

Is France Attractive for Pharma Companies?

Market Insights

Comparisons & Recommendations

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Smart Pharma Consulting has evaluated France's attractiveness for pharma companies by comparison to key European countries and has made suggestions for improvement

The attractiveness of a national market for pharma companies can be assessed through four key dimensions:



- Thus, Smart Pharma Consulting proposes to compare the French pharma market to Germany, Italy, UK and Spain and...
- ... provides recommendations likely to enhance the attractiveness of France for pharma companies

Sources: Smart Pharma Consulting



The French healthcare expenditure to GDP ratio of 12.4% compared to other Euro-5 countries reflects the high importance devoted by citizens and the government to healthcare

Healthcare expenditure – Euro-5 comparisons (2005 – 2021)



- All Euro-5 countries have increased their share of GDP related to healthcare expenditure between 2005 and 2021
- The increase of this ratio results from:
 - National economies dynamics
 - Healthcare costs evolution
 - Public health conditions and coverage²
 - Governments' investment prioritization
 - Citizens' willingness to seek for care

Sources: OECD database (January 2023) – Smart Pharma Consulting analyses



Although drugs are the 2nd largest item of healthcare expenditure after hospitals, they are the main target of cost-containment due to political reasons, and will continue to be so in the future

Healthcare expenditure breakdown – Euro-5 comparisons (2021)



% of total healthcare expenditure

- Drugs³ are the 2nd largest source of healthcare expenditure in France, while it is the 3rd in the other Euro-5 countries
- The weight of Drugs in healthcare expenditure varies from 13% in the UK to 21% in Spain
- It is typically the easiest segment to apply costcontainment measures on, as decisions are:
 - Made by payers (either public and/or private), with a limited bargaining power of suppliers
 - Much better accepted by citizens than restriction measures on the other segments
- In France, the price of reimbursable drugs fell by 48.6% between 2000 and 2021

Sources: OECD database (January 2023) – Smart Pharma Consulting analyses

¹ Incl. ancillary services, preventive care and governance, healthcare system and financing administration –² In France, 8% on average of hospital expenditures are relative to drugs purchased by institutions, representing ~2% of total expenditures (i.e., 8% of 26%) – ³ And other medical goods such as medical devices



With 85% of healthcare expenditure covered by the National Health insurance Fund and 9% of "out-of-pocket" spending, France offers one the best healthcare protection to citizens

Share of public spending – Euro-5 comparisons (2021)*

% of total healthcare expenditure



- France is the 2nd Euro-5 country offering the most extensive national health insurance
- With 85% of the healthcare expenditure covered by the government and the National Health insurance Fund, France offers one of the best healthcare public protection, just behind Germany
- All French citizens benefit from a public health insurance and 95% of them have a complementary private one¹
- As a result, "out-of-pocket" spending is the lowest amongst Euro-5 countries (and even in the world), representing only 9% of total healthcare expenditure

Sources: World Bank and OECD databases (January 2023) -Smart Pharma Consulting analyses

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* Or latest data available –



In France, pharma companies and patients must wait ~16 months after marketing authorization to get a new drug reimbursed and launched, which is higher than most Euro-5 countries

Average time to market access – Euro-5 comparisons (2020)



2022 analysis based on a sample of 160 products approved by EMA between January 2017 and December 2020

- In Europe, delays between approval and market availability vary widely, due to the time required to obtain reimbursement and a price agreement
- Except for Germany, this delay exceeds in all Euro-5 countries the **180 days** recommended by the European Commission
- Important delays are harmful both for patients who do not benefit from innovation and for pharma companies which face a loss of revenues
- Germany and the UK have smaller delays as price and reimbursement negotiations occur once the product is marketed
- France has recently decided to experiment this approach, called "Direct Access" under restricted conditions² and for a 2-year test period

Sources: Patients W.A.I.T. Indicator – EFPIA (July 2022) – Smart Pharma Consulting analyses

¹ Time between marketing authorization and price and reimbursement, excluding early access programs for breakthrough innovations (except for France) –² For products assessed by the Transparency Committee as having a clinical Added Value raked I to IV





About one third of globally approved drugs is not launched in France mainly due to market access obstacles (non-reimbursed, low price, etc.)

Market access to new drugs – Euro-5 comparisons (2020)

% of new drugs available to patients in Euro-5 countries (rates of availability)



2022 analysis based on a sample of 160 products approved by EMA between January 2017 and December 2020

- The difference of new drugs availability according to Euro-5 countries depends on:
 - Heterogeneity of procedures
 - Regulatory requirements / constraints
 - Local pricing and reimbursement conditions that can impact product launches, even when there is a centralized approval procedure
 - Market potential (e.g., epidemiology)
- In the future, availability of new drugs might be further reduced due to stricter cost containment measures applied by governments

Sources: Patients W.A.I.T. Indicator - EFPIA (July 2022) - Smart Pharma Consulting analyses

By 2027, the French pharma market should remain the 2nd largest market in Europe, accounting for ~20% of Euro-5 countries and ~2% of the global pharma market

Pharma markets size & dynamics – Euro-5 comparisons (2022 – 2027)



- In 2022, Euro-5 countries accounted together for ~13% of the global pharma market:
 - Germany: ~4%
 - France: ~3%
 - UK: ~2%
 - Italy: 2%
 - Spain: ~2%
- Over the 2022 2027 period, Euro-5 countries sales should grow at a +1.6% CAGR, vs. +5.1% for the worldwide market, due to stricter cost containment measures
- The Euro-5 country weight in the global pharma market sales should drop from 13% in 2022 to ~11% in 2027 and France from the 5th to the 6th place with a market share of 2%

Sources: IQVIA Institute (January 2023) – Smart Pharma Consulting estimates and analyses

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¹ Ex-factory price before rebates



France appears to be the least profitable Euro-5 country due to the combination of low ex-factory prices and a series of taxes imposed by health authorities on reimbursable drugs

Profitability of pharma companies – Euro-5 comparisons (2020)



Sources: Leem (2023) – INE database (2023) – Competitive Data (2022) – Insee sector studies (2022) – Smart Pharma Consulting analyses

- With an average EBTIDA rate of 10.2% in 2020, France was the least profitable pharma market, amongst Euro-5 countries
- This lower profitability is partly explained by lower prices of drugs, notably compared to:
 - Spain (prices 22% higher vs. France)
 - Italy (prices 19% higher vs. France)
 - Germany (prices 9% higher vs. France)
- Profitability of French pharma affiliates is also affected by several specific important taxes:
 - Safeguard clause (up to € 760 M in 2021)
 - Contribution on turnover of a total of 18.6% including different items (e.g., professional development HCPs fund, tax on promotion²)

 1 Earning before interest, tax, depreciation and amortization – 2 € 131 M for 2021



The French government has recently set up a specific plan to attract healthcare R&D investment and make France the leading European country for clinical research by 2030

R&D investment & employment – Euro-5 comparisons (2020)



- In 2021, Euro-5 countries accounted for ~23% of the number of clinical trials carried out in the world
- The January 2022² European regulation on clinical research harmonization aims at strengthening European attractiveness for R&D investment...
- ... to limit the increasing competition from Asia (incl. China and Korea)
- France is a leading country for clinical trials in oncology with its 20 CLCC³ and in rare diseases with 473 Excellence and Reference Centers⁴
- In 2021, the French government has set up a plan to invest € 3.5 B to boost healthcare R&D by 2030⁵
- In addition, ~€ 800 M p.a. of tax credit are granted in France for the healthcare industry

Sources: EFPIA Key Data (2022) – VFA (2022) – The UK Pharmaceutical Sector, Enterprise Ireland (2020) – Leem (2022) – Farmindustria Italy (2019) – Farmindustria Spain (2022) – WHO website (2023) – Sante.gouv.fr (March 2023) – Smart Pharma Consulting analyses ¹ Domestic sales – ² (EU 536/2014) A period of 3 years is foreseen for a complete transition on January 31st, 2025 – ³ Centres de Lutte Contre le Cancer (hospitals specialized in oncology research and care, brought together in a health cooperative group) – ⁴ Including 32 state-of-the-art University Hospitals – ⁵ Based on a proposition of the CSIS (Strategic Council for the Healthcare Industries)



Cellectis is a genome engineering company, developing new generation Car-T cells to cure various types of cancer with currently 6 candidates in Phase I clinical trial

French cell & gene therapy companies – Cellectis





Allogene



- Cellectis is a genome engineering company specializing in the development of immune therapies based on CAR-T cells, created in 1999 through a technology transfer from the Pasteur Institute
- In 2014, Pfizer acquired 10% of Cellectis, which has been listed since 2007 on the Euronext Paris and since 2015 on the Nasdaq in the US
- Cellectis is co-developing 2 of its products in partnership with **Servier** and **Allogene Therapeutics**

Products & Technologies

- The company is developing the first-of-its-kind allogeneic approach for immunotherapies in oncology, pioneering the concept of off-the-shelf and ready-to-use gene-edited CAR-T cells to cure cancer
- Cellectis is using its internal gene editing technology, Talen, and its own electroporation system, PulseAgile, showing its expertise in the field of cell therapies
- 6 candidates are currently in Phase I clinical trials in various indications (e.g., multiple myeloma, acute myeloid leukemia)

Sources: Cellectis website (March 2023) – Pfizer press release – Smart Pharma Consulting analyses



OSE Immunotherapeutics is developing immune therapies, with 5 of them in clinical-stage, and the most advanced one being a therapeutic vaccine in phase III for non-small cell lung cancer

French cell & gene therapy companies – OSE Immunotherapeutics









Company description & Partnership	erships
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- OSE Immunotherapeutics is a biotechnology company founded in 2012
- OSE Immunotherapeutics has signed partnerships with Boehringer Ingelheim, Servier and Veloxis Pharmaceuticals representing a potential of up to € 1.6 B of revenues and additional royalties on future sales
- Based in Nantes (Head Office) and Paris, OSE Immunotherapeutics has more than 65 employees and is listed on the Euronext Paris

Products & Technologies

- OSE Immunotherapeutics is focused on developing immune therapies in 3 areas: Immuno-oncology, Auto-immunity and T cell-based vaccines
- The pipeline includes 5 clinical assets, the most advanced one being a therapeutic vaccine that stimulates T cells to attack cancer cells, currently in Phase III for non-small cell lung cancer



The company is also exploring the potential of artificial intelligence in drug discovery through collaboration with the CLCC¹ Léon Bérard (Lyon) and the French firm MAbSilico²

Sources: OSE Immunotherapeutics website (March 2023) – Company's annual report (2022) – Smart Pharma Consulting analyses

 1 Centre de lutte contre le cancer: center to fight against cancer – 2 Al company focusing on biologic drugs discovery and development



GenSight Biologics is developing 2 gene therapies, one of which is currently being registered in Europe for a severe inherited disease of the eye

French cell & gene therapy companies – GenSight Biologics





Company description & Partnerships

- Gene therapy company, founded in 2012, dedicated to the discovery and development of gene therapies for the treatment of severe inherited eye diseases
- At the end of 2022, GenSight received different fundings:
 - € 35 M from the European Investment Bank to support the launch of Lumevoq (lenadogene nolparvovec-GS010), in Europe
 - € 12 M from Heights Capital, an American private equity fund
- Analysts at Belgian fund Degroof Petercam forecast sales of up to € 310 M per year for Lumevoq and break-even two years after product's launch

Products & Technologies

- GenSight Biologics, currently has 2 gene therapies in development for a total of 7 clinical trials (completed or ongoing)...
- ...the most advanced of which, Lumevoq, is currently being registered in Europe for Leber's hereditary optic neuropathy

Sources: GenSight website (March 2023) – GenSight press release – Smart Pharma Consulting analyses



Vivet Therapeutics is a clinical-stage company, developing gene therapies in rare metabolic diseases, that is supported by "big pharma" companies such as Novartis, Pfizer and Roche

French cell & gene therapy companies – Vivet Therapeutics



Company description & Partnerships

- Vivet Therapeutics is a clinical-stage emerging biotechnology company developing novel gene therapy treatments for rare, inherited metabolic diseases
- The company is supported by international life science investors such as Novartis Venture Fund, Pfizer and Roche Venture Fund

Products & Technologies

- Its portfolio is diversified and based on a novel recombinant adeno-associated virus as a vector
- Vivet's lead program, VTX-801, is currently under Phase I/II clinical development for Wilson Disease...
- ...and has been granted Orphan Drug designation by the FDA and the EMA, as well as Fast Track designation by the FDA
- Vivet is also working on technological platforms addressing key challenges of gene therapy (e.g., sustained therapeutic gene expression, immune responses towards the viral vector)

Sources: Vivet Therapeutics website (March 2023) – Pfizer press release – Smart Pharma Consulting analyses



Despite a high know-how in drug and vaccine production, France is lagging behind other Euro-5 countries, what the French government is trying to fix with a special funding decided in 2021

Pharma production – Euro-5 comparisons (2020)



Pharma production in € B

Sources: EFPIA Key Data (2022) – Leem (2023) – CDMO France website (as of March 2023) Smart Pharma Consulting analyses

- French pharma production is supported by 271 sites with strong technological and logistical expertise
- 32 of them are specialized in the production of biologic substances for human or animal purposes
- However, France faces an increasing competition from other European countries. Out of the 488 drugs authorized in Europe¹ only 42 were produced in France (vs. 112 in Germany or 48 in Spain)
- With 35,171 jobs, of which ~16,000 in CDMO², manufacturing accounted for ~35% of pharma employment in France in 2020
- This share rises to ~44% if we add "Quality, Environment, Health and Safety" functions³
- The French "Healthcare Innovation 2030" plan⁴ will support industrial investment with a fund of € 3.5 B

 1 Between 2016 and 2021 – 2 Contract Development and Manufacturing Organization – 3 Functions closely linked to production – 4 Based on a proposition of the CSIS (Strategic Council for the Healthcare Industries)



The financial support of the French government to the manufacturing of healthcare products, as decided in its "Healthcare Innovation 2030" plan, focuses on biotherapies

Biopharma production – Euro-5 comparisons (2022)

Number of biotherapies manufactured per country as of 2022¹



- ~95% of biotherapies dispensed in French hospitals are imported
- The production of biotherapies in France is the lowest amongst the EU-5 countries
- This situation is mainly explained by a historical lack of investment in the past few decades
- The LEEM² proposed in 2019 the creation of a fund to strengthen the biomanufacturing capacities of pharma companies, CDMOs³ in France
- The French government "Healthcare Innovation 2030" plan launched in 2021, includes the financial support of industrial investment through calls for projects and the financial leverage of Bpifrance⁴
- An objective of 20 biotherapies manufactured in France, by the end of 2030, has been set

¹ Out of 167 approved by the EMA between 2012 and 2019 – ² Association of the pharmaceutical companies in France – ³ Contract Development and Manufacturing Organizations – ⁴ Public investment bank supporting innovative projects carried out by SMEs (Small- and Medium-sized Enterprises)



The positive French pharma trade balance does not precisely reflect the gap between production, import and export due to significant parallel exports and distribution platforms

Pharma trade balance – Euro-5 comparisons (2020)



- The share of French drug export in the Euro zone has fallen from 20.8% to 9.5% between 2001 and 2020 (-11.3 pts)
- Given the low prices imposed on reimbursed drugs, France is an important source of parallel exports
- France exports drugs mainly to the US, Belgium and Germany
- Germany is the largest exporter of drugs in world, which is mainly explained by its:
 - Expertise and skilled workforce
 - Favorable investment climate
 - Distribution platforms
 - Excellent infrastructures (e.g., Hamburg Port, Frankfurt Airport)
 - Geographical location, in the heart of Europe

Sources: EFPIA Key Data (2022) – LEEM export and import (2023) – The pharmaceutical industry in Germany (gtai.de) (2022) – Smart Pharma Consulting analyses



Most of the key pharma manufacturers in France are French companies and amongst the top 5 CMDOs¹ the majority of their revenues come from local sales

Key pharma manufacturers in France

	Pharma Companies	CDMOs			
sanofi 🕕	 # of factories in France: 16 # of employees in French production sites: 13,570² 	 DELPHARM 2021 Global turnover: € 950 M 2021 France turnover: € 545 M # of factories in France: 12 # of employees in France: 3,766 			
S Pierre Fabre	 # of factories in France: 11³ # of employees in French production sites: data not available 	 FAREVA ● 2021 Global turnover: € 900 M⁴ 2021 France turnover: € 650 M # of factories in France: 13 # of employees in France: 3,700 			
GSK 🏶	 # of factories in France: 3 # of employees in French production sites: 2,375 # of factories in France: 3 	 2022 Global turnover: € 380 M 2021 France turnover: € 214 M # of factories in France: 4 # of employees in France: 1,164 			
	 # of employees in French production sites: 1,500 # of factories in France: 2 # of employees in French production sites: data 	CECEXI creating innovative partnerships			
	 not available # of factories in France: 2 # of employees in French production sites: 1,700 	Synerlab GROUP GROUP • 2021 Global turnover: € 145 M • 2020 France turnover: € 108 M • # of factories in France: 5 • # of employees in France: 706			

Sources: Companies websites – "Le marché du façonnage pharmaceutique et ses mutations", Xerfi (September 2022) – CDMO France.com – pharmaboardroom.com – Smart Pharma Consulting analyses ¹ Contract Development and Manufacturing Organizations –² Excluding employees from the Tours factory (data not available) –³ Including dermo-cosmetic facilities –⁴ Pharmaceuticals and API



France is considered as one of the most attractive countries in terms of public incentives, thanks to the wide range of incentives proposed, notably its "CIR" tax credit¹

Incentives to attract investments - Euro-5 comparisons

Incentives types					
Tax credits	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
Cash grants (for R&D or industrial projects)	\checkmark	\checkmark		\checkmark	\checkmark
Loans	\checkmark	\checkmark		\checkmark	\checkmark
Reduced tax rates	\checkmark				\checkmark
Reduced social security contributions	\checkmark			\checkmark	
Accelerated depreciation on R&D assets	\checkmark			\checkmark	\checkmark
Tax deduction			\checkmark		\checkmark
Tax exemptions				\checkmark	
Patent-related incentives	\checkmark		\checkmark	\checkmark	\checkmark

Sources: Worldwide R&D incentives, EY (July 2022) – PwC study for the Leem (2022) – Overview of tax incentives for health R&D, KPMG (October 2021) – Smart Pharma Consulting analyses

¹ "Crédit Impôt Recherche" is a research tax credit on 30% of eligible R&D expenses (incl. staff costs and other operating expenses, depreciation of R&D fixed assets, etc.) up to € 100 M expenditure, and 5% of expenditure beyond that

To strengthen its position as a global hub for health technologies, France has recently taken initiatives to foster investments in manufacturing (notably in bioproduction) and research

Key recent initiatives – France

Key recent initiatives to enhance France attractiveness

- € 3.5 B fund to support industrial investment by 2030
- € 1.2 B budgetary envelope for the decarbonation of industry



- € 25 B additional public investment in the French research system over the next 10 years
- € 3.5 B fund to boost pharma R&D by 2030
- € 800 M R&D tax credit per year for the health industry (30% of annual R&D expenditure up to \in 100 M per company)
- € 300 M to facilitate bridges between private and public research through temporary placement (12 to 14 months) of private R&D personnel in public laboratories with 80% of the salary covered by the State

Sources: "Shaping France as one of the most competitive, innovative healthcare hubs", Choose France (June 2021) – Smart Pharma Consulting analyses

Strategic priorities

Ambition

Be recognized as a global hub for

country to produce innovative

biological therapies

health technologies (e.g., digital

health, AI) and the first European

- Welcome more foreign investors
- Attract and develop disruptive technologies (e.g., digital health, AI)
- Lower bioproduction costs
- Create a network of starts-ups and SMEs¹
- Reinforce offer in new technologies training



March 2023





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Germany's recent initiatives aim at enhancing local manufacturing (to reduce its dependency on other countries) while fostering R&D, notably in oncology, immunology and infectious diseases

Key recent initiatives – Germany



Ambition

- Develop complete value chain to boost "self-sufficient" production
- Achieve 3.5% GDP in R&D expenditure (vs. 3.2% in 2018)

Strategic priorities

- Achieve self-sufficient pharmaceutical production
- Foster research & innovation, while prioritizing oncology, immunology and infectious diseases research
- Attract new foreign investments
- Strengthen partnerships and alliances at national and international levels

Key recent initiatives to enhance Germany attractiveness



- € 1 B invested in 2020 for economic stimulus to expand production capacity and reduce the dependency on global supply chains
- Vaccine Production Taskforce launched to become a major vaccine production site in the world
- ► > € 7 B yearly investment in pharma R&D to strengthen Germany's research excellence position
- Funding options (e.g., grants, loans with attractive interest rates, public funding programs) to incentive biopharma players
- Labor-related incentives and subsidies to build strong R&D teams (e.g., financial support in recruitment, training and wages)
- <u>)</u>
- Multi-sectoral collaborations to trigger creative R&D solutions
- Intensification of collaborations between international and leading German cancer research institutions
- Germany's large population size leveraged to attract clinical research in **orphan diseases** where participant recruitment is difficult

Sources: "Global Heath Strategy", German Federal Government (October 2020) – "The Pharmaceutical industry in Germany", Germany Trade & Invest (Issue 2021-2022) – Smart Pharma Consulting analyses

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UK initiatives aim at fostering sciences and research (through increased investment in R&D, innovation fund and patient enrollment facilitation) and developing skills in AI, data and digital

Key recent initiatives – UK



Ambition

- Achieve 2.4% GDP in R&D expenditure by 2027 (vs. 1.8% in 2019)
- Develop skills in AI, data and digital

Strategic priorities

- Invest in sciences, research & discovery to make UK a leading hub for advanced therapies
- Attract long-term investments
- Provide access to the largest healthcare and research datasets worldwide, notably in genomic, phenotypic, biological and health data



Key recent initiatives to enhance UK attractiveness

- € 4.6 B¹ yearly investment in R&D to boost science, research & discovery in the UK (notably fundamental biology, genomics and genetics research)
- € 570 M innovative medicines fund
- Patient enrollment facilitation (e.g., setting up of 5 patient recruitment centers, implementation of data-enabled processes, launch of DigiTrials, incentivizing GPs for participant identification)
- € 684 M scale-up investment program in cooperation with British Business Bank and private finance partners
- "2030 Skills strategy" developed with a focus on R&D, medicines manufacturing and emerging technologies



- > 6,000 doctoral and research fellowship awards funded every year
- € 11.4 M pilot scheme to enable NHS consultants with PhD or master's degree to participate in collaborative research partnerships
- Boosted skills in AI through new PhD and master's programs
- NHS involvement in the development of digital skills

 1 GBP 1 = € 1.14



Several levers can be activated to strengthen France's attractiveness in an international context where more and more countries seek to boost R&D investment and relocate drugs manufacturing

How to enhance the attractiveness of France for pharma companies?



Sources: Smart Pharma Consulting analyses

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Consulting firm dedicated to the pharmaceutical sector operating in the complementary domains of strategy, management and organization

Market Insights Series

- The Market Insights Series has in common to:
 - Be well-documented with recent facts and figures
 - Highlight key points to better understand the situations
 - Determine implications for key stakeholders
- Each issue is designed to be read in 15 to 20 minutes and not to exceed 25 pages

Is France attractive for Pharma companies?

Comparisons & Recommendations

- Smart Pharma Consulting proposes to evaluate France's attractiveness for pharma companies vs. other Euro-5 countries
- To do so, the following topics have been assessed:
 - 1. Pharma market potential
 - 2. R&D capabilities
 - 3. Manufacturing capacities
 - 4. Public incentives

Smart Pharma Consulting Editions



- Besides our consulting activities which take 85% of our time, we are strongly engaged in sharing our knowledge and thoughts through:
 - Our teaching activities in advanced masters (ESSEC B-school, Paris Faculty of Pharmacy)
 - Training activities for pharma executives
 - The publication of articles, booklets, books and expert reports
- Our publications can be downloaded from our website:
 - 41 articles
 - 65 position papers covering the following topics:
 - 1. Market Insights
- 5. Marketing

2. Strategy

- 6. Sales Force Effectiveness
 7. Management & Trainings
- Market Access
 Medical Affairs
- Our research activities in pharma business management and our
- consulting activities have shown to be highly synergistic
- We remain at your disposal to carry out consulting projects or training seminars to help you improve your operations

Best regards

Jean-Michel Peny