SCIENCES ECONOMY*; EY. (2017, 2010, 2009, 2006, 2003). *Biotechnology Report: Beyond borders*; Capital IQ – Extraction on 02/08/17 and 09/17/17; Evaluate Ltd – Extraction on 08/30/2017; MBC. (2017). *2016 Industry Snapshot*; BCG Analysis

²² OECD. OECD Databank. Database consulted on 09/28/2017

²³ DARES

²⁴ LEEM. (2017). *L'économie du médicament*; BMI Research. (2017). *France Medical Device Report Q4 2017*

²⁵ France Biotech. (2016). *Panorama 2015 de l'industrie des sciences de la vie en France*

²⁶ MBC and BCG. (2001). MassBiotech 2010, *ACHIEVING GLOBAL LEADERSHIP IN THE LIFE-SCIENCES ECONOMY*; EY. (2017, 2010, 2009, 2006, 2003). *Biotechnology Report: Beyond borders*; Capital IQ – Extraction on 02/08/17 and on 09/17/17; Evaluate Ltd – Extraction on 08/30/2017; MBC. (2017). *2016 Industry Snapshot*; LEEM. (2017). *L'économie du médicament*; BCG Analysis

²⁷ INSEE

**"HEALTH TECH
SHOULD ENABLE
DEVELOPMENT
OF A STRONG
BIOPRODUCTION
INDUSTRY AND
REINFORCE FRANCE'S
HEALTH CARE
INDEPENDENCE"**

CHRISTIAN BÉCHON,
LFB

France can already count on a robust biopharmaceutical production industry: the country is fourth in Europe in pharmaceutical production (in value)²⁸. The development and production requirements of homegrown big pharmaceuticals has supported the growth of local biomanufacturing capacities.

Still, multiple countries are ramping-up their investments in industrial bioproduction. The additional business brought by a thriving biotechnology industry would help sustain France's role in Europe as a major bioproduction center in an increasingly competitive environment.

The emergence of several French leaders is a necessary step to achieving this potential

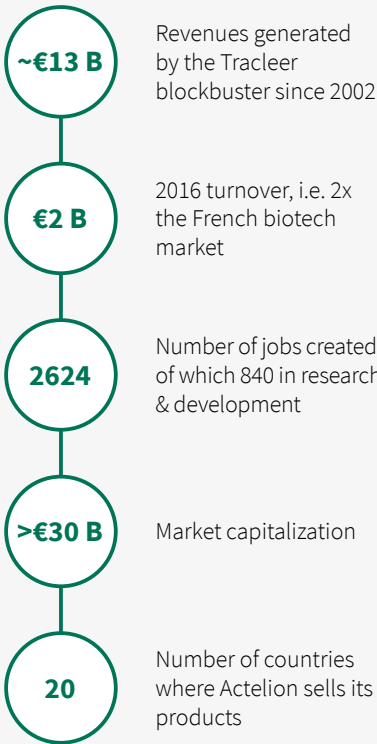
In order to fully achieve this potential, the number of startups and SMBs must increase, yet that alone is insufficient. It is vital that some startups grow and become international leaders with access to global markets. In Boston, Biogen and Genzyme were the first biotechs to have emerged, and then drove the whole sector.

Today, France has several companies ideally positioned to play the same role, with high-potential products that are soon to arrive on the market. Supporting these future leaders is key to benefitting from their full economic and social potential.

²⁸ Efpia (2016). The pharmaceutical industry in figures

FRENCH LEADING INTERNATIONAL SUCCESSES

ACTELION, A EUROPEAN SUCCESS



ACTELION AT A GLANCE – BEFORE ACQUISITION BY J&J IN 2017

- The biggest European biotech, based in Switzerland
- Founded and led by a couple of French scientists: Jean-Paul Clozel (cardiologist, CEO) and Martine Clozel (pediatrician, Chief Scientific Officer)
- Its blockbuster, Tracleer, treats pulmonary arterial hypertension (HTAP), an orphan disease

FROM FUNDAMENTAL RESEARCH TO MEDICAL AND INDUSTRIAL SUCCESS

- 1990** - Discovery of bosentan by Dr. Martine Clozel
- 1997** - Creation of Actelion
- 1999**: 1st clinical trial with patients affected with HTAP with bosentan (Tracleer)
- 2000** - Actelion IPO
- 2000-2002** - Status of orphan drug and obtaining of marketing authorization in the US and in Europe
- 2007** - Acquisition of CoTherix
- 2008** - Jean-Paul Clozel named Entrepreneur of the year by EY
- 2017** - Sold to J&J for €28 B - Création of Idorsia

FRENCH AT THE HEAD OF THE TWO LARGEST US START-UPS IN BIOTECHNOLOGIES

Incyte

Led by Hervé Hoppenot since 2014:

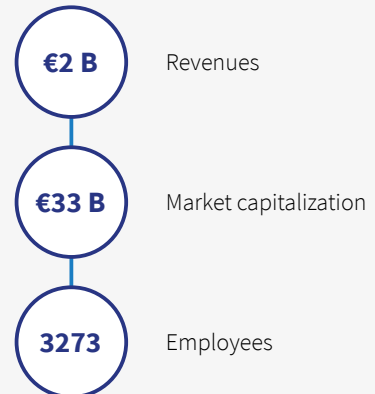
- One of the global leader in oncology
- Ranked 6th most innovative company in the world (1st in health care) by Forbes

BIOMARIN

Led by Jean-Jacques Bienaimé since 2005:

- One of the global leader in orphan genetic diseases
- Ranked 12th most innovative company in the world (3rd in health care) by Forbes

BIOMARIN AND INCYTE IN 2016



Note: capitalization on 10/24/2017; *then Rhone-Poulenc Rorer Pharmaceuticals; Sangstat, Genencor and Biomarín are three US biotechs
 Source: Bloomberg, J&J Woos Billionaire Doctors Who Don't Need Cash in Actelion Bid, 6/12/2016; Actelion official website; Bloomberg; Actelion 2016 Annual Report; Forbes, The world's most innovative companies, 2017 ranking

France has many of the assets required to become a global hub

3.1 EXCELLENCE OF FRENCH SCIENTIFIC RESEARCH

France is a country with proven scientific and academic excellence in many domains relating to life sciences. Evidence of this lies in the numerous French Nobel Prize and Fields Medal winners – the country respectively ranked fourth and second for the number of these two prestigious distinctions²⁹. Although the Nobel Prize can be given for disciplines as different as medicine and literature, it remains a global recognition of a country's academic excellence and innovation level.

In the field of “hard sciences,” France is also recognized for its world-class research institutes and laboratories. The Spanish SCImago agency, which measures and ranks research institutions based on project excellence, impact, and innovation, has put CNRS (National Center for Scientific Research) at the top of its ranking for eight consecutive years from 2009 to 2016. If we limit the analysis to research institutes in the health care sector, INSERM was ranked second, and AP-HP seventh in 2016 – the only non-US institutions in the top ten³⁰.

GLOBAL RANKING OF THE BEST RESEARCH CENTERS

Global Ranking*	Institutions	Countries
1 st	National Institute of Health (NIH)	United States
2 nd	INSERM	France
3 rd	Veteran Affairs Medical Centers	United States
4 th	Massachusetts General Hospital	United States
5 th	Howard Hugues Medical Institute	United States
6 th	American Cancer Society	United States
7 th	Assistance Publique Hôpitaux de Paris (AP-HP)	France
8 th	Brigham and Women's Hospital	United States
9 th	Mayo Clinic	United States
10 th	University of Texas M.D. Anderson Cancer Center	United States

*Source: SCImago Santé, 2016

²⁹ Audrey Dufour. *Les Prix Nobel, quels pays sont les plus récompensés ?*, La Croix (2014). *Médaille Fields : la France, pays le plus titré avec les Etats-Unis*, Le Monde (2014)

³⁰ SCImago Institutions Ranking in Health (2016)

"THE QUALITY OF FRENCH HEALTH TECH IS EXCEPTIONAL – WE HAVE SIGNED 25 PARTNERSHIP AGREEMENTS IN 2016"

CHRISTIAN DELEUZE,
SANOFI-GENZYME

Finally, these exceptional standings are the result of high-quality higher education that rests on two main pillars: public universities and "Grandes Ecoles" (similar to private universities in other countries). This system, however poorly adapted to the criteria of rankings such as the Shanghai one, is very competitive. Ecole Normale Supérieure has trained the second most Fields Medal recipients in the world, after Princeton University in the US.

This multidisciplinary academic excellence is an undeniable asset for France, as it is an essential prerequisite in the Health Tech sector – and it usually takes a long time to build.

3.2 ONE OF THE BEST HEALTH CARE SYSTEM IN THE WORLD, WITH TREATMENTS-RESEARCH-TRAINING CENTERED IN ACADEMIC HOSPITALS

France also benefits from a base of exceptional public and non-profit academic hospitals which could be a real launching pad for innovative treatments and their delivery to patients.

Doctors in France are both required and exceptionally willing to be innovative research players, notably through clinical research. Having such a national network is an undeniable asset for the French biotech and medtech sector from a market-access perspective.

At the same time, a dynamic and open health tech network may be an exceptional source of motivation for doctors and health care practitioners in academic hospitals because it cultivates innovative research on topics where international scientific competition is fierce and highly rewarding.

3.3 STRONG SUPPORT FOR INNOVATION

France has progressively built a very favorable environment for startup creation, the result of an energetic and partnership-based public policy. Entrepreneurs in France can thus benefit from an ecosystem and a framework that support business creation and from numerous world-renowned incubators. This is also one of the numerous assets health tech shares with French tech in general, and which enabled the latter to experience the strong dynamics observed in the last few years. Several public systems are particularly recognized and play an essential role in the development of startups in the sector.

Tax credit for research (CIR - Crédit d'Impôt Recherche)

The purpose of CIR is to support companies' research and development activities, independent of size. A set of expenditures related to fundamental research, or applied to experimental development activities, can thus benefit from a tax credit of up to 30% for amounts lower than €100 million. In 2013, the CIR enabled companies to deduct over €6 billion in taxes³¹.

This tax relief plays an essential role in the competitiveness of French companies by encouraging them to invest in innovation and settle their research centers in France, thus creating jobs.

Bpifrance investments

Bpifrance is a corporate funding and accompaniment entity which intervenes by funding and investing in innovative companies. In 2016, Bpifrance invested its own funds in 14 new health tech companies for a total amount of almost €161 million—and finances in parallel more than 500 projects with €171 million in aids to innovation³².

Numerous companies benefit from Bpifrance's offerings at various stages of their evolution (help in innovation, investment funds in innovative biotherapies or rare diseases, biotech acceleration fund, InnoBio fund), up to and including the final steps in their development (large venture fund, Société de Projet Industriel).

³¹ *Le Crédit d'Impôt Recherche, L'essentiel en 10 points*. Diplomatie.gouv

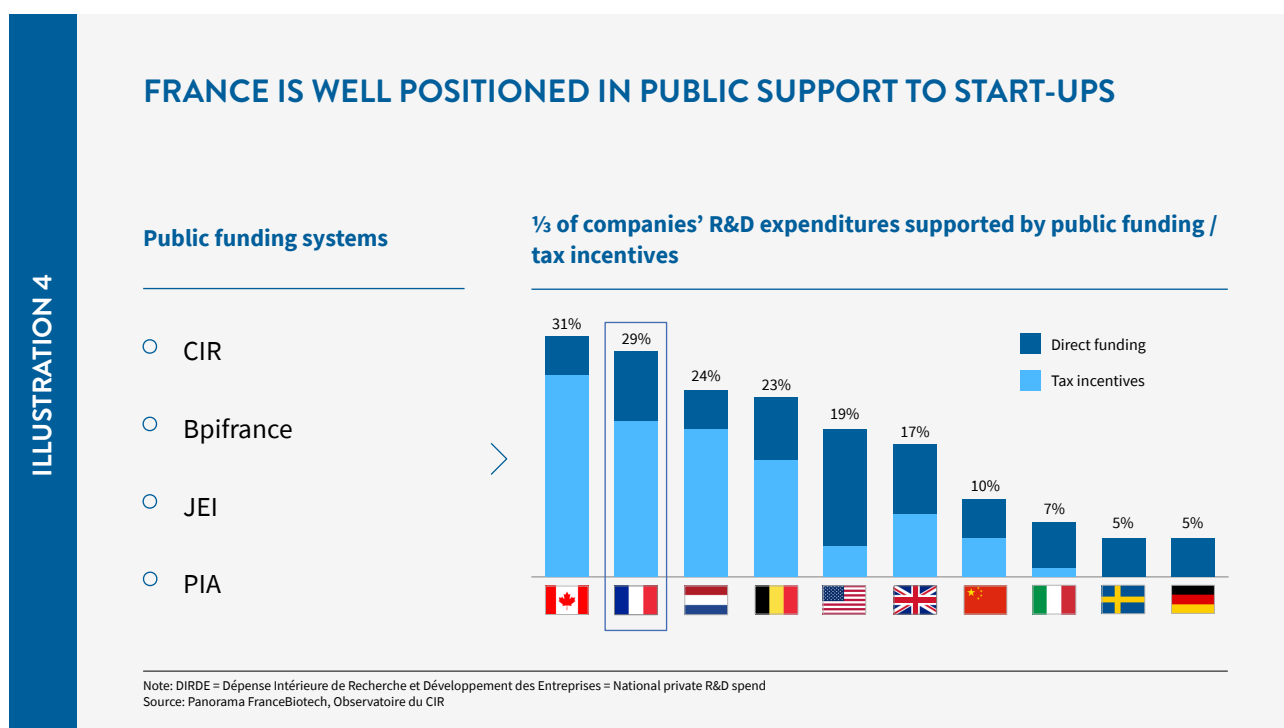
³² Bpifrance data (2016)

Young Innovative Company status (JEI – Jeune Entreprise Innovante)

This status, created in 2004 as part of France biotech initiative, enables SMBs under eight years old to benefit from multiple types of tax relief and exemptions when their expenditures in research and development represent at least 15% of their costs. In 2013, more than €100 million had been submitted for exemption³³.

Investment programs for the Future (PIA - Programmes d'Investissement d'Avenir)

Health care and biotechnologies were among the strategic axes identified by the State in which to invest the €47 billion allocated to the Programmes d'Investissement d'Avenir (PIA – investment programs for the future) since 2010. With €3 billion allocated to the sector, the State supported ten academic hospital research projects in 2016 alone, with close to €80 million invested³⁴. These investments also benefit academic hospital institutions (IHU), whose funded activities enable to influence research projects at internal level and significantly increase publishing activity.



3.4 PARIS, A SIGNIFICANT FINANCIAL LOCATION FOR THE SECTOR

The possibility of companies financing themselves through IPOs is also encouraged in France, a financial location that is part of the Euronext system. The main criteria for being included in the list are generally linked to the location of company activities, access to investors, presence of companies from the same industry, and coverage by analysts.

For these reasons Euronext, formed by a merger of the Amsterdam, Brussels, and Paris Stock Exchanges, is the financial operator most often chosen for IPOs of European life science companies. In the last six years, 75% of the money raised through IPOs in this domain specifically came from Euronext Paris³⁵. To date, more than 60 French biotechs and medtechs are listed at Euronext Paris. With this dynamic financial situation, French companies can be agile and open to new investors.

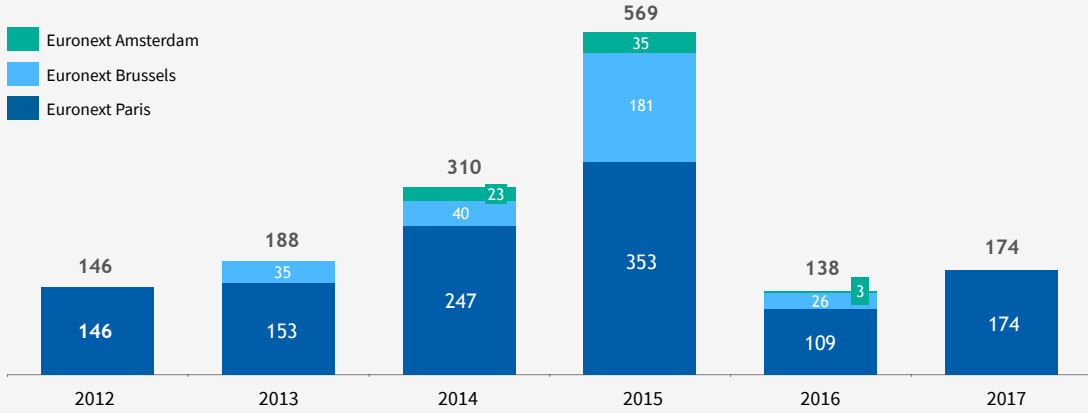
³³ Ministry of Higher Education, Research, and Innovation. *Appui aux entreprises innovantes, JEI*

³⁴ Commissariat Général à l'Investissement. *Rapport d'Activité 2016*

³⁵ Panorama France Biotech. (2016)

PARIS, PREDOMINANT MARKETPLACE WITHIN EURONEXT

Amount raised in IPO by European Health Tech (M€)



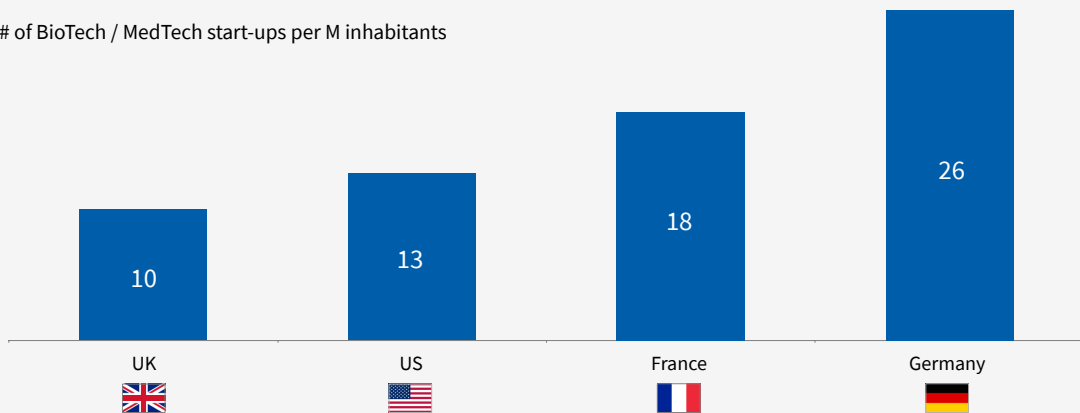
1. All IPOs of life science companies in Europe of minimum value of €2,5M
Source: France Biotech, Panorama 2016

3.5 STRONG ENTREPRENEURIAL DYNAMICS

An assessment to date shows that France is one of the most dynamic countries in terms of health tech creation. The country has almost 18 biotech and medtech startups per million inhabitants, more than the US with 10 and the UK with 13 companies per million inhabitants³⁶. This fact is very promising as it facilitates the development of a rich ecosystem and the rise of new initiatives in the domain.

FRANCE HAS INITIATED A STRONG ENTREPRENEURIAL DYNAMIC, LEADING TO NUMEROUS START-UP CREATIONS

of BioTech / MedTech start-ups per M inhabitants



Sources : Evaluate Pharma, Orbis, Capital IQ

³⁶ Capital IQ, Orbis, Evaluate Pharma. Data extracted on 9/21/2017

France holds all the cards required to become a global epicenter of health tech: a full pipeline of innovative therapies and technologies, top-notch scientific research, generous public funding, and an efficient and accessible health care system. Thanks to a strong entrepreneurial dynamic, multiple players now exist to use these assets and convert budding startups into industrial leaders. The emergence of a French health tech hub is near, and with it will come the potential to deliver paradigm-shifting treatments to patients as well as strong gains to the economy.



THERAPEUTIC POTENTIAL OF FRENCH BIOTECH / MEDTECH

To evaluate the potential, we analyzed the pipeline of the top 20 French health techs (as of September 2017) and estimated the number of patients that could be treated and/or cured by 2030.

Oncology

Acute leukemia, multiple myeloma, lymphoma, pancreas cancer, non-small cell lung cancer: number of patients who are likely to die from these diseases between 2018 and 2030

Source: WHO. Global Health Estimates (2013), Deaths by age, sex and cause, Anticancer Fund – ESMO. Non-small cell lung cancer: a guide for patients (2016)

Neuro-ophthalmic diseases

Alzheimer's: number of patients who are likely to die from this disease between 2018 and 2030

Source: WHO. Global Health Estimates (2013), Deaths by age, sex and cause

Glaucoma, AMD: number of patients with glaucoma in 2030

Source: INSERM, INSEE. Demographic balance (2016)

Metabolic diseases

NASH: number of patients diagnosed with NASH in US & EU5 (France, Germany, UK, Italy, Spain)

Source: Intl. Diabeted Federation; Decision Resources PatientBase 2013; Ratziu et. al., J Hep. 2012/2010; KOL interviews (Hepatologists)

Diabetes: number of patients diagnosed with a Type 2 Diabetes & with HbA1c > 7 (poorly regulated diabete)

Source: DRG database. Diagnosed Prevalent Cases of T2 Diabetes

Cardio-vascular diseases

Heart failure: number of patients who are likely to die from this disease between 2018 and 2030

Source: WHO. Global Health Estimates (2013), Deaths by age, sex and cause

Others

Food allergies: number of people with food allergies (worldwide)

Source: Health Ministry. Food allergies – knowledge, clinics & prevention

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