# The French Generics Market

## (Including Biosimilars)

Excerpts

Smart Pharma Consulting

Perspectives 2017 – 2022

*Business Report*

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1, rue Houdart de Lamotte – 75015 Paris – France
Tel.: +33 6 11 96 33 78 – Fax: +33 1 45 57 46 59
E-mail: jmpeny@smart-pharma.com – Website: www.smart-pharma.com

# Contents

# This report describes and explains the dynamics of the French generics and biosimilars markets and evaluates their attractiveness by 2022

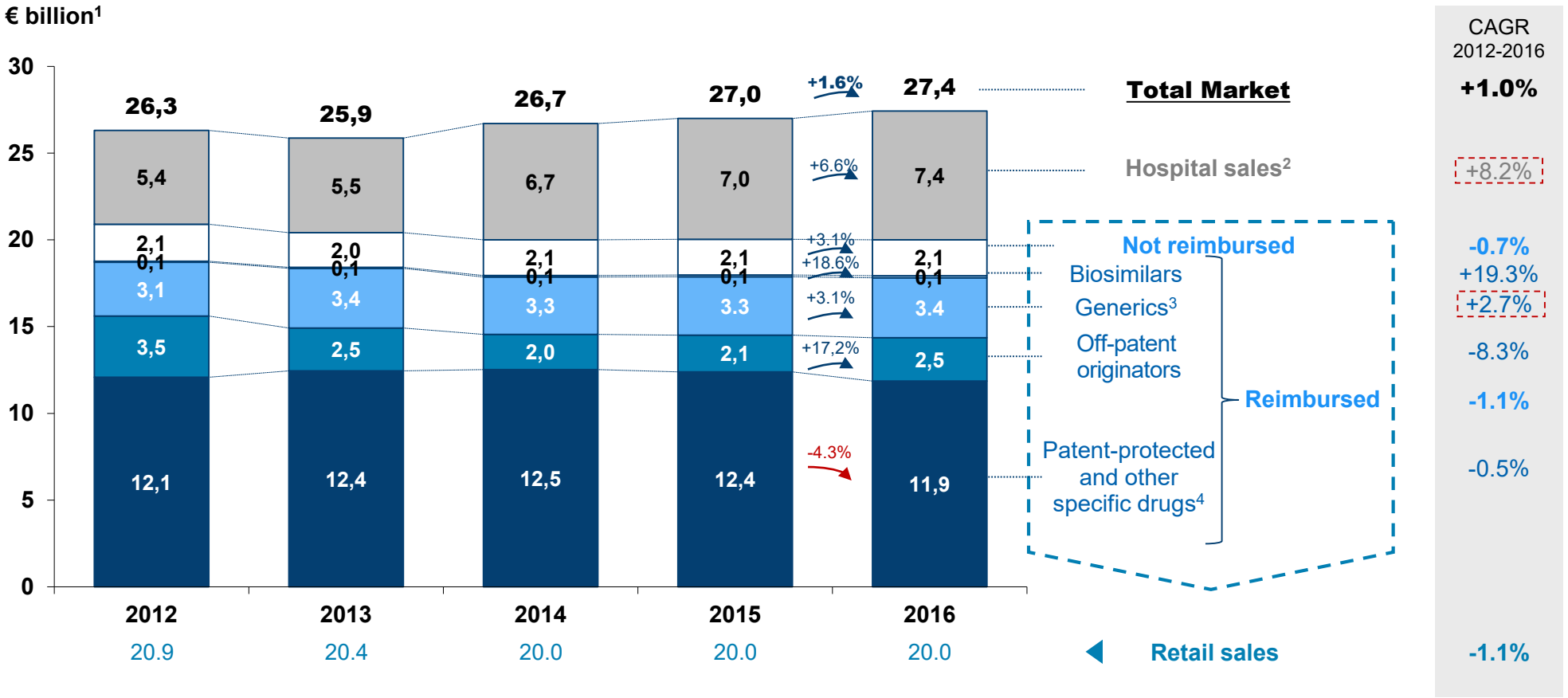
## Context and objectives

- **In this report, Smart Pharma Consulting proposes to cover the following questions:**
  - What is the definition and status of generic drugs in France?
  - What are the recent dynamics, changes and trends on the retail generics market?
  - What are the recent dynamics, changes and trends on the hospital generics market?
  - What is the behavior of the different stakeholders towards generics and how should it evolve?
  - What are essentially similar drugs and what is their performance?
  - What are biosimilar drugs and what is their performance?
  - Who are the major generics manufacturers?
  - What are the main drivers to market generics?
  - What would the French drugs market look like in 2022?

*Sources: Smart Pharma Consulting*

# Spending on drugs is mainly driven by hospital sales and by generics sold in retail pharmacies

## Evolution of drug sales by segment (2012 – 2016)




*Sources: GERS and Top Pharma data – Smart Pharma Consulting analyses*

*[1] Constant ex-factory prices – [2] Estimated rebated sales including hospital sales of biosimilars and products invoiced in top of "T2A"and reassigned medicine sales – [3] Reimbursable generics and quasi-generics – [4] Sales of drugs whose patents have not expired and of other specific products (calcium, sodium, potassium, paracetamol, etc.)*

# Substitution of biosimilars by retail pharmacists, at treatment initiation, is legal since 2014, but the absence of the corresponding decree does not allow its implementation

## Characteristics of the four statuses of "copies" in France

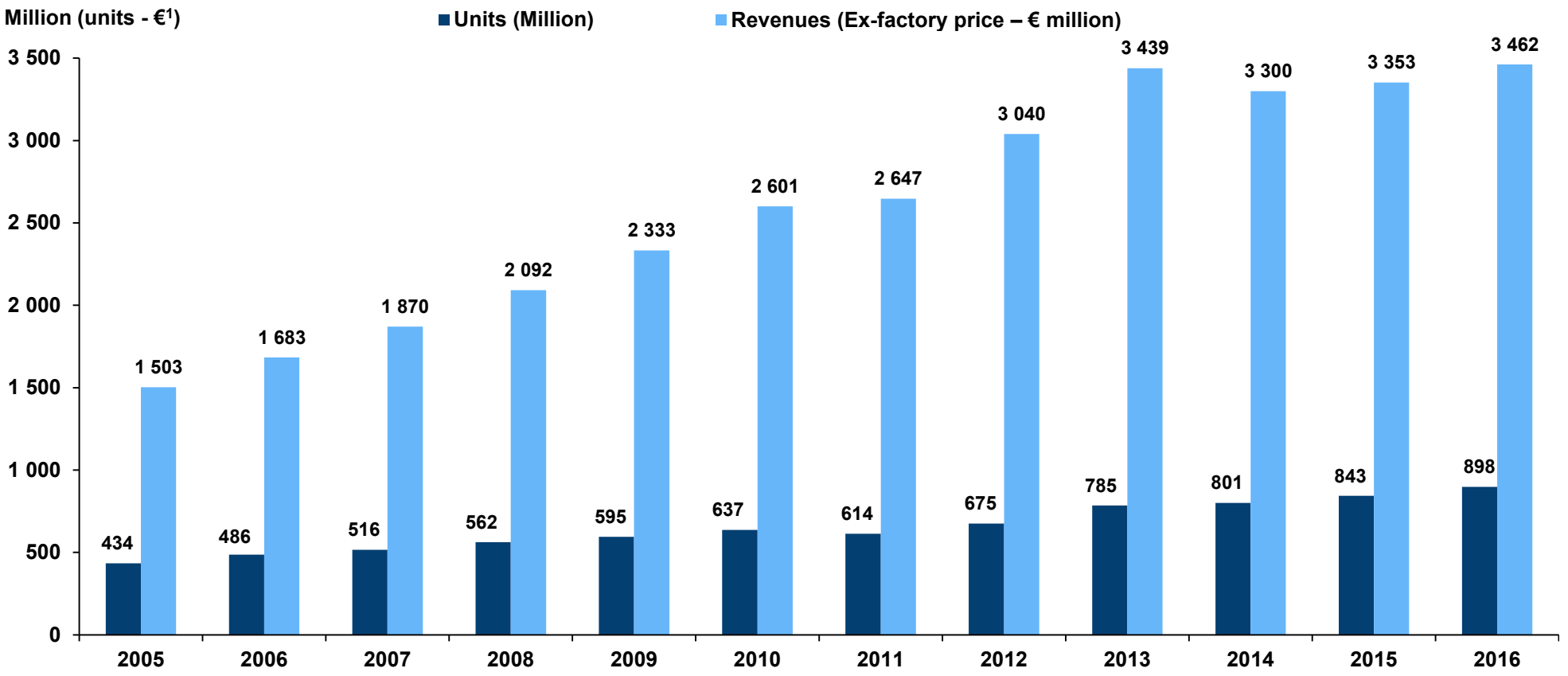
| | Generics | Quasi-generics / Generic FOLM[1] | Essentially similar drugs | Biosimilar drugs |
|---|---|---|---|---|
| **Description** | ▪ Copies of synthetic drugs<br>▪ Bioequivalence has been proven | ▪ Copies of oral modified release form drugs<br>▪ Bioequivalence (has not or) cannot be proven | ▪ Copies of synthetic drugs<br>▪ Bioequivalence (has not or) cannot be proven | ▪ Copies of biotech products<br>▪ Bioequivalence cannot be proven |
| **Market approval requirements** | ▪ Abridged procedure with simplified dossier reproducing original brand's clinical outcome | ▪ Same as for generics<br>▪ Necessity to respect the modified form of the originator (i.e. prolonged, delayed or sequential) | ▪ Minimal clinical development to document safety/ efficacy profile (e.g. with specific device used) | ▪ Complete clinical development (excluding phase 2 studies) |
| **Substitution[2]** | Allowed | Allowed | To be allowed only at treatment initiation, pending application decree[3] | To be allowed only at treatment initiation, pending application decree |
| **Examples** | OMEPRAZOLE MYLAN (generic of MOPRAL) | ESOMEPRAZOLE BIOGARAN (Quasi-generic of INEXIUM) | VITALOGINK (Essentially similar of TANAKAN) | BINOCRIT (Biosimilar of EPREX) |

*Sources: Legifrance, Article L.5125-23 CSP – Senate, November 2016 – LFSS 2017 – Smart Pharma Consulting analyses*

*[1] "Formes orales à libération modifiée" = Modified-release oral forms – [2] Substitution of original brands by their generic / essentially similar / biosimilar drug, in retail pharmacies – [3] For anti-asthmatic drugs only*

# In 2016, sales of reimbursable generics reached € 3,5 billion and 898 million units in the retail market…

## Evolution of reimbursable generics' sales in the retail market (1/2)



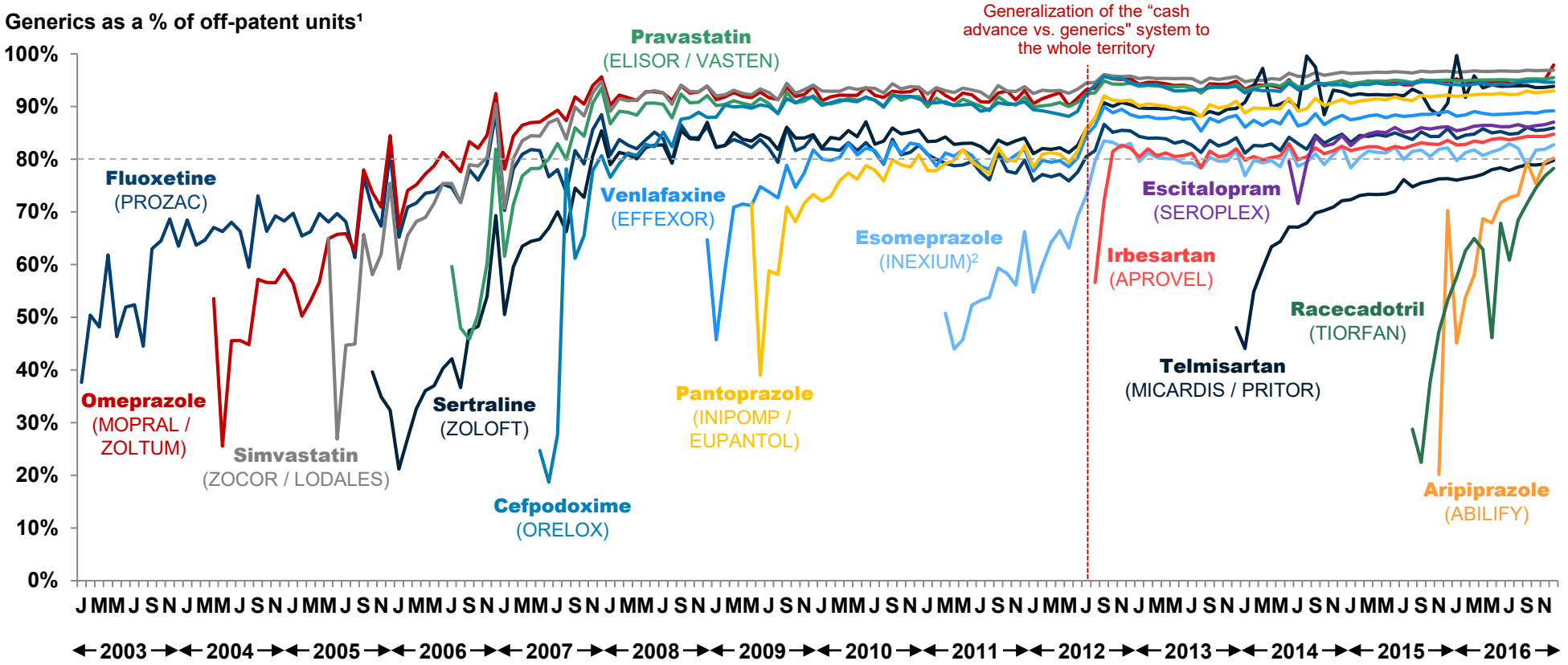

*Sources: GERS dashboard (December 2016) – Smart Pharma Consulting analyses*

*[1] Ex-factory prices, excluding taxes*

# The speed of penetration has accelerated since 2003, reaching ~80% within a few months for brands with no particular barriers to substitution

## Generics penetration trends on the retail market

### Generics penetration for selected high volume drugs

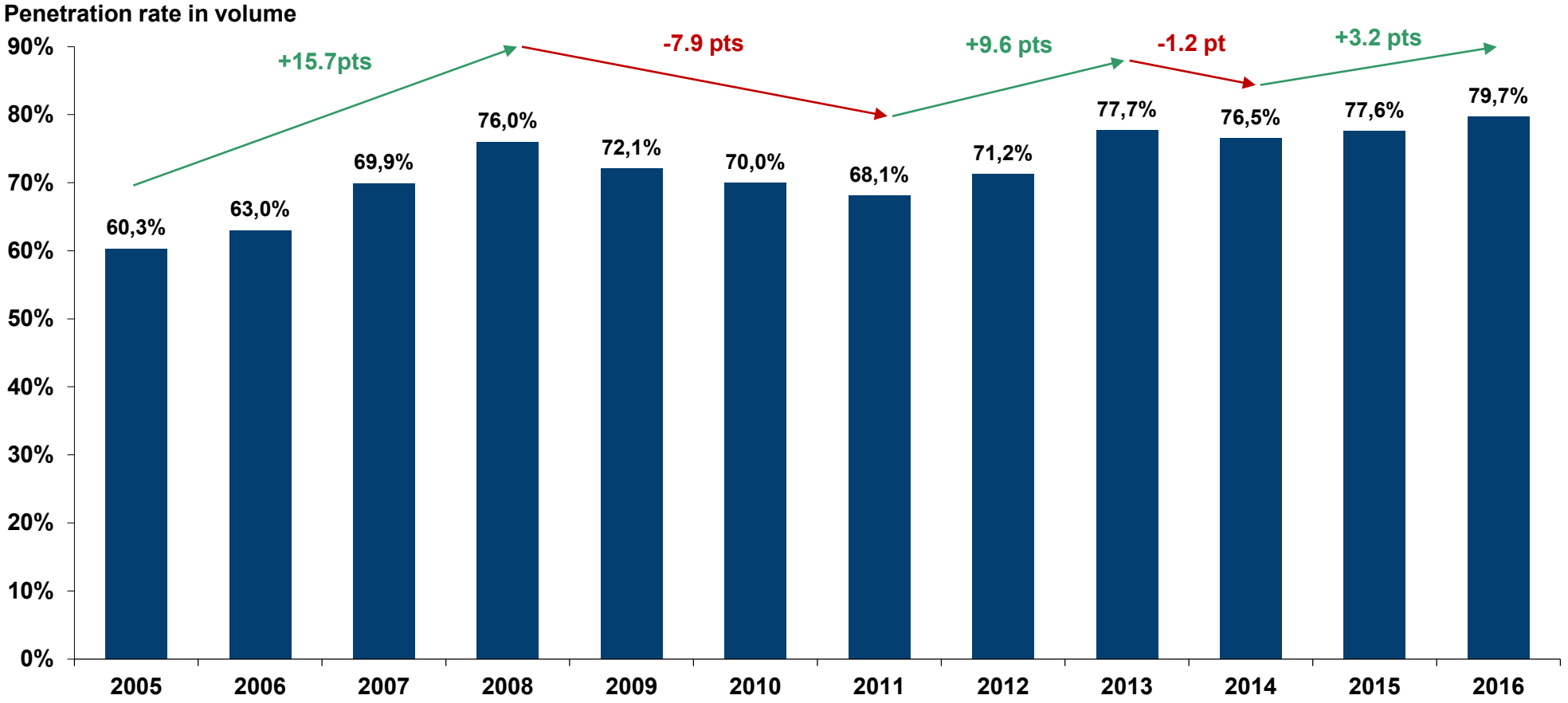



*Sources: GERS – Smart Pharma Consulting analyses*

*¹ Compounded average of the different forms and dosages – ² Quasi-generics*

# The penetration rate, which had slightly declined in 2014 due to various political issues[1], has been increasing steadily during the last two years

## Evolution of the generics penetration in the retail reimbursable market (2005 – 2016)

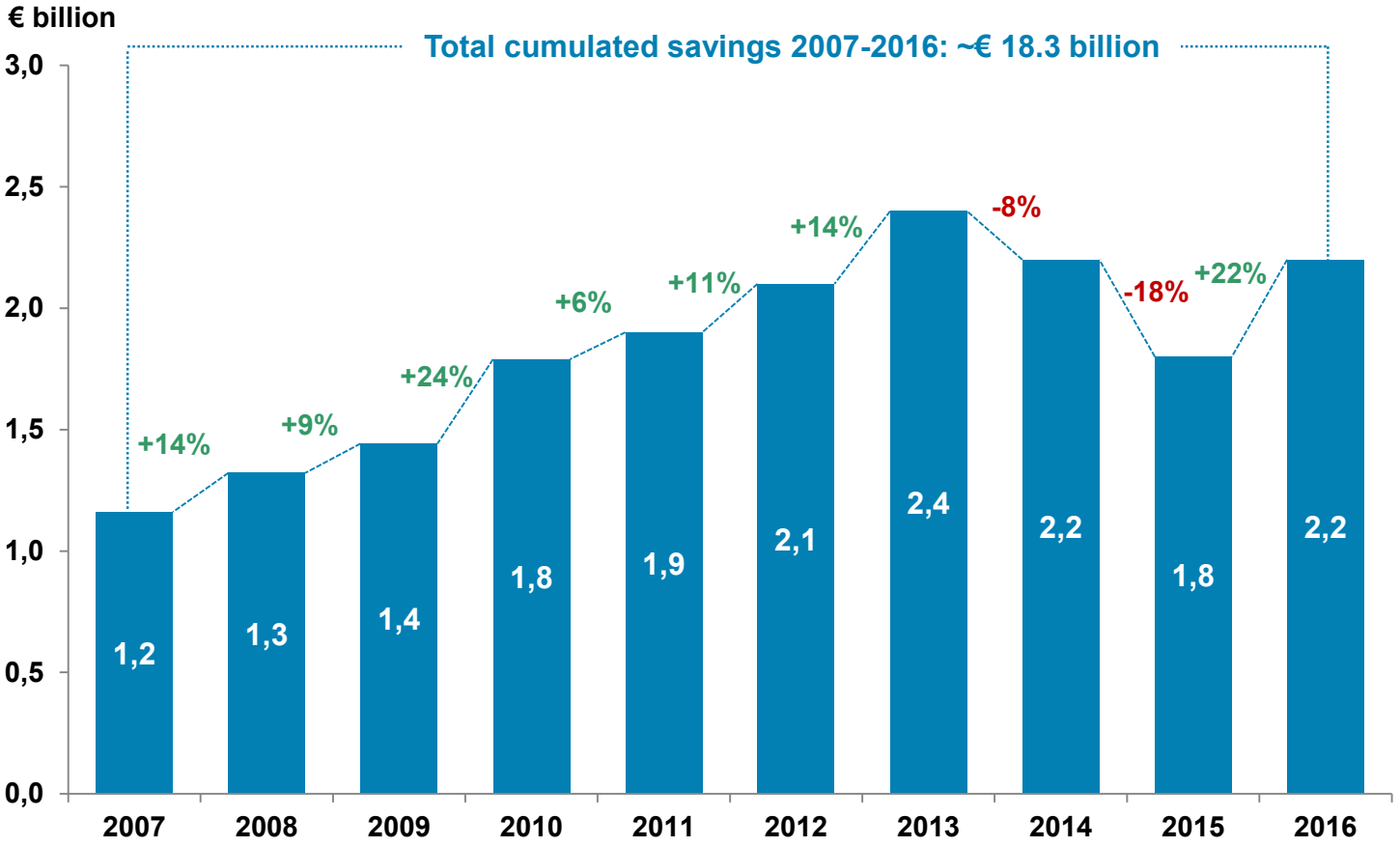



*Sources: GERS data (December 2016) – Smart Pharma Consulting analyses*

*[1] Delayed signature of the amendments "remuneration" and "generics", reconsideration of the monopoly of retail pharmacies, etc.*

# Savings generated by the use of generics reached ~€ 2.2 billion in 2016 and accounted for a cumulated ~€ 18.3 billion over the 2007-2016 period

## Savings generated by generics (2007 – 2016)



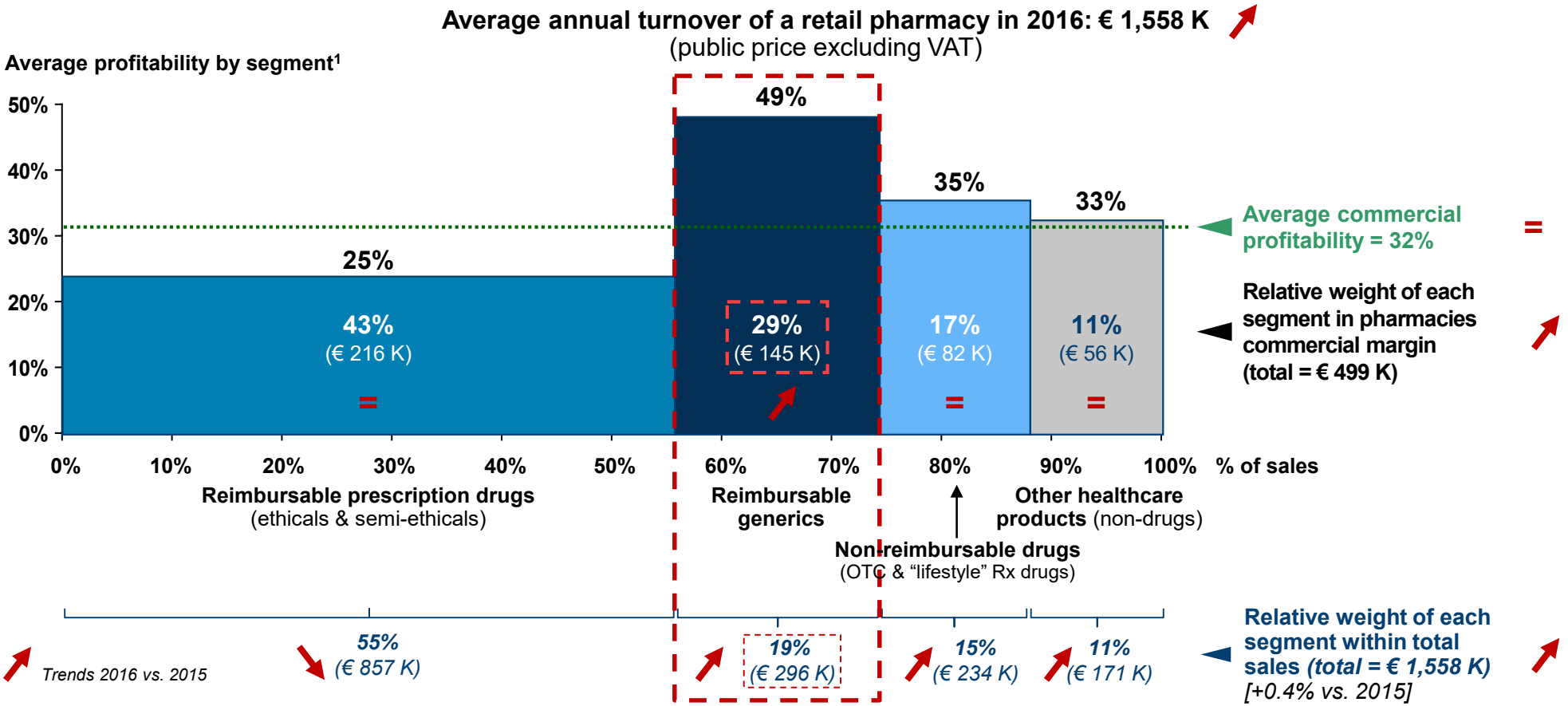

- In 2014, the launch of new generic medicines enabled the market to maintain an **upward dynamic in volume** (+ 2%) and a **fall in value** (-4%) due to price cuts on generics over the period (~ € 220 million)
- Nevertheless, price cuts have impacted even more reimbursable originators, reducing the price differential between originators and generics, and for the first time in 2014, the savings generated by generics decreased (-8%)
- The trend of price cuts in 2015 led to a further decline in savings (-18%) to € 1.8 billion, i.e. the level of 2010 but was reversed in 2016 to reach the level of 2014

*Sources: GEMME[1] – Smart Pharma Consulting analyses*

*[1] "Générique, Même Médicament": association gathering the main generics companies in France*

# In 2016, generics accounted for 19% of retail pharmacies sales on average, and for 29% of their margin, due to the high rebates offered by generics companies

## Economic structure of retail pharmacies in France (2016)



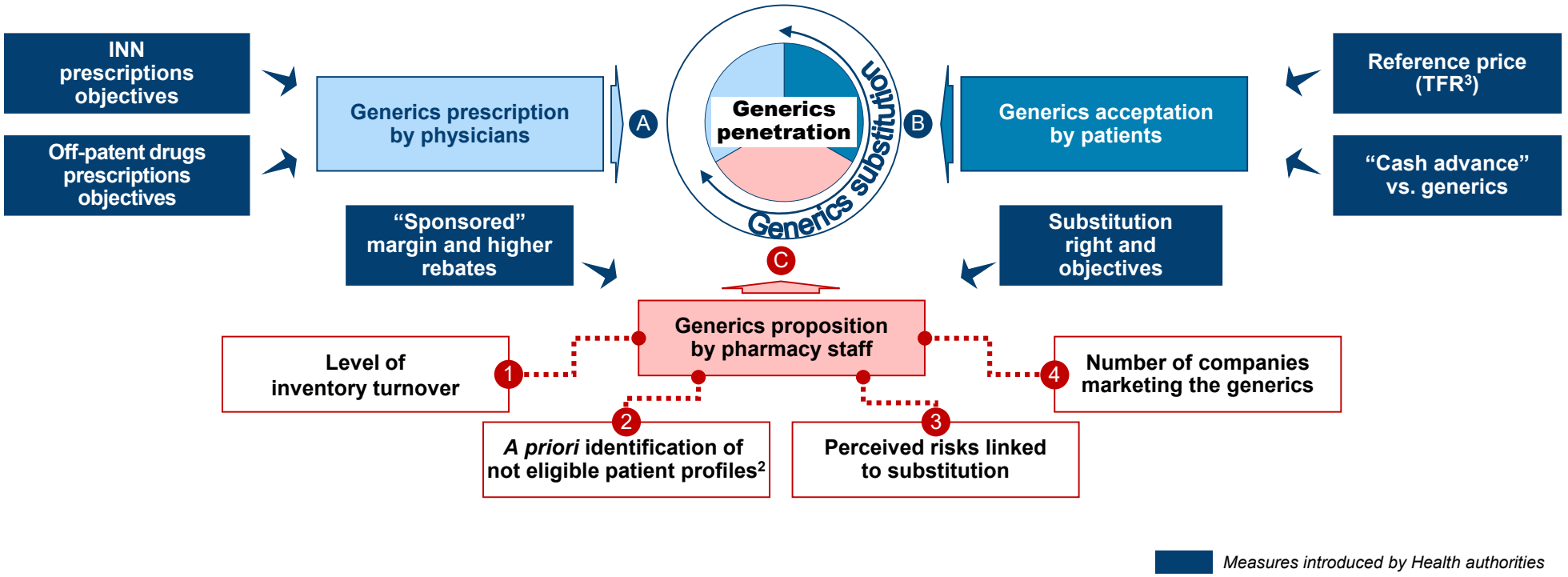

*Sources: KPMG (2016) – Smart Pharma Consulting analyses*

*[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.)*

# Generics penetration is facilitated by INN[1] prescription and substitution, both of which are enhanced by a favorable support from health authorities

## Key drivers of generics penetration on the retail market

### Health authorities measures supporting generics penetration

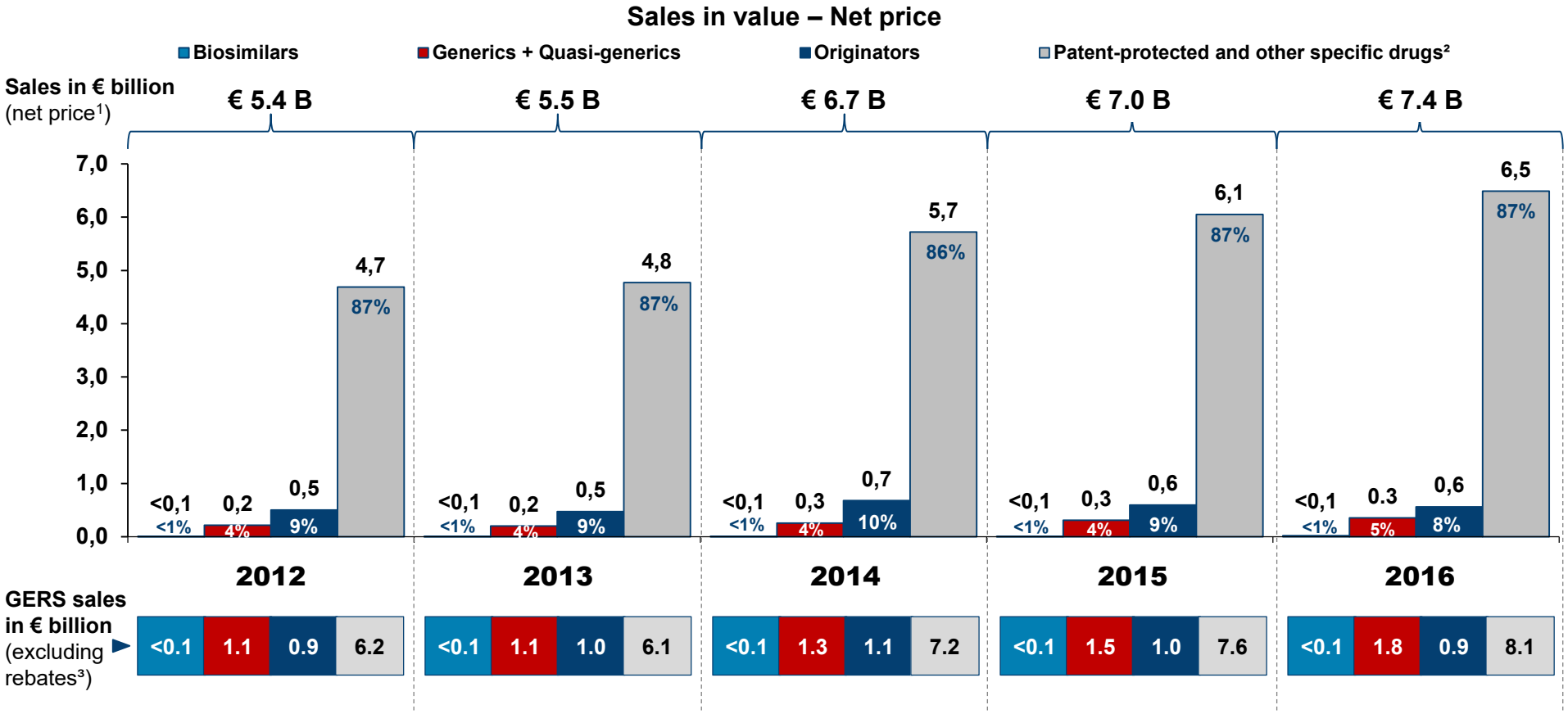



Sources: Smart Pharma Consulting analyses

[1] International non-proprietary name – [2] To whom substitution will not be proposed (e.g. patients having refused substitution several times) – [3] "Tarif forfaitaire de responsabilité": single reimbursement price for a generic group as a whole, based on the cheapest generic price

# The share of generics in the hospital market in value weights for 4-5% and has been relatively stable since 2012

## Hospital market dynamics




*Sources: GERS – Smart Pharma Consulting analyses*

*¹ Net sales estimated based on GERS sales on which theoretical discounts have been applied: 20% for patent-protected and other specific drugs, 40% for originators and 80% for generics and biosimilars – ² Drugs not listed in the ANSM generics directory, including particular products (calcium, sodium, morphine, etc.) – ³ GERS price excluding taxes and rebates*

# Since the substitution right granted to retail pharmacists in 1999, the different governments have introduced several measures to favor the development of generics

## Main governmental measures related to generics

Authorities

Objective of 25% INN prescriptions incentivized through an increase in consultation fees

Adoption of EU Directive 27/2004, which accelerated the registration process for generics

Launch of "Tiers-Payant[1]" system (not compulsory and limited to departments where generics penetration is low), that entails a delayed vs. immediate reimbursement for patients who buy originator instead of its generics

Price reduction for drugs included in the official generics directory

- Increase of the national objective of average generics penetration
- Introduction of individual incentives for retail pharmacists achieving substitution objectives on a selection of generic groups
- Systematization of the "Tiers Payant" system

A Treasury report proposes several measures to improve the financial situation of generics companies which are:
- To make the prices of originator and generics converge as soon as the patent falls
- To systematically put generic groups under reference price (TFR)
- To guarantee higher prices for the most expensive generics to be produced
- To promote generics prescription
- To accelerate the market authorization procedures

1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018

- Introduction of generics substitution right for retail pharmacists
- Revision of distribution margins

Introduction of the TFR (reference price), which entails a unique reimbursement fee for patients for both branded and generics, regardless of the actual price

10-year protection for clinical data of a molecule, starting at its first MA in Europe, for all forms, dosages and indications

Limitation of rebates granted to pharmacists to 17% (Loi Dutreil II / Chatel)

- INN prescriptions facilitated by certified prescription assistance software
- Exception to patent rights allowing generics manufacturers to use similar packaging to those used by brands ("Bertrand Law")

Limitation of generics rebates granted to retail pharmacists to a cap of 40%

General public campaign to promote generics medicines

CAQES[4] setting generics and biosimilars prescription objectives at hospital level at respectively 45.5% and 70%

- Compulsory prescriptions in INN
- Setting of annual objectives of prescription of generics within hospitals
- Launch of the National Plan for the Promotion of Generic Medicines[2] with different priorities to increase the penetration of generics in the open care market, in hospitals and EHPADs[3]

*Positive impact for generics* | *Neutral impact for generics* | *Negative impact for generics*

*Sources: Smart Pharma Consulting analyses*

*[1] Cash advance vs. generics – [2] Launched in March 2015 and included in the 2015-2018 French stability program presented in April 2015 – [3] EHPAD: Institution taking care of dependent elderly people – [4] CAQES: contracts between hospitals, Regional Health Agencies and Health Insurance to enhance healthcare quality and efficiency*

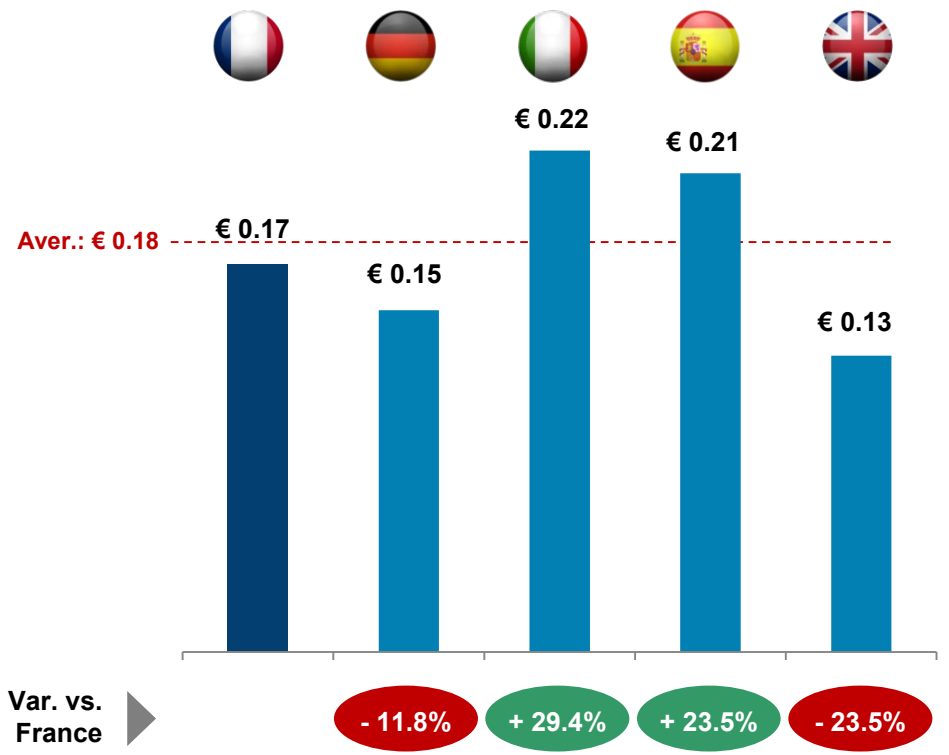
# With an average price of generics of € 0.17 per standard unit, France is now aligned with its European neighbors

Authorities

## Comparative study of generics prices – Overall result

| Scope of the study | |
|---|---|
| **Studied reference countries** | ▪ Germany ▪ Spain ▪ France ▪ Italy ▪ United Kingdom |
| **Studied generics classes** | ▪ 4 studied classes: statins, proton pump inhibitors (PPI), angiotensin-converting enzyme (ACE) inhibitors and sartans<br>▪ In 2014, these classes represented a turnover of € 735 M in France, i.e. ~22% of the generics market |
| **Selected samples** | ▪ Generics marketed in retail |
| **Data sources used** | ▪ For France, the data come from the GERS and the price base of the CEPS (taking into account the price cuts achieved in 2015)<br>▪ For the 4 other reference countries, the 2014 data come from the IMS MIDAS database (price data) |
| **Unit of measure used** | ▪ The unit of measure of the price is the average ex-factory price (in standard unit) charged in a country weighted by the French units in order to neutralize the structural effects |

**Average ex-factory price / unit of main generics classes[2]**



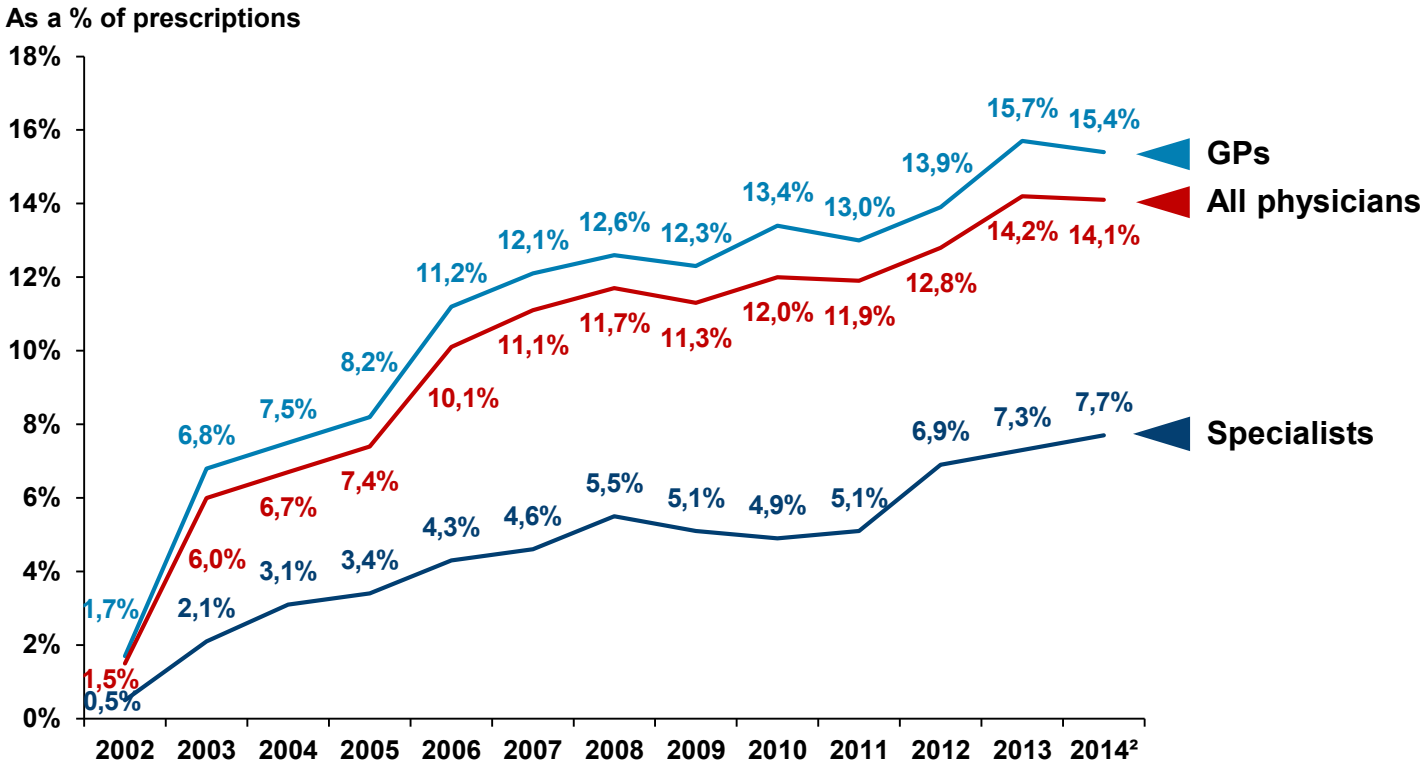

*Sources: Annual report of CEPS 2014/2015 (September 2015) – Smart Pharma Consulting analyses*

*[1] Average price of 4 studied generics classes (statins, PPI, ACE inhibitors, sartans)*

# Since physicians' INN[1] prescription rates are relatively low, generics penetration is mainly due to substitution in retail pharmacies

Physicians

## Evolution of the INN[1] prescription rate (2002-2014)




**Mesures affecting INN prescriptions**

- **LFSS 2009:** imposes physicians to mention the INN for generic drugs prescriptions (measure not well respected)
- **Medical agreement signed with the National Health Insurance, July 2011:** provides a remuneration based on physicians' performance on, among other things, generics prescription objectives
- **"Bertrand law", December 2011:** stipulates that all the prescriptions must mention the INN from January 2015. However, the prescription can be supplemented by the brand name
- **2015:** Mandatory INN prescription

*Sources: "Baromètre de la prescription en DCI", Mutualité française based on IMS data – Smart Pharma Consulting analyses*

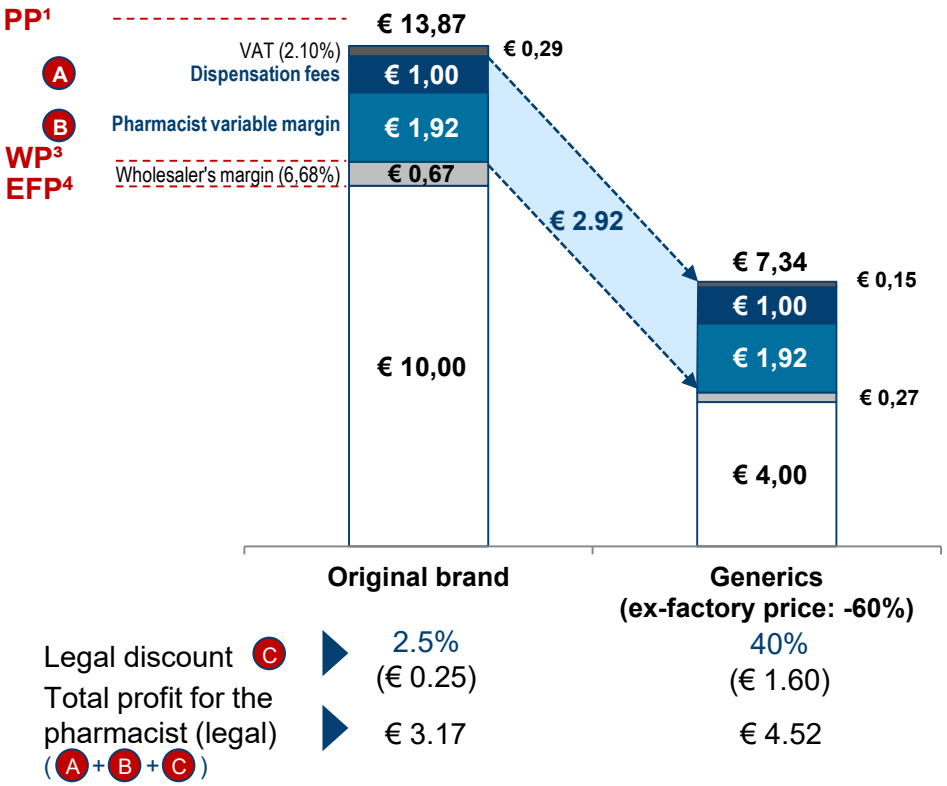
*[1] International non-proprietary name, without associated brand name*
*[2] Moving Annual Total as of August 2014 (No update since)*

# The levels of margins and rebates set by the CEPS for drugs sold on the retail market contribute to regulate the evolution of cost of reimbursed drugs

## Legal margins and discounts for reimbursed generics (2018)

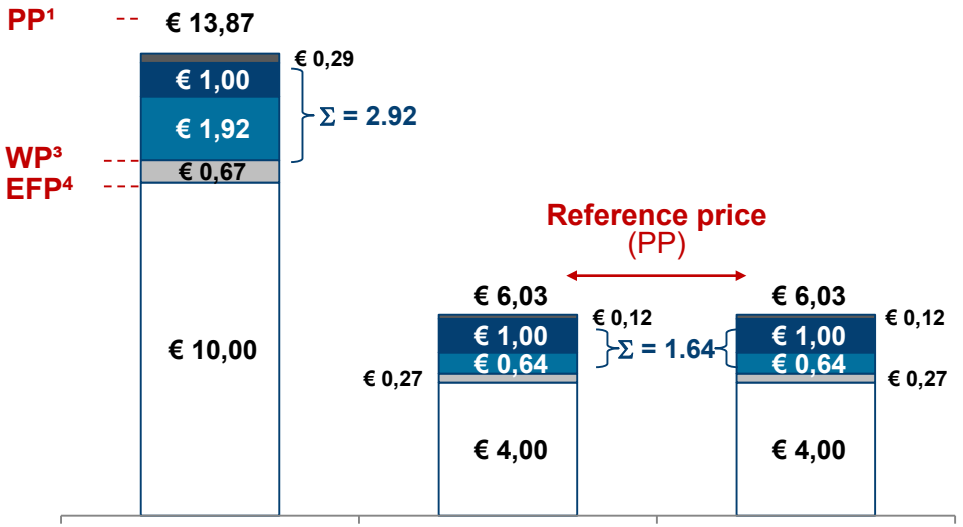
Pharmacists

### Without reference price (TFR)




| | Original brand | Generics (ex-factory price: -60%) |
|---|---|---|
| Legal discount (C) | 2.5% (€ 0.25) | 40% (€ 1.60) |
| Total profit for the pharmacist (legal) (A+B+C) | € 3.17 | € 4.52 |

### With reference price (TFR)




| | Original brand 1 | Original brand 2 (Alignment of reference brand prices) | Generics (Ex-factory price: -60%) |
|---|---|---|---|
| Legal discount (C) | 2.5% (€ 0.25) | 40.0% (€ 1.60) | 40.0% (€ 1.60) |
| Total profit for the pharmacist (legal) (A+B+C) | € 3.17 | € 3.24 | € 3.24 |

*Sources: Smart Pharma Consulting analyses*

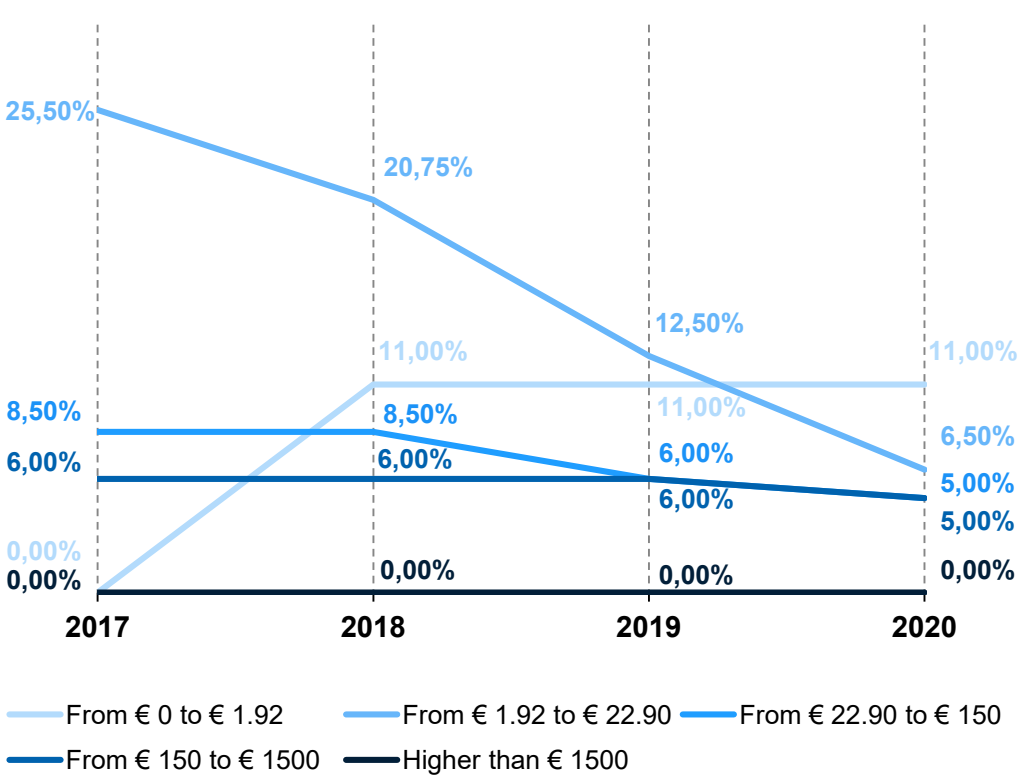
*[1] Public price, incl. taxes and dispensing fees –[2] Dispensing fee as applicable since January 1st, 2016, i.e. € 1.02 incl. taxes – [3] Wholesaler price, excl. taxes – [4] Ex-factory price, excl. taxes*

# The 11th amendment to the National Pharmaceutical Agreement provides for reducing margin on ex-factory price of drugs over the 2018-2020 period for pharmacists

## The 11th amendement to the National Pharmaceutical Agreement

Pharmacists

**Evolution of the smoothed digressive margin on ex-factory price (2017-2020)**




- The main priority of the 11th amendment[1] to the National Pharmaceutical Agreement is to change the remuneration of pharmacies and make them **less dependent on the price and volume of reimbursable drugs**
- Thus, it proposes **progressive transfer** of a significant part of the regulated margin on the price of medicines to **new forms of remuneration** related to dispensing and to the improvement of patients' management
- Thus, three successive waves of **margins** on price **decreases** are expected in January of each year from 2018 to 2020
- The creation of **3 new dispensing fees** will only be settled from 2019 and only 2 of the 3 fees are expected to be re-evaluated in 2020:

| New dispensing fee | 2019[2] | 2020[2] |
|---|---|---|
| Fees for the delivery of a prescription | € 0.51 | € 0.51 |
| Fees related to the age of the patient (youth children and elderly people) | € 0.51 | € 1.58 |
| Fees for the delivery of specific drugs (e.g. immunosuppressive drugs) | € 2.04 | € 3.57 |

*Sources: Le moniteur des pharmacies, August 26th, 2017 – 11th amendment to the National Pharmaceutical Agreement*

*[1] The 11th amendment was signed on July 20th, 2017 by only one of the three French pharmaceutical unions – [2] All taxes included*

# The resistance of some drugs to generics substitution can be explained by several factors such as the complexity of the pathology and the narrow therapeutic margin

## Main limiters of substitution for selected drugs

| | Complexity / Severity of pathology | Narrow therapeutic margin | Low inventory rotations | Frequent "not substitutable" scripts | Difference of chemical forms in comparison with generics | Protection of an indication |
|---|---|---|---|---|---|---|
| **Durogesic** (fentanyl) | ✓ | ✓ | ✓ | | | |
| **Levothyrox** (levothyroxine) | ✓ | ✓ | | | | |
| **Epitomax** (topiramate) | ✓ | | | ✓ | | |
| **Neurontin** (gabapentin) | ✓ | | | ✓ | | |
| **Plavix** (clopidogrel) | | | | ✓ | ✓ | ✓ |
| **Risperdal** (risperidone) | ✓ | | | ✓ | | |

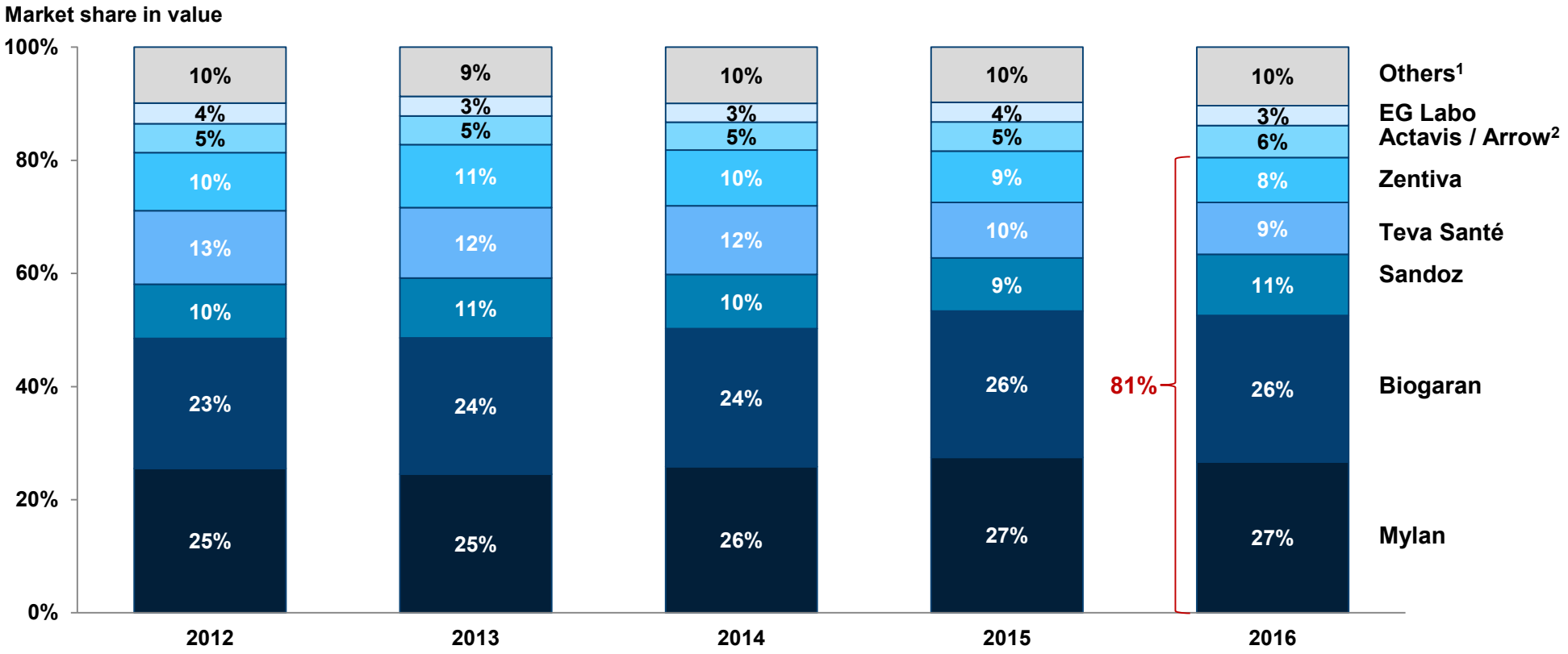
- For those drugs with specific conditions, in order to limit prosecutions engaging their responsibility, pharmacists tend to:
  - Follow the ANSM[1] recommendations regarding narrow therapeutic margins
  - Respect generic groups as defined in the ANSM directory
  - Respect substitution rules regarding protected indications (protection of intellectual property)

*Sources: Phone interviews with 21 pharmacists (April 2011) and 50 pharmacists (May 2010) – Smart Pharma Consulting analyses*

*[1] "Agence nationale de sécurité du médicament": National Agency for the Safety of Medicines and Health Products*

# The French generics market is concentrated with 81% of the sales captured by the top 5 players, whose market shares have been relatively stable since 2012

## Market share of generics companies in the retail market (2012 – 2016)

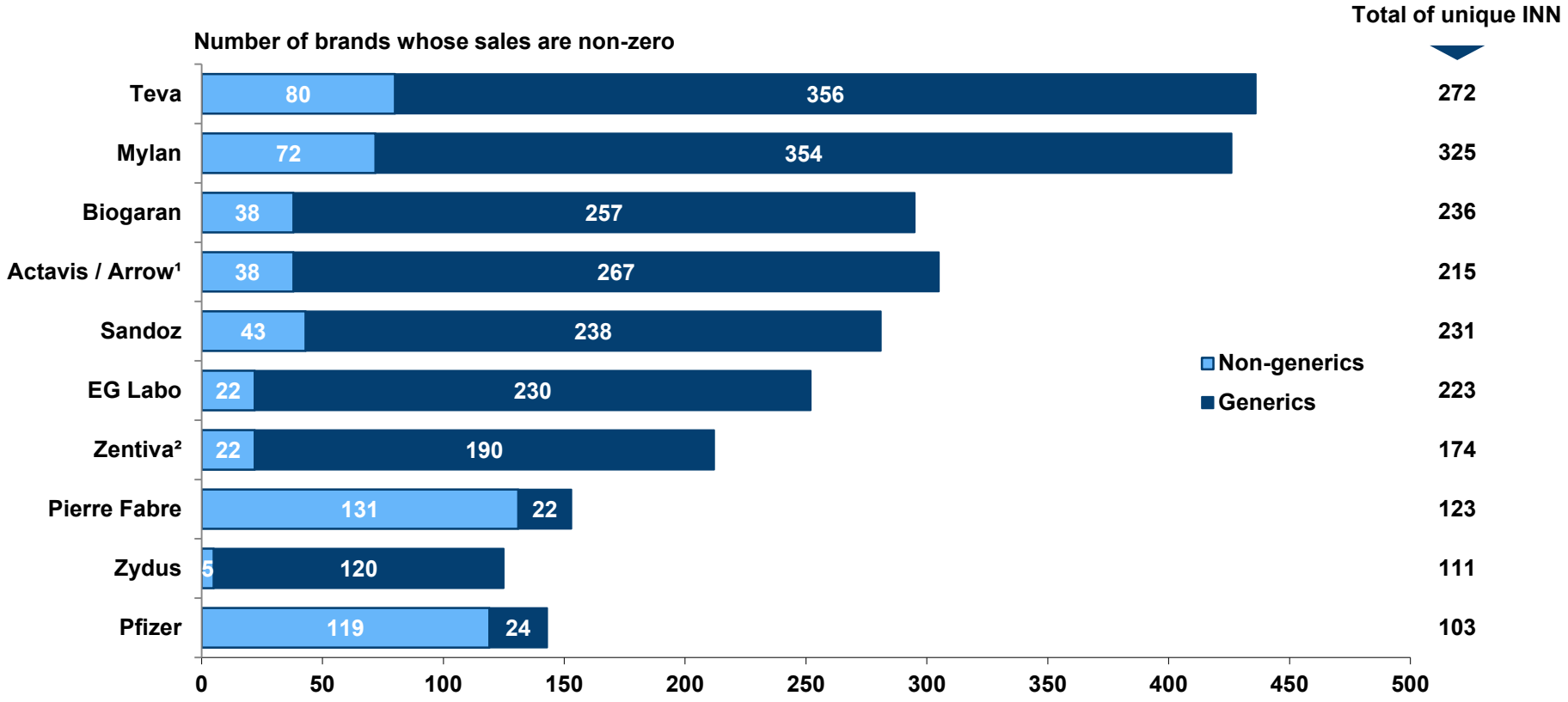



*Sources: GERS – Smart Pharma Consulting analyses*

*[1] Mostly Pierre Fabre, Pfizer, Cristers and Zydus – [2] Acquired by Teva on August 2nd, 2016*

# The scope of the portfolio proposed by the generics companies is a determining factor in their referencing by retail pharmacies

## Product portfolio of generics companies in retail pharmacies (2016)



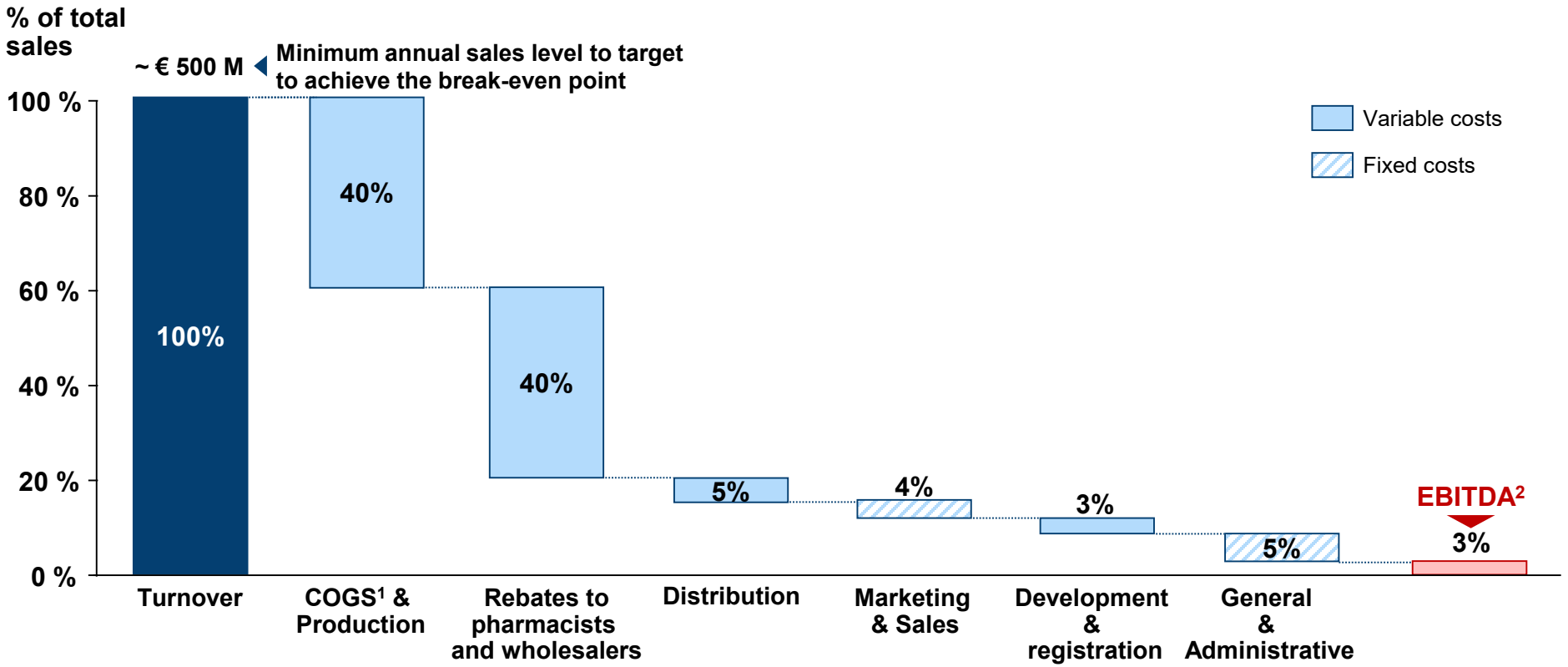

*Notes: The ANSM directory contains 524 different INNs in September 2017*
*Some INNs may be registered as generic or non-generic depending on the presentation (dosage, packaging, form)*

*Sources: GERS – ANSM – Smart Pharma Consulting analyses*

*[1] Acquired by Teva on August 2nd, 2016 – [2] The Zentiva group includes all the generic products of Sanofi*

# The average turnover to generate operating profitability (EBITDA[1]) is estimated at ~ € 500 M for generics companies operating in the retail market

## Estimated cost structure of generics companies in France




*Sources: Smart Pharma Consulting analyses and estimates*

*[1] Cost of goods sold – [2] Earnings before interests, taxes, depreciation and amortization*

Mylan

## Key data for the French affiliate

### Key financial data (2012-2016)[1]

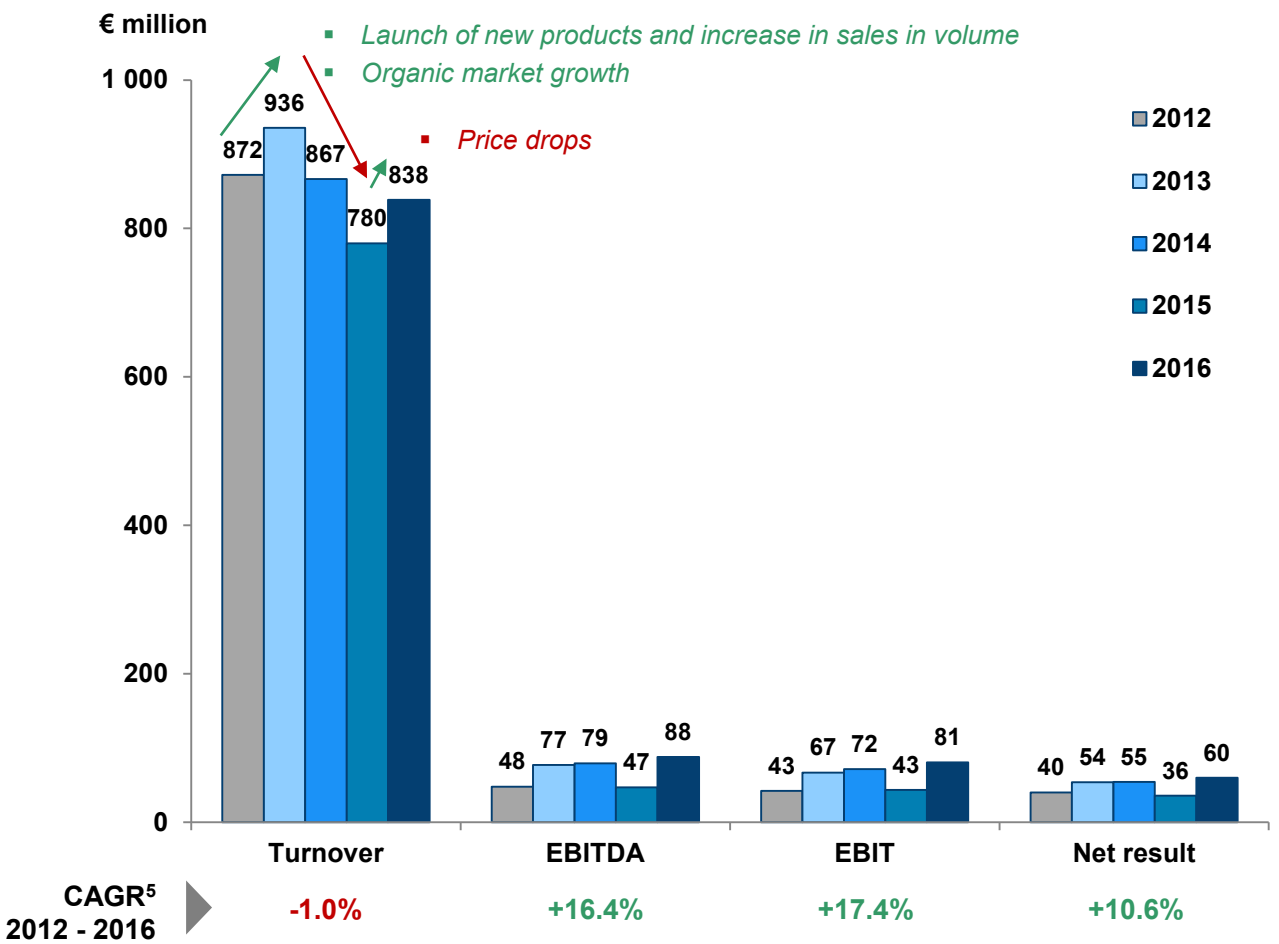
| € million | 2016 | 2015 | 2014 | 2013 | 2012 |
|---|---|---|---|---|---|
| Turnover | ***838*** | *780* | *867* | *936* | *872* |
| EBITDA/Turnover | ***10.5%*** | *6.1%* | *9.1%* | *8.3%* | *5.5%* |
| EBIT/Turnover | ***9.6%*** | *5.6%* | *8.3%* | *7.1%* | *4.9%* |
| Net result/Turnover | ***7.1%*** | *4.6%* | *6.3%* | *5.8%* | *4.6%* |

### Sales data (2016)[2,3]

| | Sales (€ million) | YoY change | Share of turnover |
|---|---|---|---|
| Generics | *1,594* | *+4.9%* | *86.6%* |
| Quasi-generics | *30* | *+5.2%* | *1.6%* |
| Biosimilars | *0* | *N/A* | *N/A* |
| Originators | *218* | *+11.7%* | *11.8%* |
| **Total** | ***1,842*** | ***+5.7%*** | ***100.0%*** |
| **Top 3 generics therapeutic areas[4]** | | | |
| 1. Injectable corticosteroids | *88* | *+29.0%* | *4.8%* |
| 2. Proton pump inhibitors | *71* | *+9.3%* | *3.9%* |
| 3. Non-narcotics & anti-pyretics | *67* | *+0.4%* | *3.6%* |

| Field team | ~ 100 pharma reps |
|---|---|

### Profitability analysis (2012-2016)[1]



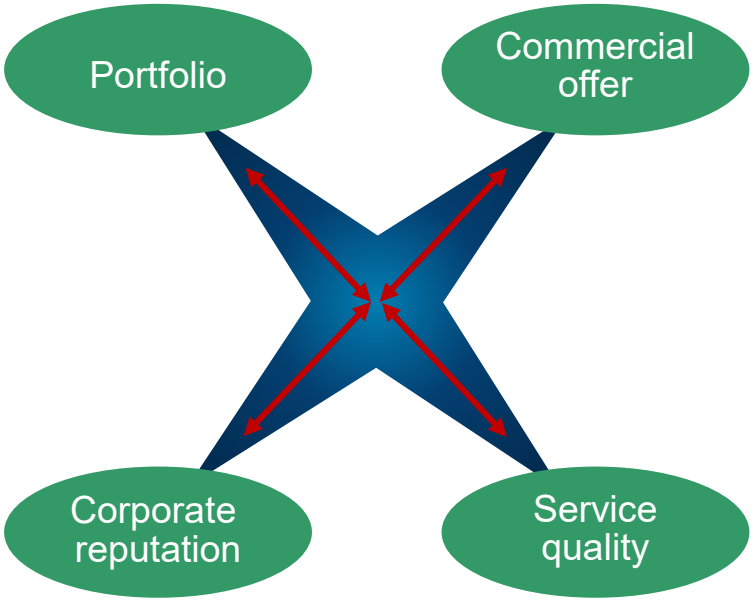

*Sources: societe.com – GERS – Smart Pharma Consulting analyses*

*[1] Data from company financial statements – [2] Ex-factory prices, excluding taxes and rebates – [3] Including Mylan Medical – [4] EphMRA level 4 – [5] Compound Annual Growth Rate*

# The Generics Preference Mix allows generics companies to identify and evaluate the drivers of pharmacists' preference at the time of listing and handing out generics

## Generic Preference Mix: Description

**The 4 components of the *Generic Preference Mix***



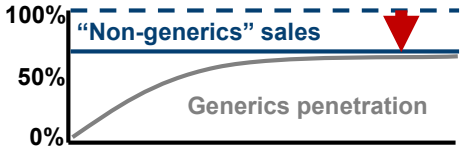

- The *Generics Preference Mix* (GPM) has been developed by Smart Pharma Consulting
- To the extent that retail pharmacists generally focus the great majority of their generics orders on a single supplier and that they have an increasingly important role through counseling and the right of substitution ...
- ... it is essential for generics companies to increase the preference of pharmacists for their brands
- To develop and strengthen pharmacists' preference for their products, generics companies must seek to optimize their *Generics Preference Mix*, which relies on pharmacists' perception of:
  - The breadth and quality of their product portfolio
  - The attractiveness of their commercial offer
  - The quality and the interest of their offered services
  - Their reputation
- The links between the 4 components of *the Generic Preference Mix* should be well established in the minds of clients

*Sources: Smart Pharma Consulting*

# Pharma companies can follow 4 directions and use 10 strategic levers to protect the value of their brand despite the arrival of generics...

## Strategic options of the pharma companies

### Direction n°1 — Reduce the size of the market accessible to generics



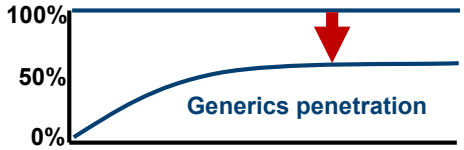

1. **New formulation** (e.g. Actonel)
2. **New combination** (e.g. Glucovance, Inegy)
3. **"Back-up" brand** (e.g. Inexium)
4. **Rx-to-OTC switches** (e.g. Zyrtec)

### Direction n°2 — Delay the arrival of generics


5. **Extension of pediatric exclusivity** (e.g. Tareg / Nisis)
6. **Patent litigation** (e.g. CoAprovel)

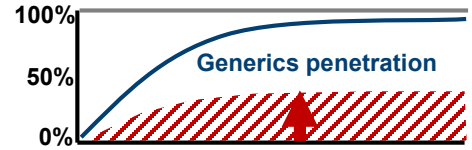
*An agreement with generics companies to delay their arrival is illegal*

### Direction n°3 — Limit the penetration of generics




7. **Commercial offer to pharmacists** (e.g. Mopral)
8. **Price adjustment** (e.g. Brands with or without reference price)

### Direction n°4 — Take part in the generic business




"Royalties" granted to pharma companies

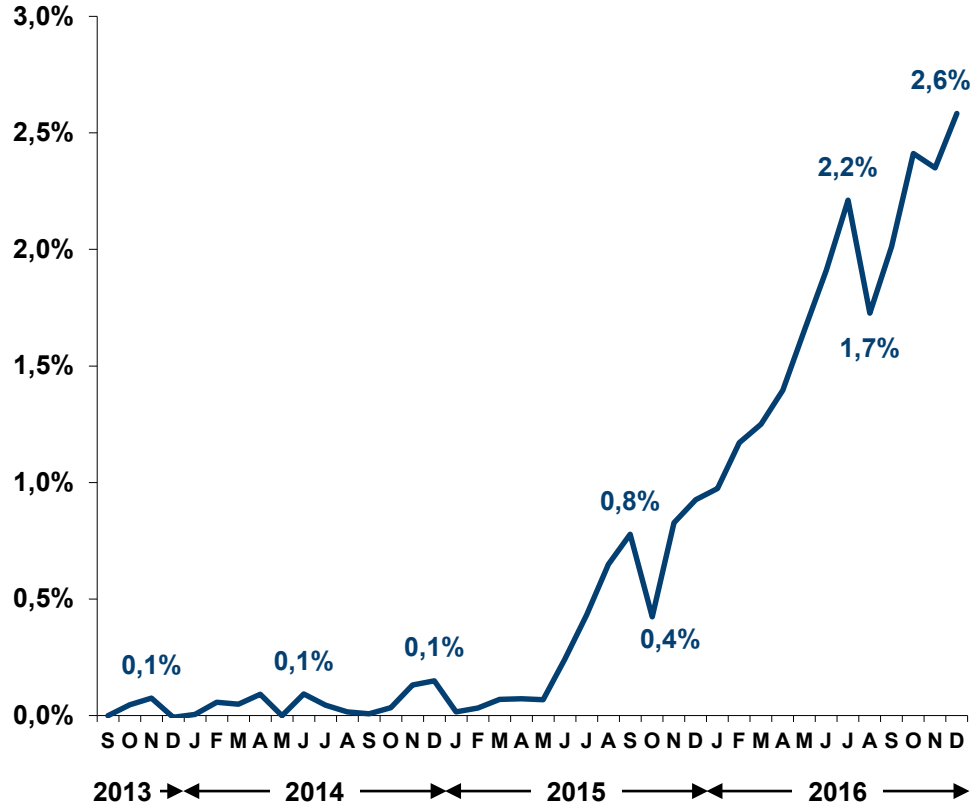
9. **Launch of self-generics** (e.g. Stilnox - Plavix)
10. **Licenses granted to generic companies** (e.g. PROZAC - Fluoxetine RPG)

*Sources: Smart Pharma Consulting analyses*

# The example of the immunosuppressive drug Adoport shows that it is very difficult for an essentially similar with narrow therapeutic index to penetrate

## Adoport example – Penetration of generics companies

**Penetration on Prograf in volume**




### Comments

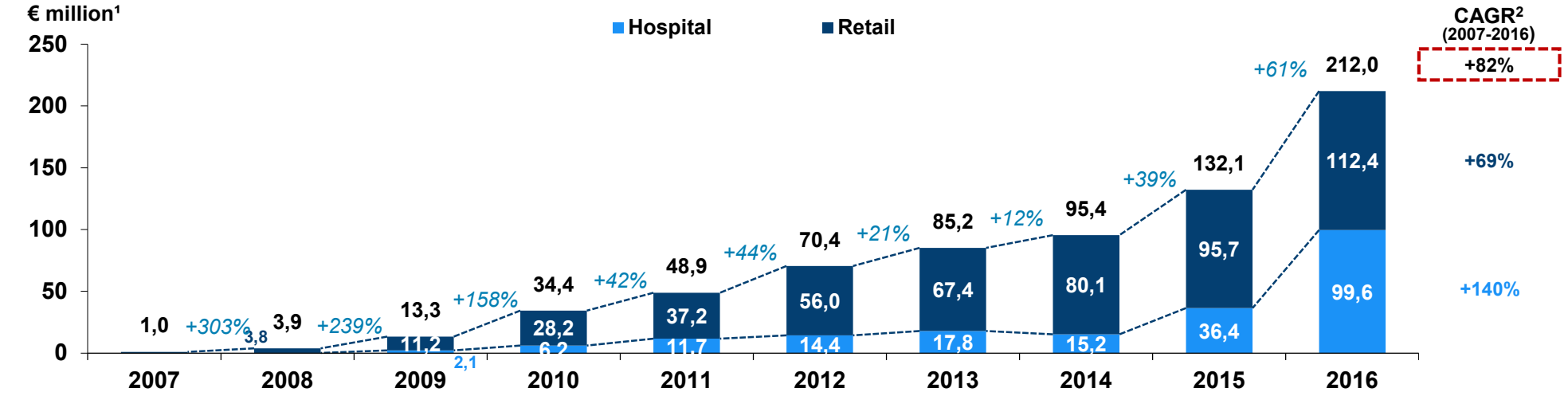
- **Adoport** is an **immunosuppressive agent** containing tacrolimus, indicated in the prevention or treatment of organ transplant rejection, marketed by **Sandoz** in August 2013 after the patent loss of exclusivity of tacrolimus Astellas, but whose first sales were referenced in October 2013 on the GERS database
- Astellas markets three tacrolimus drugs in capsules:
  - **Modigraf** (0.2 mg, indicated for children)
  - **Prograf** (0.5 mg, 1 mg and 5 mg)
  - **Advagraf**, **sustained-release form** (0.5 mg, 1 mg, 3 mg and 5 mg)

  … while **Adoport** is available at 0.5 mg, 1 mg and 5 mg
- Tacrolimus is a drug with a **narrow therapeutic index**, its major adverse event is its nephrotoxicity and it has a high inter- and intra-pharmacokinetic variability
- Thus, no tacrolimus generics group was created in the directory of ANSM, so Adoport is considered as an "**essentially similar**" of Prograf
- At the end of December 2016, i.e. more than 3 years after launch, Adoport's market share in volume in the 0.5 mg, 1 mg and 5 mg market (excluding prolonged-release form) reached **2.6%**
- A third player, **Chiesi**, entered the market in September 2015 with **Envarsus** and proposes 3 sustained-release doses: 0.75 mg, 1 mg and 4 mg

*Sources: GERS – Smart Pharma Consulting analyses*

# Sales of biosimilars, which were launched in 2007 and belonged to six types of products in 2016, reached a total of ~ € 212 million on the overall market in 2016

## Evolution of the biosimilars market (2007 – 2016)



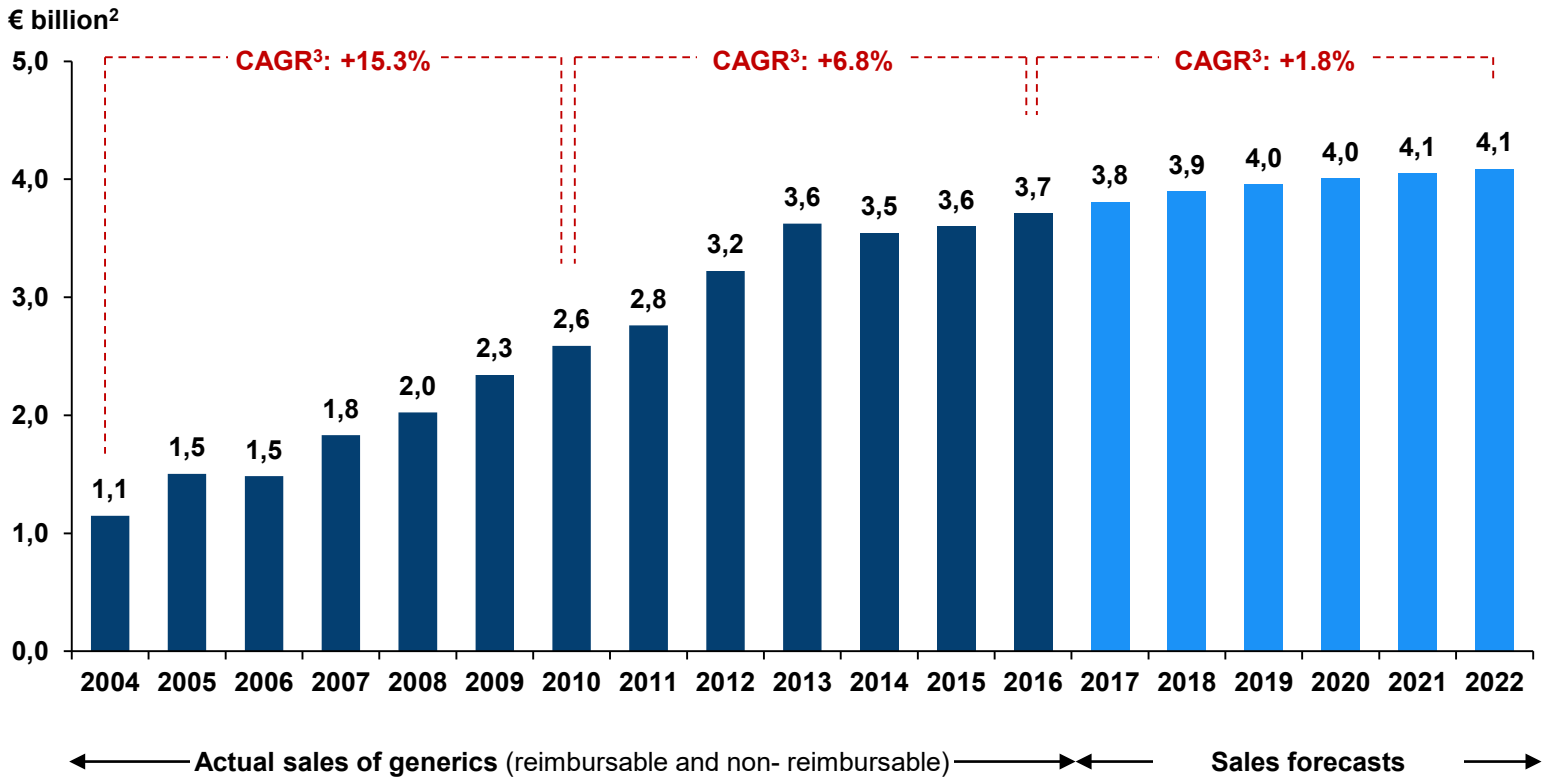

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| GH[3] | **Omnitrope**, *Sandoz* (May) | | | | | | | | | |
| ESA[4] | | **Binocrit**, *Sandoz* (July) | **Retacrit**, *Hospira* (March) | **Eporatio**[9] *Teva* (May) | | | | | | |
| G-CSF[5] | | | **Ratiograstim**,[8] *Teva* (March) **Zarzio**, *Sandoz* (October) | **Tevagrastim**, *Teva* (March) | **Nivestim**, *Hospira* (September) | | | | | |
| Anti-TNF α (mAb[6]) | | | | | | | | | **Remsima**, *Biogaran* **Inflectra**, *Hospira* (February) | **Benepali**, *Biogen* (October) |
| FSH[7] | | | | | | | | | **Bemfola**, *Gedeon Richter* (May) | **Ovaleap**, *Teva* (May) |
| Insulin | | | | | | | | | | **Abasaglar**, *Lilly / Boehringer Ing.* (January) |

*Sources: GERS – Smart Pharma Consulting analyses*

*[1] Ex-factory prices excluding rebates – [2] Compound annual growth rate – [3] GH: Growth hormones – [4] ESA: Erythropoiesis stimulating agents – [5] G-CSF: Granulocyte colony stimulating factors – [6] mAb: Monoclonal antibodies – [7] FSH: Follicle Stimulating Hormone – [8] Ratiogastrim was removed from market in 2016 – [9] Eporatio is not a biosimilar per se but is rather a « me-too » product. It was first launched by Ratiopharm, before to be acquired by Teva in March 2010*

# The average annual growth in value of the generics retail market is expected to remain below 2% by 2020, in particular as a result of price cuts

## Forecasts of generics sales[1] in the retail market – Value




### Comments

- **The low CAGR in value, estimated at 1.8% between 2016 and 2022 can be explained by two factors:**

1. The number of molecules with high potential for the generics market that will lose their patents during the period will be relatively limited
2. The authorities will continue to regularly impose drastic price cuts

*Sources: GERS retail – Smart Pharma Consulting forecasts*

*[1] Reimbursable and non-reimbursable – [2] Ex-factory price, excluding rebates and taxes – [3] CAGR: Compound annual growth rate*

# The market of biosimilars will benefit from the launch of new products in existing classes and in new classes by 2022

## Evolution of the biosimilars market in France

- No new biosimilar class was commercialized between 2009 and February 2015, when **the first two biosimilars of infliximab**, whose originator brand is Remicade, were launched after an **EMA authorization** in September 2013:
  - **Inflectra**, developed by Hospira and marketed by Pfizer (Pfizer acquired Hospira in early 2015)
  - **Remsima**, developed and produced by Celltrion and marketed by Biogaran in France
- If these two products have the same indications as Remicade...
  - In **rheumatology**: rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis
  - In **gastroenterology**: hemorrhagic ulcerative colitis (HRC) in adults and children and Crohn's disease in adults and children
  - In **dermatology**: psoriasis

  ... the **bioequivalence** of these biosimilars has been **demonstrated** in a pharmacokinetic study carried out **only in patients with ankylosing spondylitis** and its **clinical equivalence** has been **evaluated only in patients with rheumatoid arthritis**
- Inflectra and Remsima have the **same dosage**, the **same pharmaceutical form**, the **same route of administration** and **the same composition in excipients** as Remicade
- In May 2015, **Majorelle commercialized Bemfola[1], the first biosimilar of follitropin alfa** (Gonal-F), bringing to five the number of therapeutic classes on the French market
- In January 2016, the launch of **Abasaglar**, a biosimilar of **Lantus** (**insulin glargine**) by **Eli Lilly** / **Boehringer Ingelheim** implies the arrival of a sixth class
- The last one to enter the market was **Benepali (etanercept)**, marketed by **Biogen** (Samsung Bioepis), biosimilar of **Enbrel**, in October 2016
- By 2022, new biosimilars classes are expected. The total biosimilar market will notably be developed thanks to the **launch of hospital biosimilars** (bevacizumab, trastuzumab, rituximab) but also through penetration of classes **already commercialized** (e.g. ESA, G-CSF) and/or recently launched on the retail market (etanercept and insulin glargine)

*Sources: External interviews – GERS – Smart Pharma Consulting analyses*

*[1] Marketed by Gedeon Richter since November 2016*

# Authorities and payers will continue to lower the prices of reimbursed drugs, generics or non-generics, and promote the use of generics and biosimilars

## 1 Position of health authorities and payers

### 2017 – 2022 Trends

***Optimization***

- Recent initiatives to stimulate generics growth
  - Substitution of inhaled drugs[1,3] and biosimilars[2,3]
  - Extension of the generic directory to inhaled respiratory drugs as well as for drugs of plant or mineral origin
  - Prescription objectives within the generics directory at hospital level (45.5%, conforming to the CAQES objective for 2018)
  - Prescription objectives within the biosimilars reference list at hospital (70.0%, conforming to the CAQES objective for 2018)
  - Simplification of generics instruction and notification processes
  - Prioritization of the generics dossier instruction
- Continuous price pressure on reimbursed drugs, originators and generics (price cut, reference prices (TFR[4]))
- Toughening of reimbursement and price attribution rules for originators (e.g. comparative studies, medico-economics data)

### Rationale

- The "pact of responsibility", launched in January 2014, foresees savings of € 3.5 billion over the period 2015 - 2017 due to lower drug prices and the development of generics. However, generics will also be subject to price cuts, tariff convergences with originators and new TFRs
- The 2018 social security finance law includes measures to push further efficiencies. Over the € 4.2 billion potential savings, € 340 million should come from promotion and development of generics and € 40 million should come from biosimilars prescriptions
- Healthcare expenditure objectives set by the government at an average of + 2.3% per year by 2022
- Drugs accounted for only 17.4% of healthcare expenditure in 2016, but since price cuts have no negative political and social impact and are easy to implement, they are used as an adjustment variable

***Quality control of drugs***

- Control of generics quality, particularly best-selling drugs, in comparison to originators

- The objective is to show the safety of generics present on the French market, these controls being part of the national action plan for the promotion of generics 2015-2017

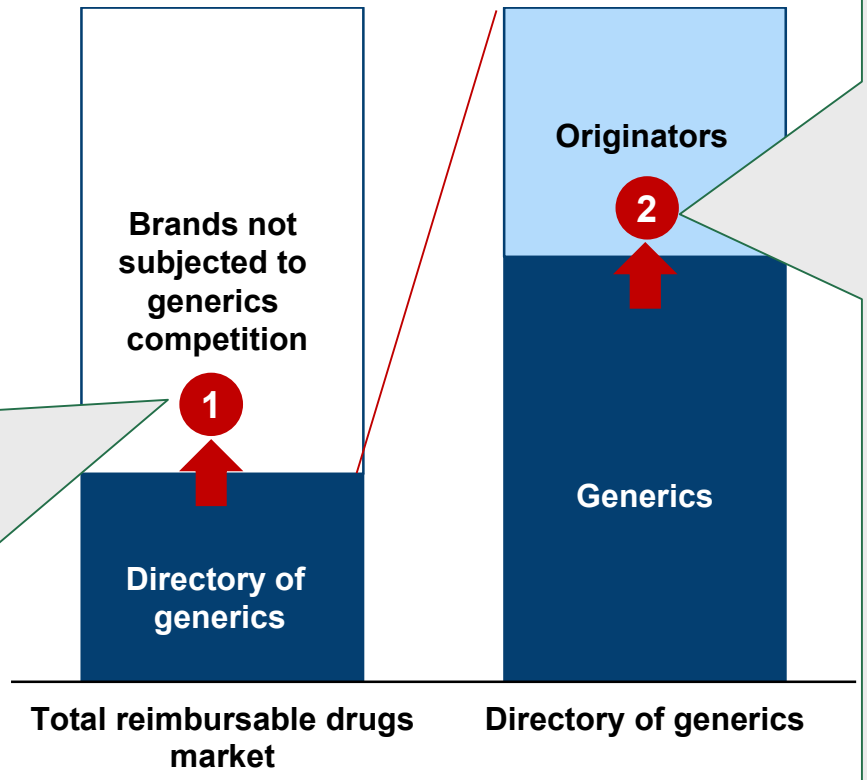
*Sources: Smart Pharma Consulting analyses*

*[1] According to LFSS 2015, substitution may be allowed (at initiation only) for inhaled device – [2] According to LFSS 2014 and PLFSS 2015, biosimilars substitution could be allowed – [3] According to several institutional sources, implementing decrees should not be published in the short term – [4] "Tarif forfaitaire de responsabilité": single reimbursement price for a generic group as a whole, based on the cheapest generic price*

# ... these measures follow two distinct axes: the expansion of the directory of generics and the gain of market shares of generics against originators

## Possible government measures[1] to boost the generic market

- Broadening of the directory of generics by including inhaled sprays, mineral and vegetable substances as provided in the LFSS 2015, or even the various salts, esters, ethers, etc.
- Financial incentives for physicians to increase their prescriptions in the directory and / or prescribe in INN and introduction of “jumbo classes”[2]




- Obligation and financial incentives for physicians to prescribe in INN
- Penalties for physicians writing "Not Substitutable" without adequate reason
- Initiatives in prescribing software to automatically record on each prescription that the pharmacist is authorized to supply generics for substitutable drugs
- Controls to demonstrate the safety of generics present on the French market to reassure prescribers and patients
- General public campaign on generics over time from the Ministry of Health and Solidarity, National Health Insurance or GEMME
- Reduction of health insurance contributions against 100% coverage of generics
- Automatic substitution by restricting the “cash advance vs. generics” system[3]
- Removal of the rebates of generics companies to increase competition
- Indemnities for pharmacists for the denunciations of non-substitutable mentions[4]

*Sources: Smart Pharma Consulting analyses*

*[1] Non-exhaustive list – [2] Drugs are grouped into broad classes in which the products are presumed to have an equivalent benefit for patients and can thus claim the same rate of reimbursement – [3] Measure on the initiative of the CPAM of the Tarn but which meets the hostility of the three trade unions of pharmacists – [4] Proposal by the National Health Insurance Fund decried by the National Union of Pharmacies of France*

# Smart Pharma Consulting

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

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  - Highlight the key points to better understand situations
  - Propose in-depth analyses
  - Determine the business implications for stakeholders

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- This report has been conceived as a working tool to:
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  - Facilitate communication within companies
  - Support strategic decisions over the 5 upcoming years
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  - 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,

Jean-Michel Peny

1, rue Houdart de Lamotte – 75015 Paris – France • Tel.: +33 6 11 96 33 78 • E-mail: jmpeny@smart-pharma.com • Website: www.smart-pharma.com