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The French Pharma Market 2020 – 2025

BUSINESS REPORT

Strategic Implications for Pharma Companies

Excerpts

May 2021

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Section 2. The French pharmaceutical market p. 234

This report analyzes the current situation and the key trends on the French Pharma market by the end of 2025 to provide pharma companies with key strategic insights

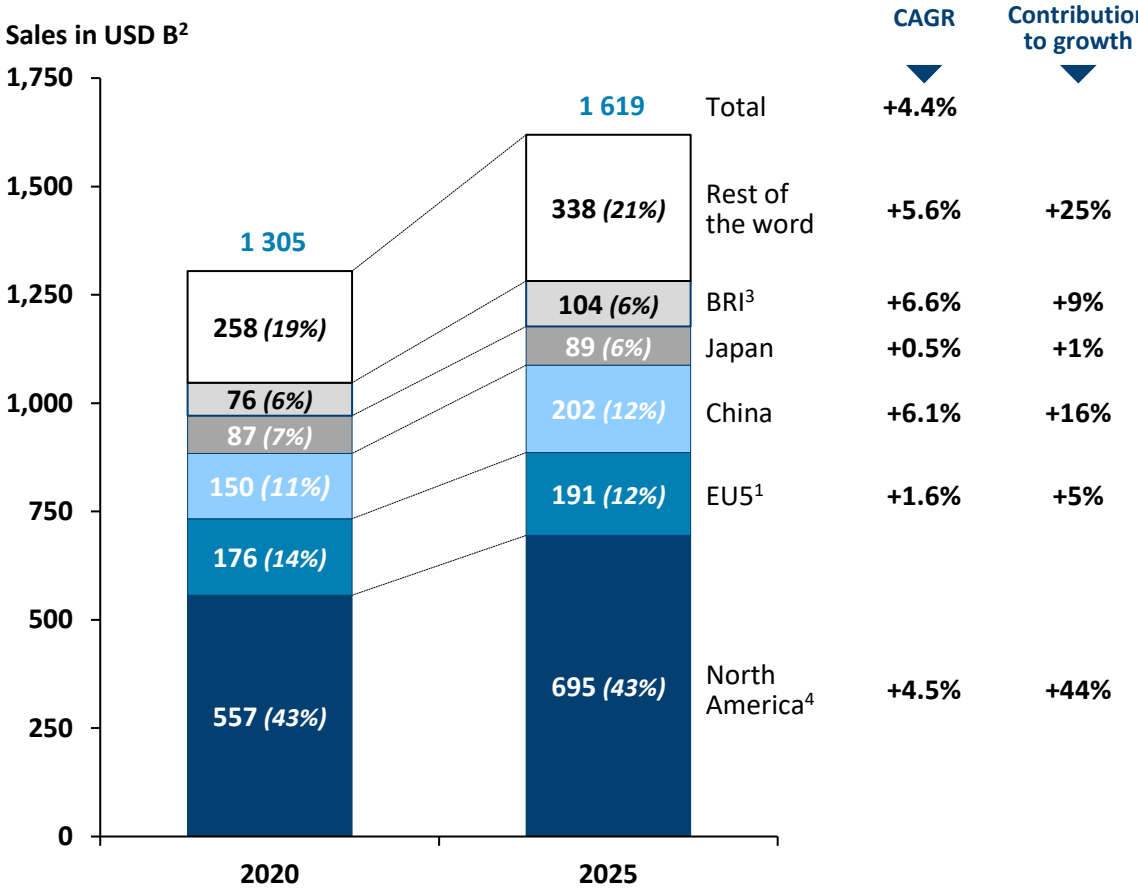
2020 – 2025 French pharma market prospects & strategic implications

- Despite an ever-tougher environment, the French pharma market should remain a key priority for most of pharma groups
- Smart Pharma Consulting proposes to address the following key issues related to the French healthcare system and pharma market evolution by the end of 2025, to better grasp its strategic impacts for pharma companies

- How is the French healthcare system organized at national and regional levels?
- What are the key recent measures introduced by health authorities and their impact?
- What are the behavioral trends of key stakeholders and their impact by 2025?
- What are the estimated sales forecasts by strategic segment on the French pharma market by 2025?
- What could be the strategic and organizational implications for pharma companies by 2025?

Sales of EU5[1] should grow slowly by 2025 due to stringent cost containment measures leading to a two-point decrease of their weight in the global pharmaceutical market

Global pharmaceutical market size and growth by geographic area (2020 – 2025)



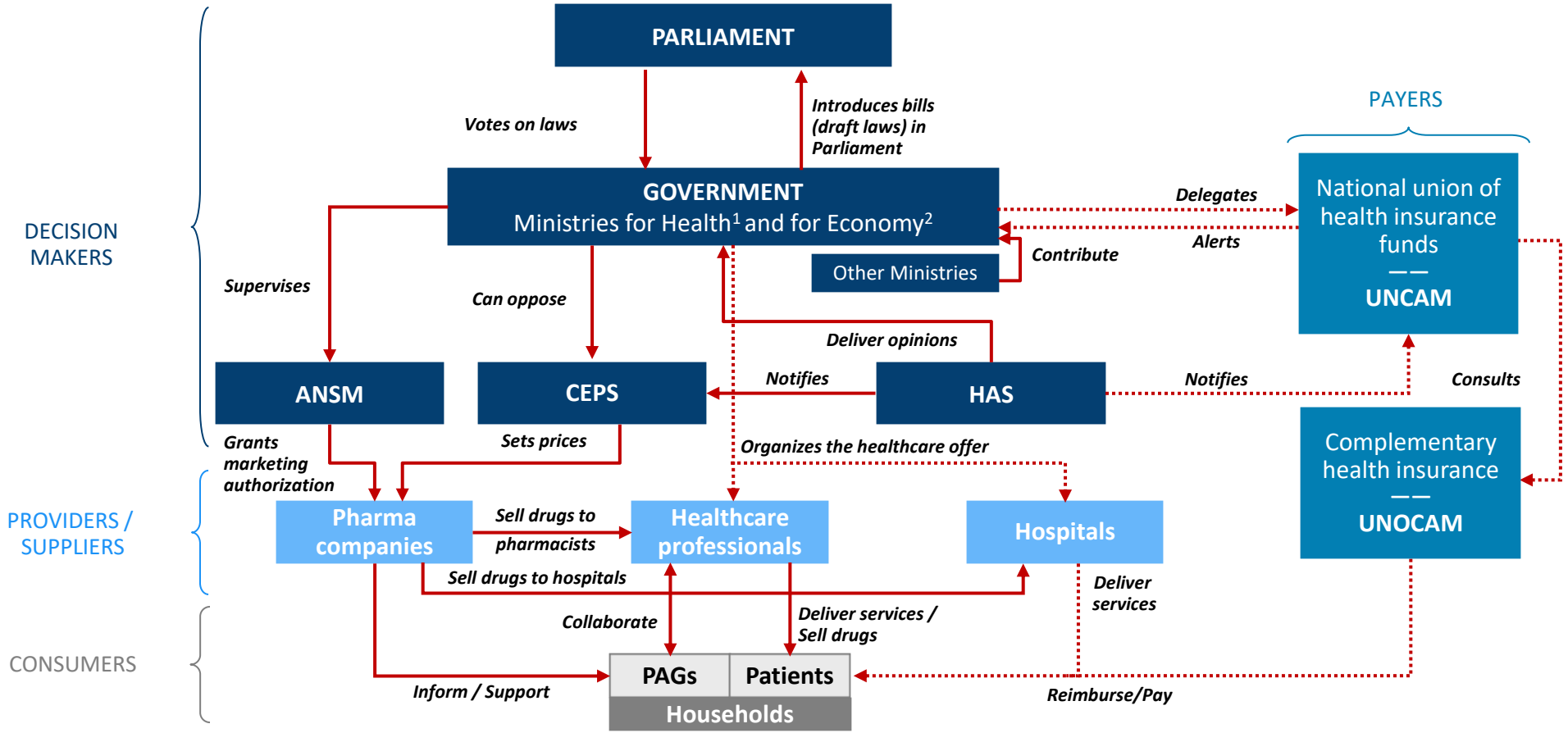
- The global pharma market is expected to grow with of a **CAGR of +4.4%** by 2025 including the impact of Covid-19, that should lead to **higher pressure** on **prices** worldwide in the next 5 years
- **EU5** countries account together for only 14% of the global pharma market (Germany: 4%, France: 3%, Italy: 3%, UK: 2% and Spain: 2%) and should see their **weight drop by 2 points** by 2025, **due** to higher **price pressure** than in the average of the other countries
- **North America** should continue to weigh for 43% of the global pharma market in value and contribute to **44% to worldwide market growth** over the 2020 – 2025 period

Sources: IQVIA Institute (March 2020) – Smart Pharma Consulting estimates

[1] France, Germany, Italy, Spain, UK – [2] Ex-factory price before rebates – [3] Brazil, Russia, India – [4] USA and Canada

Stakeholders in the French healthcare system can be divided according to their role as decision makers, payers, providers / suppliers and consumers

Mapping of key stakeholders

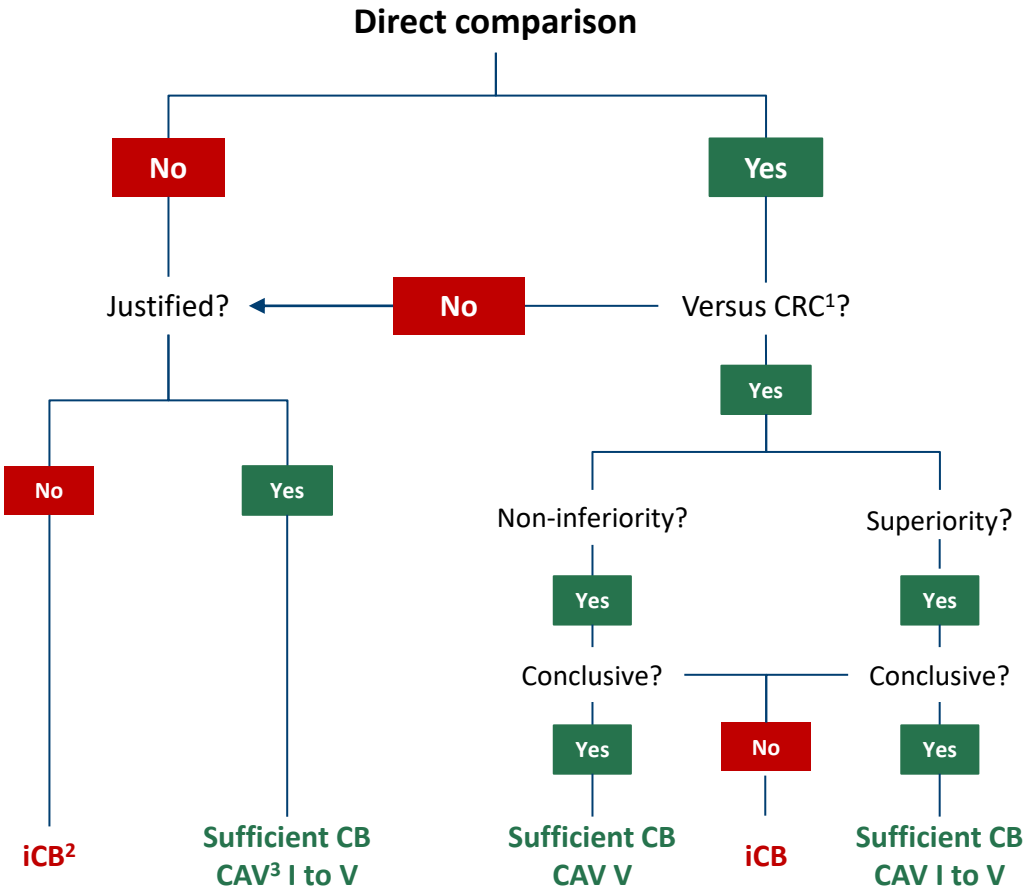


Sources: Smart Pharma Consulting analyses

[1] The exact name of this ministry is: Ministry of Solidarity and Health – [2] The exact name of this ministry is the Ministry for the Economy and Finance which includes the budget and the industry

To assess the therapeutic progress of a product, the Transparency Committee will expect direct comparison – whenever possible – in terms of efficacy and safety with existing relevant therapies

Transparency Committee – Clinical added value (CAV) assessment



- The Transparency Committee (TC) will particularly pay attention to the following criteria, in view of medical need:
  - The quality of the demonstration:
    - The choice of comparator(s)
    - The methodological quality of the study
    - The appropriateness of the population included
    - The relevance and significance of clinical endpoints
  - The effect size in terms of clinical efficacy, quality of life and safety in view of the demonstration robustness
  - The clinical relevance of this effect compared to clinically relevant comparators
- Double-blind, randomized controlled studies is a prerequisite
- The absence of direct comparison to comparator must be justified and may be accepted by the TC in certain situations
- The absence of a direct comparison, which the TC believes was possible, may lead to an ASMR V
- The TC reasoning presented in this figure is not fixed and is adapted to the context of each evaluation

Sources: Transparency Committee doctrine December 2020 – Smart Pharma Consulting analyses

[1] Clinically Relevant Comparator – [2] Insufficient Clinical Benefit – [3] Clinical Added Value

The framework agreement signed between CEPS and Leem in March 2021 aimed at improving patient access to innovation, encouraging investments in France and simplifying access processes

CEPS – Framework agreement signed with the Leem (2021 – 2024)

Context & objectives

- Framework agreement signed on **March 5, 2021** by Philippe Bouyoux (**CEPS**) and Frédéric Collet (**Leem**), in the presence of Olivier Véran (Minister of Health) and Agnès Pannier-Runacher (Delegate to the Minister of Economy in charge of Industry)
- This new agreement, that replaces the previous one which had been signed in 2016, has been concluded for a **3-year period**, i.e., until March 5, 2024
- **3 main objectives** pursued:
  - Improve **patient access** to **innovation**
  - Encourage **productive investments** in France
  - Simplify **market access** processes

Patient access to innovation

Innovative drugs

- Guidance on the duration of effect of comparators, the inclusion on uncertainty, the setting of rebates and the splitting of payments

Orphan drugs

- Possibility of renegotiating the terms of conventional rebates if target population evolves
- Commitment to come to a contractual amendment within 6 months with an adjusted budget package

Drugs that meet public health needs

- Possibility for ASMR IV drugs meeting a non- even partially-covered medical need to access to an EU price[1]

Productive investments in France

Support for investment and export

- Creation of a specific chapter intended to support for investment and export
- Authorization for investing pharma companies to proactively meet with the CEPS President to be informed of conventional terms

Pricing counterparties

- Possibility of granting a EU price[1] to ASMR I to III drugs whose manufacturing activities[2] are mainly carried out in France
- List price stability guaranteed over 2 years (renewable once) for products manufactured in Europe (notably in France) for which more than 60% of volumes are exported

Market access processes

Fast-track

- Access guaranteed within a maximum period of 15 days for:
  - ASMR I to III with dominant efficiency
  - ASMR IV with dominant efficiency & allowing savings
  - ASMR V with prices lower than comparators

Price stability and predictability

- 5-year stability of the EU price[1] for ASMR I to III drugs, covering both list and net prices

Transparency

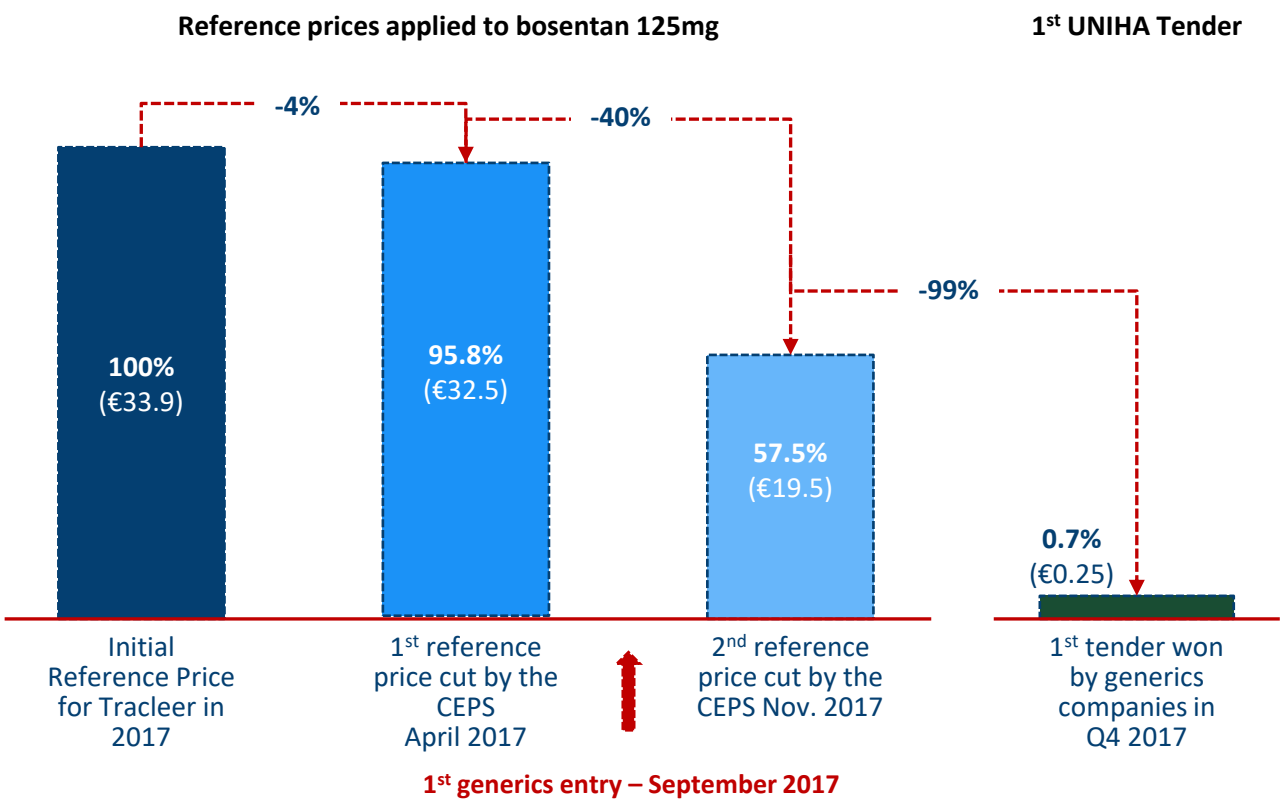
- Statement by pharma companies of the amount of both R&D investment made, and public incentives received

Sources: Framework agreement signed between CEPS and Leem (March 5, 2021) – Smart Pharma Consulting analyses

[1] In this case, French price cannot be lower than the lowest price in the rest of EU5 (Germany, UK, Italy and Spain) –
[2] Including the manufacturing of active components, finished goods and/or packaging

Bosentan net price has dropped drastically as soon as the 1st call for tender, enabling the best bidder to discard competitors while taking the risk to make this "market" little or even non profitable

CEPS – Hospital generics pricing: Bosentan (Tracleer)



Comments

- For bosentan, the purchasers did not really value the quality of the dossier
- **UNIHA**[1] and the **AGEPS**[2] account for **80%** of the total bosentan market
- The UNIHA market has been won at €0.25, Teva offered €0.50, and the originator price was €19
- The prices on generics **should go up** for the future calls for tender
- The prices should not remain at this level, which is **unlikely to generate profits**
- Such a **drastic** drop was not expected by Actelion (Janssen)
- Few small accounts do not list generics of bosentan
- Janssen doesn't discount beyond -75%

Sources: Business Intelligence – Smart Pharma Consulting analyses

[1] Purchasing group for the Regional Teaching hospitals and other public hospitals – [2] Purchasing group for largest public hospitals in Paris and close suburbs

The prices, margins and level of rebates are regulated by the CEPS throughout the value chain of the reimbursable products, either originators or generics

CEPS – Prices, margins and rebates for reimbursable drugs

	Originator without TFR[1]	Originator with TFR	Generic without TFR	Generic with TFR
Ex-factory price	▪ Price negotiated / set by the CEPS ▪ Generics are priced 60% below originator price at patent expiry ▪ After generics launch, originator price is cut by 20%			
Wholesalers' margins	▪ Minimum of € 0.30 per pack if ex-factory price below € 4.33 ▪ 6.93% of ex-factory price if ex-factory price from € 4.33 to € 468.97 ▪ 0% beyond € 468.97, representing a maximum of € 32.50 margin per sold unit			
Pharmacists' margins	▪ Variable margin: – 10.0% of ex-factory price below € 1.92 – 7.0% from € 1.92 to € 22.90 – 5.5% from € 22.91 to € 150.00 – 5.0% from € 150.01 to € 1,930.00 – 0% above € 1,930.00 ▪ Dispensing fees (VAT excluded): – € 1.00 per pack – € 0.50 per prescription including at least 1 reimbursable drug – € 1.00 per prescription with at least 5 medicines – € 1.55 if the patient is 3 years or under or over 70 years old – € 3.50 for specific drugs (e.g., immunosuppressive drugs)	Margin in absolute terms identical to the corresponding originator	Calculation identical to the originator's one
Pharmacists' rebates[2]	▪ Maximum legal rebate: 2.5% of ex-factory price	▪ Maximum legal rebate: 40% of ex-factory price, since September 2014 (17% before)		
	▪ Possibility to add up to 100% of the wholesaler margin in case of direct sales			

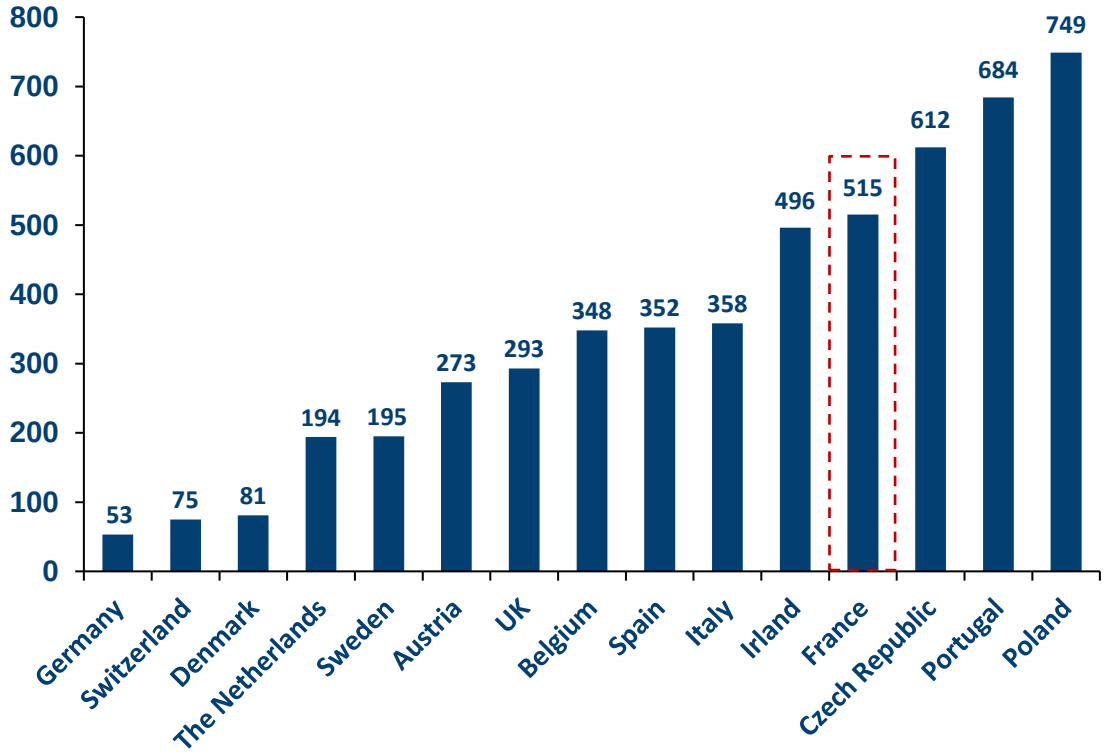
Sources: CEPS annual report (September 2020) – Legifrance (e.g., decree on September 14, 2020 intended to reevaluate wholesalers' margin from February 1, 2021) – Ameli – Leem –Smart Pharma Consulting analyses

[1] Tarif Forfaitaire de Responsabilité (Reference price) – [2] Including cooperation and other commercial rebates

In France, pharma companies and patients must wait ~17 months after marketing authorization to get a new drug reimbursed and launched[1]

Average time to market access – European comparisons

Median time in days between marketing authorization and price and reimbursement[1,2]



2019 analysis based on a sample of 172 products approved by EMA (European Medicines Agency) between January 2015 and December 2018

- In Europe, the delay between marketing authorization of a drug and its availability on the market may vary widely, due to the time required to obtain its inclusion on reimbursement list and a price agreement
- In countries such as France, Italy or Spain, this delay exceeds the 180 days recommended by the European Commission
- An important delay may be harmful both for patients who do not have full access to innovative therapies and for companies which face a loss of revenues[1]
- The UK and Germany have no delay since the price and reimbursement negotiations occur once the product has reached the market

- In 2018, the Leem (French association of pharmaceutical companies) has carried out a study on 67 new products, showing an average time between marketing authorization and price & reimbursement of 563 days

Sources: Patients W.A.I.T. Indicator – EFPIA (June 2020) – Smart Pharma Consulting analyses

[1] Excluding early access programs for breakthrough innovations (e.g., ATU in France) – [2] For drugs receiving their first marketing authorization between 2015 and 2017

Since the introduction of the T2A reform in 2004, the allocation of resources of public and private hospitals is based on the nature and on the volume of the activities carried out by hospitals

Hospital funding system: Activity-based financing (T2A) principles

Objectives	Means	Expected results
Increase the efficiency of hospitals	▪ Converge funding systems to be able to compare public and private sectors ▪ Gradually implement the T2A to facilitate the adaptation of both structures and players ▪ Harmonize funding arrangements between public and private sectors ▪ Expand the clarity and the visibility of the role of the players, for both managers and supervisors	Greater involvement of medical players in financing
Address the inequity of resources allocation across structures		Accountability of health players
Optimize the funding of the most active structures		Development of quality management and medico-economic tools
		Fairness of treatments between public and private sectors

Major drawback

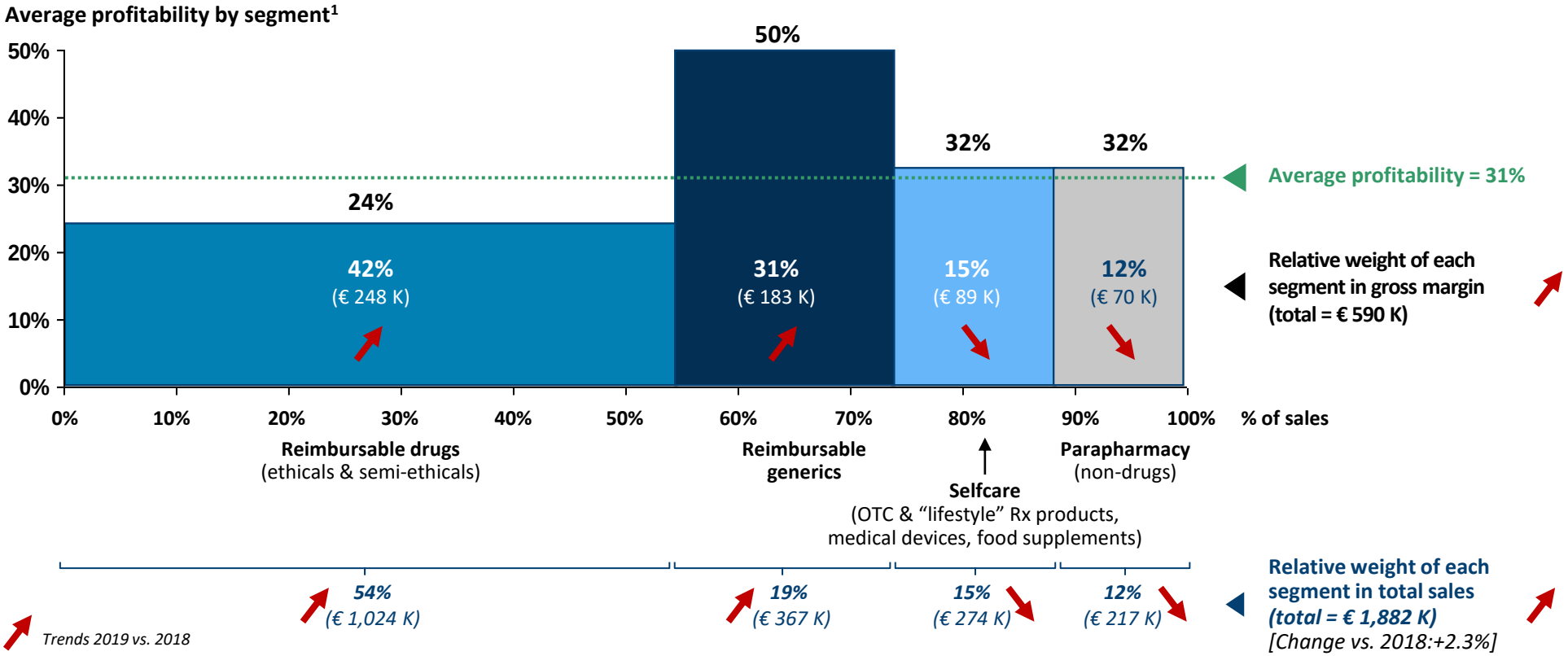
The T2A has led to an inflationary effect; hospitals being prompted to increase their level of activities and notably of the most profitable medical procedures, for maintaining adequate funding

Sources: French Ministry of Health, as of February 2021 – Smart Pharma Consulting analyses

In 2019, originators accounted for ~54% of the retail pharmacies sales on average and for ~42% of their gross margin

Economic structure of retail pharmacies in France (2019)

Average annual turnover of a retail pharmacy in 2019: € 1,882 K
(public price excluding VAT)



Note: Dispensing fees and ROSP accounted for ~48% of the retail pharmacy margin on reimbursed drugs

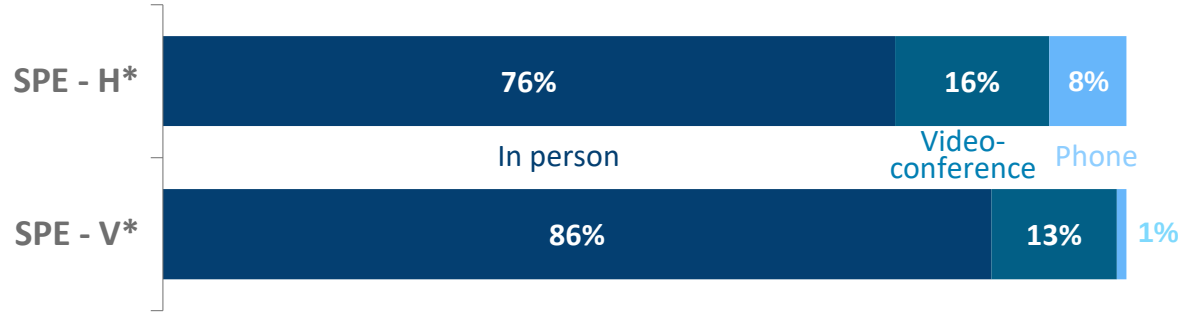
Sources: CGP Experts Comptables – KPMG – Smart Pharma Consulting estimates

[1] Inclusive of legal margin, rebates, commercial agreements and remuneration for pharmaceutical services, notably those corresponding to the public health objectives (e.g., generics substitution objectives, pharmaceutical interviews with patients, etc.)

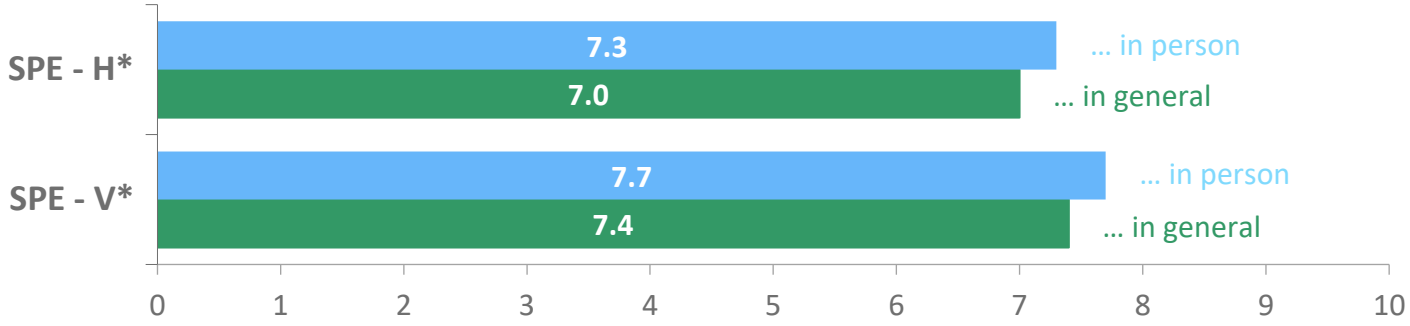
Specialists keep on preferring in person interactions with med reps to communicate about innovations and they remain attached to this communication channel

Access to HCPs in France (2020 – 2021)

Most appropriate channels for med reps to communicate about innovations (product, indications, dosage, etc.)[1]



Attachment to medical calls…



* : SPE-H (Hospital-based specialists) – SPE-V (Office-based specialists)

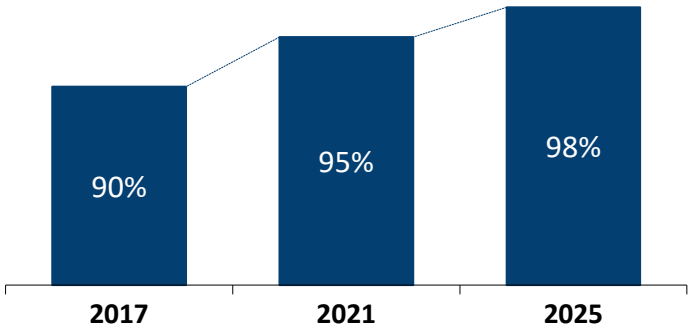
Sources: Leem (September 2020) – Smart Pharma Consulting analyses

[1] 150 office-based specialists and 150 hospital-based specialists, whom 35 dermatologists interviewed on-line in June 2020

Med reps are not viewed by physicians as a robust, updated and convenient source of scientific information, which means that they must bring high-value services to stay connected to them

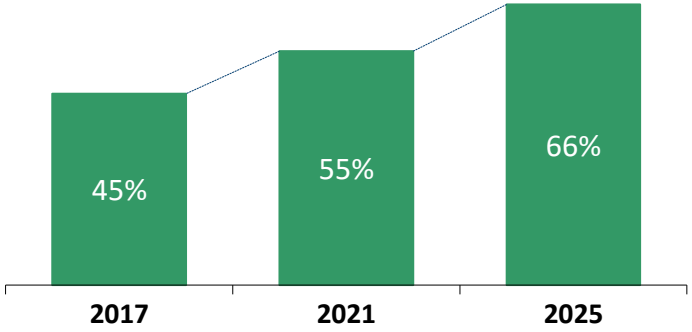
Access to HCPs in France (2017 – 2025)

Online scientific search by physicians
(% of total)



- Physicians becoming more familiar with the Internet, they are increasingly finding information online, as needed
- The Covid-19 crisis has accelerated the usage of digital channels by physicians to find scientific information
- Product-related is the most accessed website resource

Credit given to pharma websites by physicians
(% of total)



- 50% or more physicians using search engines, rely on pharma companies' digital resources
- Most of pharma companies have designed product-related websites, with objective and well-presented information
- Thus, these websites have a certain influence on physicians' prescribing decision

For scientific data, including those related to products, online websites are the first source of information, while pharma companies' websites are gaining credibility with physicians

Sources: Smart Pharma Consulting estimates and analyses based on multiple historical studies (e.g., DRGs – ZS – McKinsey)

LFSS 2020 modified the provisions to be granted an ATU, introduced constraints to prevent drug shortages and encouraged generics substitution, while quashing biosimilar substitutability law

LFSS 2020 key articles regarding drugs and pharma companies (1/2)

Safeguard clause for drugs (Article 24)

- For 2020, the safeguard clause to drugs, called the "M" rate, has been set at +0.5%, while it had been set at +1.0% for 2019

Financial sustainability of the ATU (early access program) (Article 44)

- This article concerns filings for ATUs applied before March 1, 2020 and modifies the conditions to obtain a nominative ATU (ATUn):
  - The drug efficacy should be important and clinically relevant
  - Refusal of ATUn if previous demands for cohort ATU (ATUc), clinical trial or in case of increased risk with the existing treatments have been rejected
  - Free pricing of ATUn is replaced by a compensation set by the government
- The receivability of a demand for an ATU is subject to the following conditions:
  - The number of ATUn for a given drug will be limited by a Ministerial Order
  - The drug has not yet been granted a marketing authorization or an ATUc
- Communication to the pharma company of the possible estimated amount that could be funded by the National Health Insurance Fund after the ATU ends
- The CEPS can set up a schedule a payment of discounts for a period beyond one year

Prevention of drug shortage (Article 48)

- Pharma companies must have buffer stock of 4 months located in Europe
- Financial penalty will be imposed to pharma companies in case of failure

Various measures regarding cost of drugs (Article 42)

- A ministerial order can set a maximum selling price for a drug to hospitals:
  - When there is risk of unjustified expenditure
  - In case of expensive health product
- Relaxation of the rules to substitute drugs with narrow therapeutic margins that will be clarified by an implementing decree
- Modification of the Article 66 (LFSS 2019) stipulating that if a patient refuses a generic[1], he will be reimbursed based on the price of the most expansive generic. This rule will start two years after the publication of the 1st generic's price and will be implemented on January 1, 2022, at the latest
- Repeal of the law authorizing biosimilar substitution by retail pharmacists[2]
- A working group will be set up to determine the inter-changeability between biologic drugs
- Manufacturers are authorized to file a registration dossier for a biosimilar before the patent expiry of the corresponding original biologic

Sources: LFSS 2020 – "Loi de Financement de la Sécurité Sociale pour 2020" NILE Consulting – Smart Pharma Consulting analyses

[1] For non-valid reasons – [2] This law created by the LFSS 2014 has never been implemented in the absence of a decree defining the conditions of substitution

Launched in December 2019, the Health Data Hub[1] is a new French platform designed to cross-reference existing health databases for medical research purposes

Health Data Hub

SNDS[2]
National Health Data System

- **PMSI** – Information Systems Medicalization Program (Hospital data)
- **SNIIRAM** – National Health Insurance Inter-Plan Information System (National Health Insurance Fund data)
- **CNSA** – National Solidarity Fund for Autonomy (Disability data from MDPH)
- **CépiDC-Inserm** – Electronic certification of causes of death (Medical causes of death)
- **Complementary health insurance companies** (Sample of data)

Aggregating and making these data available to promote studies, research or evaluation of a public interest nature and contributing to the :

- Information on health
- Implementation of health policies
- Knowledge of health expenditures
- Information of professionals and institutions about their activities
- Innovation in the fields of health and medico-social care

Definition
- New French **health data platform**, created in **December 2019**, that allows to cross-reference existing health database and thus facilitate their use for research and development purposes

Objective
- Based on the **Artificial Intelligence**, create a platform for accessing and sharing data, in the service of **health research** and **innovation**

Pros
- **Health issues**: improving research and development
- **Competitive advantage** at international level for research and innovation

Cons
- **Sensitive** and **personal data** that can be used if there is a public interest and after the CNIL's[3] consent
- Data hosted by **Microsoft**: **exposure to US law** (Cloud Act)

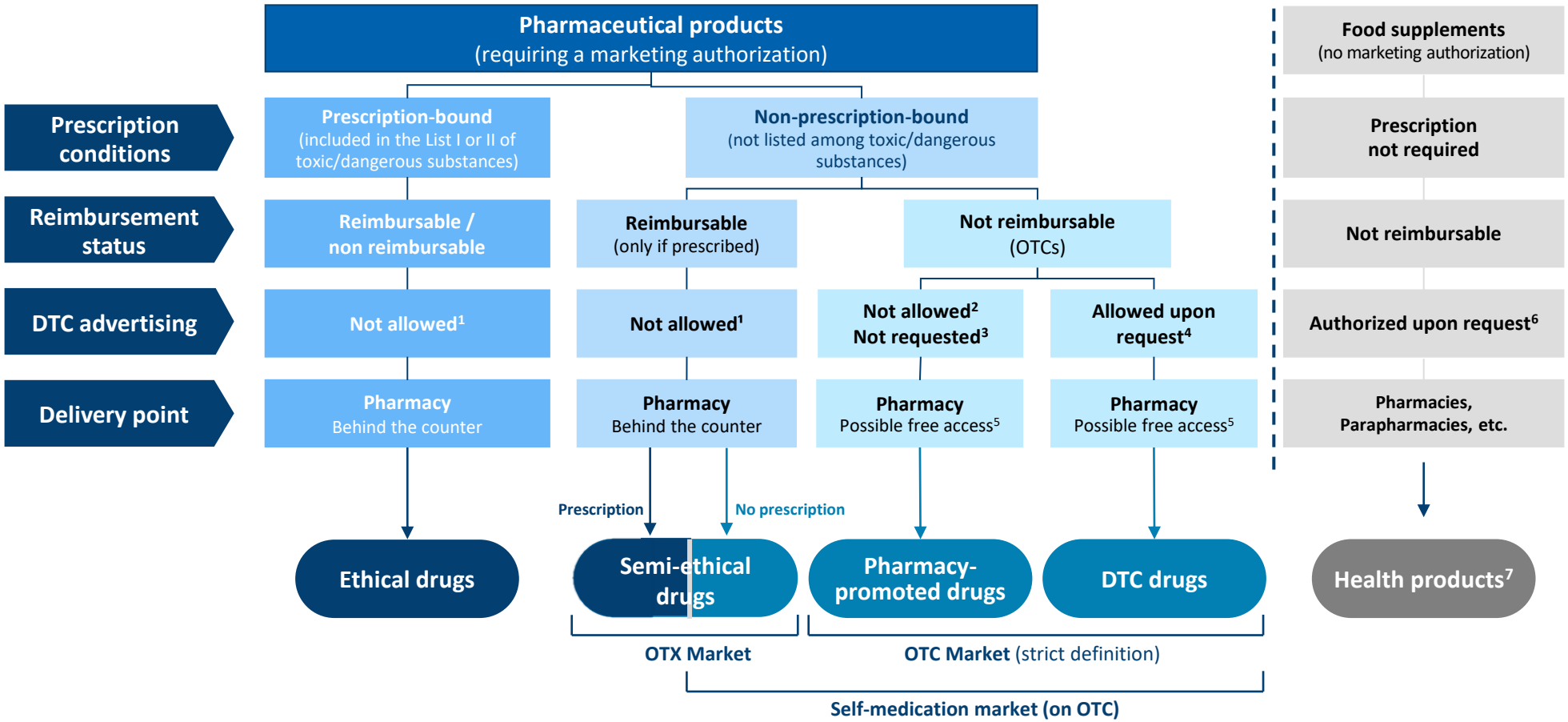
Implication for pharma companies
- **Perspectives of interest** at each stage of the drug or medical device value chain, from research to development, including monitoring the use of healthcare products in real life and organizing care pathways
- **Access to data**, not accessible as of today
- Additional place to forge **new links and partnership relations** with the players of the ecosystem, whether public or private

Sources: "La Plateforme des données de santé (Health Data Hub)", CNIL (February 2021) – "Health Data Hub : 6 questions sur la plateforme de données de santé et sa polémique", Numerama (June 2020) – "Le Health Data Hub : quelles opportunités pour l'industrie pharmaceutique ?", Alcimed (July 2020) – Smart Pharma Consulting analyses

[1] Also named PDS (Plateforme des données de santé) – [2] Système National des Données de Santé – [3] Commission Nationale de l'Informatique et des Libertés (National commission for information technology and civil liberties)

Pharmaceutical products can be split into prescription-bound and non-prescription-bound drugs, knowing that some of the prescribed drugs are not reimbursed

Classification of pharmaceutical products in France



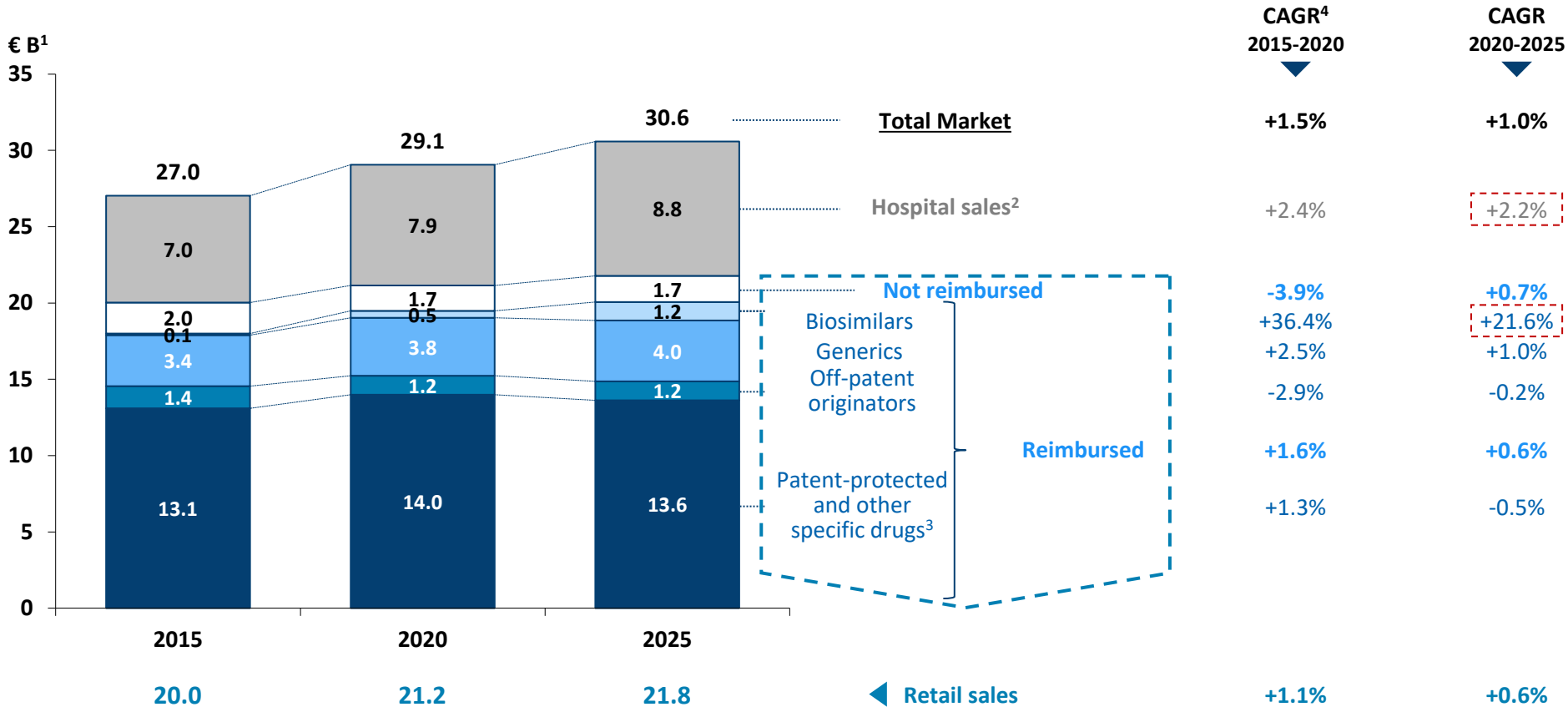
Note: OTC = Over-the-counter, OTX = combination of prescription (RX) and over-the-counter (OTC), DTC = Direct to consumer

Sources: ANSM – DGCCRF – Smart Pharma Consulting analyses

[1] Rare exceptions (e.g. vaccines) – [2] Psychotropic or narcotic drugs – [3] When the pharma company does not wish to communicate to the general public – [4] Whatever the claims – [5] Possibility of "free access" within the retail pharmacy for certain OTC products – [6] Only for claims relating to healing, alleviating or preventing diseases – [7] Other than drugs and pharmaceutical products

By 2025, the French pharmaceutical market should be mainly driven by innovative hospital products and biosimilars

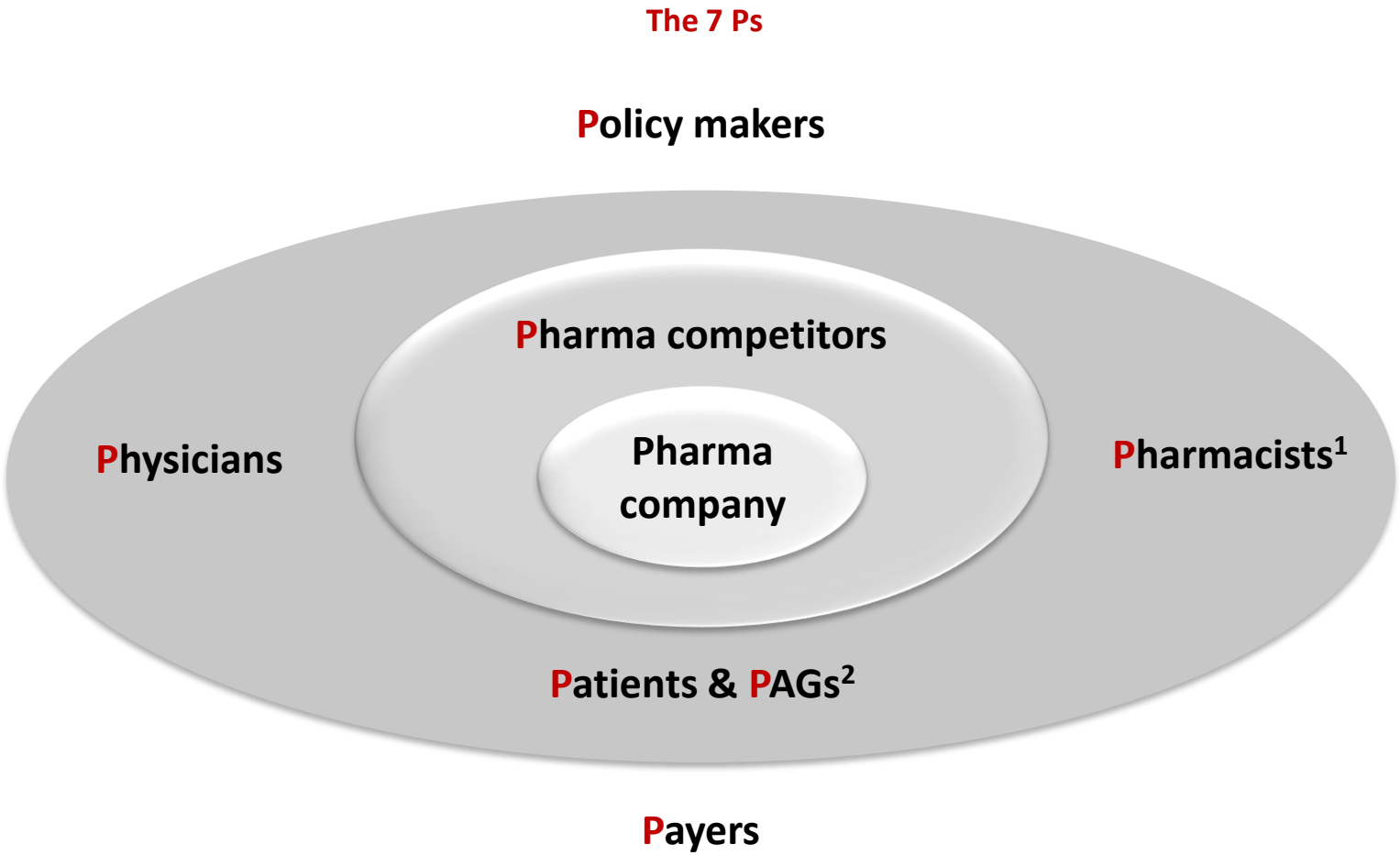
Drugs sales forecast by segment (2015 – 2020 – 2025)



Sources: GERS dashboards – Smart Pharma Consulting estimates

¹ Constant ex-factory prices – ² Estimated rebated sales including hospital sales of biosimilars, products invoiced on top of "T2A" and reassigned medicines
³ Sales of drugs whose patents have not expired and of other specific products (calcium, sodium, potassium, paracetamol, etc.) – ⁴ Compound annual growth rate

Pharmaceutical companies' strategic priorities by 2025 will be linked with the behavior of the "7 Ps" stakeholders



Sources: Smart Pharma Consulting analyses

[1] Pharmacists also play the role of purchasers and their importance will keep on increasing in the upcoming years, either on the open care or the hospital segments – [2] Patient Advocacy Groups

Policy makers & Payers will work jointly to secure the sustainability of the healthcare system, implying its redesign and the introduction of new measures and possibly new taxes

Stakeholder behavioral trends: Policy makers & Payers (1/4)

2020 – 2025 Trends

Global cost optimization

- Increase of the ONDAM in the range of +4.5% p.a. by 2025, compared to +2.5% on average between 2015 and 2020
- Research of new funding mechanisms to ensure a better sustainability of the healthcare system
- Reorganization of the healthcare system to improve its efficacy and efficiency
- Reduction / prevention of National Health Insurance Fund deficit

Driving factors

- Healthcare costs and economic turmoil induced by the Covid-19 outbreak should increase healthcare expenditure as a percentage of GDP, from ~11.2% in 2019 to 13.2% in 2025 and widen the National Health Insurance Fund deficit
- 78% of healthcare expenditure are funded by the National Health Insurance Fund; whose 90% of revenues are generated by social contributions
- € 19 B investment have been budgeted following the "Ségur de la Santé" consultation (June & July 2020) to improve the healthcare system
- The National Health Insurance Fund has cumulated a deficit reaching a total of € 193 B over the 2008-2020 period, 20% of which has been concentrated in the year 2020

Implications

- Increase of the CSG (+0.9% in 2021) and possibility to introduce new taxes to reduce dependency on social contributions and thus, on the employment
- Redesign of the healthcare system:
  - Shift from hospital to home care
  - Improve hospital / open care markets coordination
  - Improve patient journey efficiency
  - Set up a new framework for funding innovation in the healthcare system[1]
- Introduction of measures and tools:
  - Tighter control of hospital costs
  - Increase price pressure on reimbursed drugs
  - Reinforcement of the ROSP[2] contracts plan for physicians
  - Limitation of access to ALD[3]
  - Budgeting control generalization

Sources: Smart Pharma Consulting analyses

[1] As addressed in the Article 51 of the LFSS 2018 – [2] Bonus program to encourage physicians to comply with "best prescribing practices" for a better efficacy/cost ratio – [3] 100% cost coverage for chronic and long-lasting diseases

Pharma companies must position their products, services and themselves to be perceived by Policy makers and Payers as offering superior value than competition

Strategic priorities induced by Policy makers & Payers behavioral trends

Behavioral trends	Strategic priorities for pharma companies
1 Stricter control of reimbursed drug expenditure 2 Measures to boost generics & biosimilars	Enhance the global value proposition (incl. corporate identity, product and service offering) through: – Dedicated corporate reputation programs targeted at policy makers and government – Generation of data vs. standards of care, real world data and … – … high quality medico-economic studies (whenever relevant) – Initiation / support of specific projects to improve patient care
3 Shift from hospital to ambulatory care	Participate to working groups with health authorities and other stakeholders to: – Facilitate the change management (e.g., development of tools, processes, proposition of training programs) – Ensure it will benefit or be neutral on pharma company performance
4 Promotion of investments in France	Increase or maintain R&D activities to be in a more favorable position to negotiate drugs' price, and weigh – very carefully – the pros and cons before deciding to produce in France

Sources: Smart Pharma Consulting analyses

Smart Pharma
CONSULTING

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

The Smart Pharma Business Reports

- Our business reports have in common to:
  - Be well-documented with recent facts and figures
  - Highlight the key points to better understand situations
  - Propose in-depth analyses
  - Determine the business implications for stakeholders

The French Pharma Market 2020 – 2025 Prospects

- This report has been conceived as a working tool to:
  - Strengthen and align the level of knowledge and understanding of the French pharma market and its key trends by the executives of French affiliates
  - Facilitate the communication, with correspondents of affiliates at the European and/or Global headquarters, regarding the specificities and major trends in France
  - Support the strategic decisions over the next 5 years
- The purchase of this report includes:
  - A two-hour working session to address one or more specific points covered in this report
  - A free access for all collaborators of the pharma group

Smart Pharma Consulting Editions

- Besides our consulting activities which take 85% of our time, we are engaged in sharing our knowledge and thoughts through our:
  - Teaching and training activities
  - Publication of articles, booklets, books and business reports
- Since 2012, we have published **19 business reports** covering the following topics:
  - French healthcare system and pharma market (2021, 2019, 2017, 2015, 2014, 2013, 2012)
  - Market access and drug valuation (2016)
  - French generics market (2017, 2016, 2014, 2012)
  - Global biosimilars drugs market (2015, 2012)
  - Best pharma performers (2015)
  - French pharma distribution (2015, 2012)
  - Digital marketing (2012)
  - French OTC market (2012)
- We expect that this new publication will be helpful

Best regards,

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