Smart Pharma
CONSULTING

# Five Insights about the Pharma Industry

Market Insights

## Truths & Untruths

1. Pharma market attractiveness
2. Drug price pressure intensification
3. Cost of R&D
4. Impact of drugs on people's life
5. Pharma companies' reputation

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

## Smart Pharma Consulting has selected 5 characteristics of the pharma industry that are essential to know and understand to make informed opinions and relevant decisions

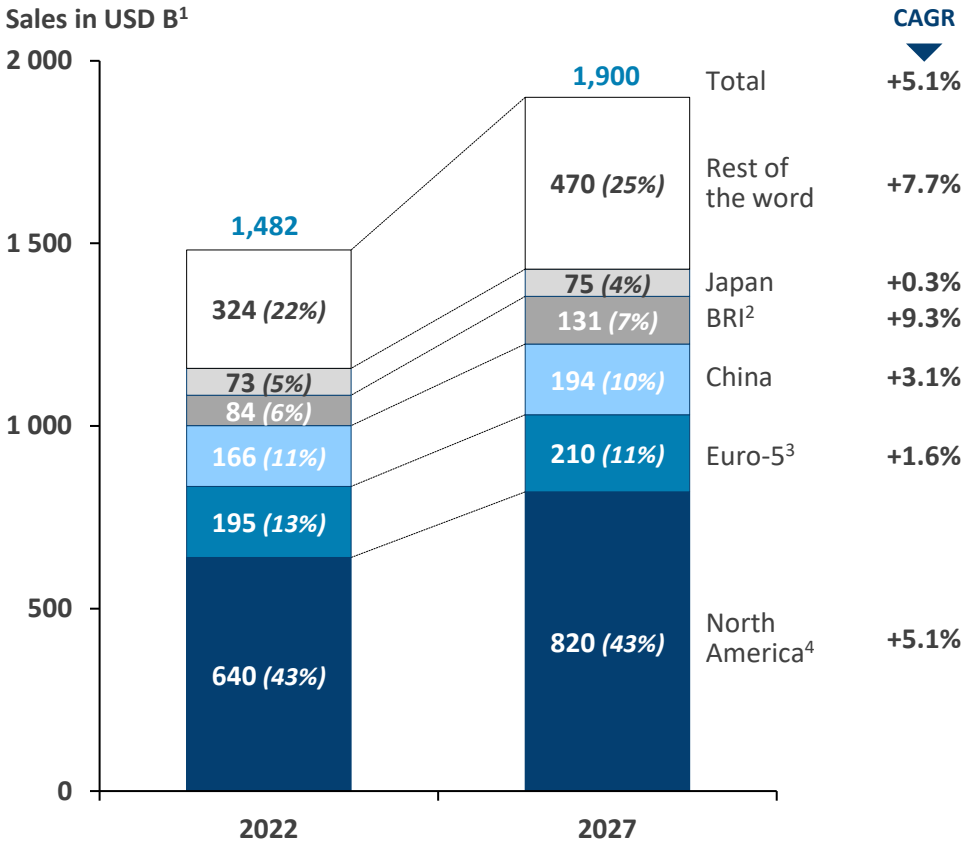
Smart Pharma Consulting proposes to cover 5 key insights that are specific to the pharma industry:

1. Why is the pharma market so attractive?
2. Why will the pressure on drug price intensify?
3. What is the R&D cost of drugs?
4. Do drugs really improve people's life?
5. Why do pharma companies have a poor reputation?

*Sources: Smart Pharma Consulting*

# The pharma market should keep on growing by the end of 2027, at a pace of ~5% per annum, with North America being the main contributor of growth

## Pharma market structure and dynamics (2022 – 2027)




- The pharma market is expected to grow with a **CAGR of +5.1%** by 2027 vs. +3.2% for the worldwide economic growth
- **Euro-5** countries account for 13% of the market:
  - Germany: 4%
  - France: 3%
  - Italy: 2%
  - UK: 2%
  - Spain: 2%

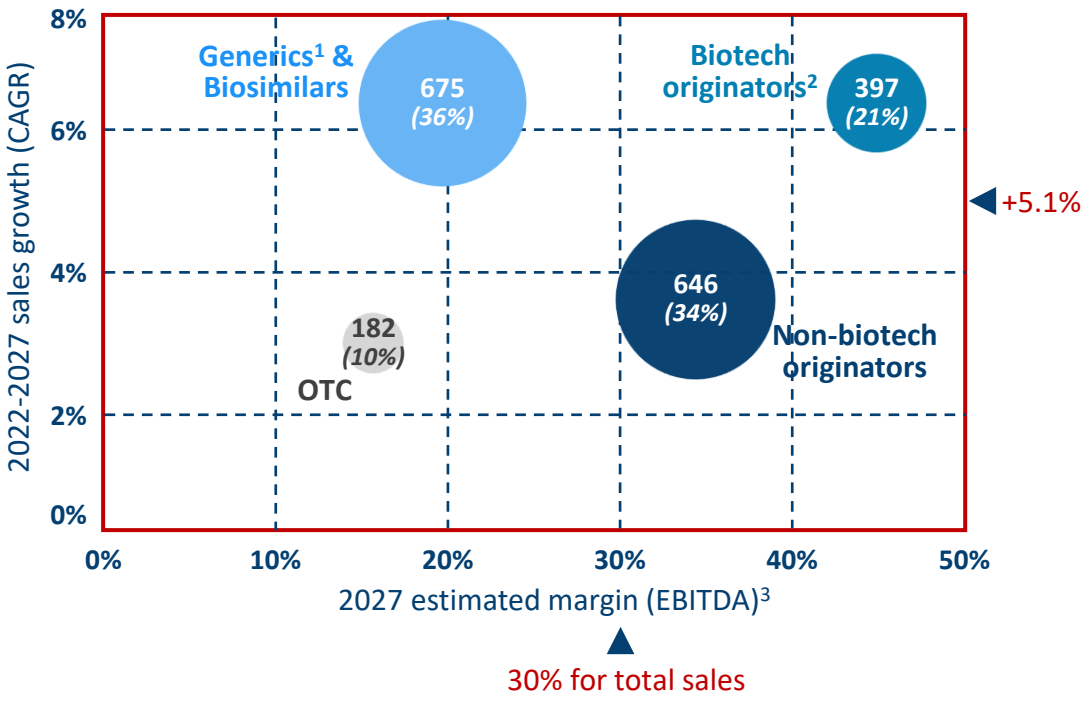
  and they should see their **weight drop by 2 points** (i.e., to 11% of the market) by 2027, **due** to higher **price pressure** than in the average of other countries
- **North America** should continue to weigh for 43% of the global pharma market in value and remain **the key contributor** to the **worldwide pharma market growth**

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

*[1] Ex-factory price before rebates – [2] Brazil, Russia, India – [3] France, Germany, Italy, Spain and UK – [4] USA and Canada, the former accounting for 41% of the total*

# Over the 2022 – 2027 period, the pharma market growth should be essentially driven by generics and biotech originators, while the profitability of the industry should decrease from ~32% to ~30%

## Pharma market attractiveness by strategic segment (2022 – 2027)




- The strategic segment of "**Generics & Biosimilars**" is the **largest** and the **most dynamic**
- The **biotech** segment will **remain attractive** despite the **ramp up** of **biosimilars**
- The **OTC** segment will remain the **least attractive** one
- The average **EBITDA** of the pharma industry should **decrease** from **~32%** in 2022 to **~30%** in 2027, mainly as a result of **increasing price pressure**, and **inflation**

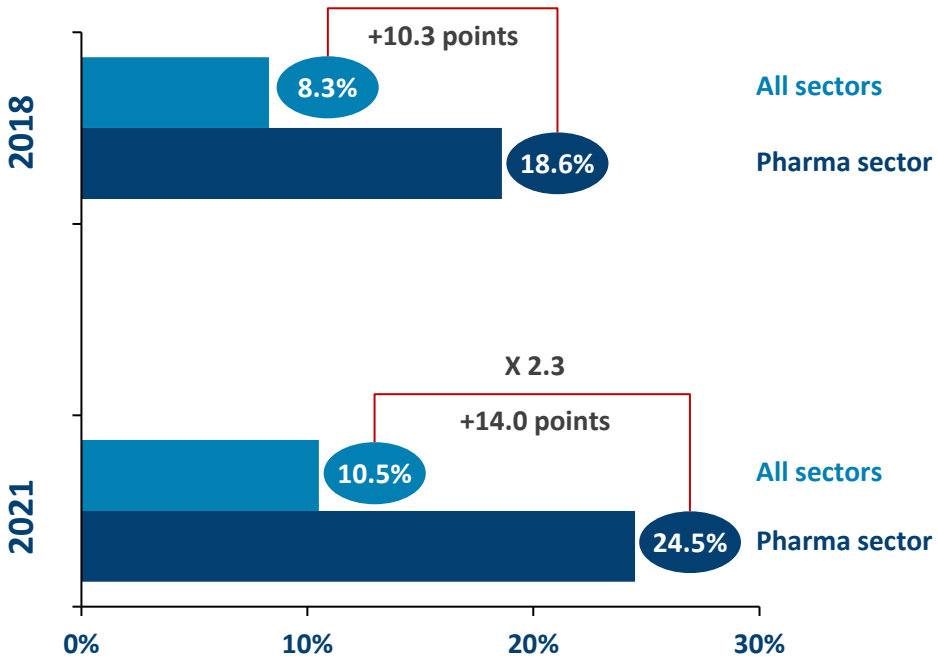
*Sources: IQVIA Institute (January 2023) – World economic outlook, IMF (October 2022) – Smart Pharma Consulting estimates*

*[1] Including branded and unbranded generics and excluding OTCs – [2] Excluding biosimilars, already combined with Generics in a single segment – [3] Earnings before interest, taxes, amortization and depreciation*

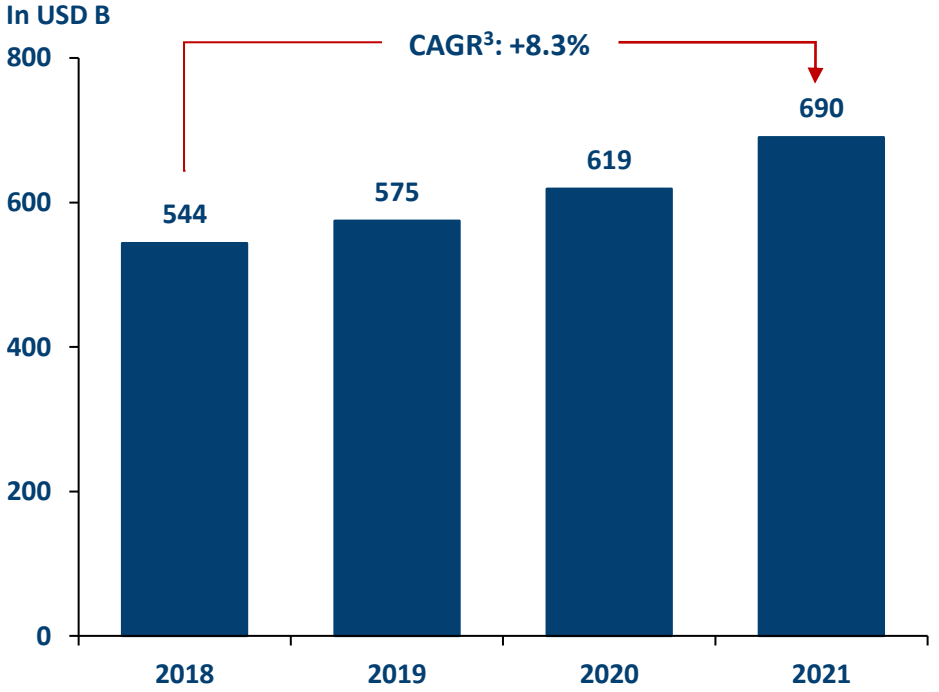
# In 2021, the net profitability of the pharma sector was 2.3 times higher than the average of all other sectors, and revenues of top 20 companies grew by +8.3% p.a. between 2018 and 2021

## Net profitability and sales dynamics of the pharma sector (2018 – 2021)

**Net profitability in 2018 & 2021**
(Of top Rx pharma companies[1] and of the global economy)




**Market sales trend**
(Cumulated revenues of top 20 Rx pharma companies)

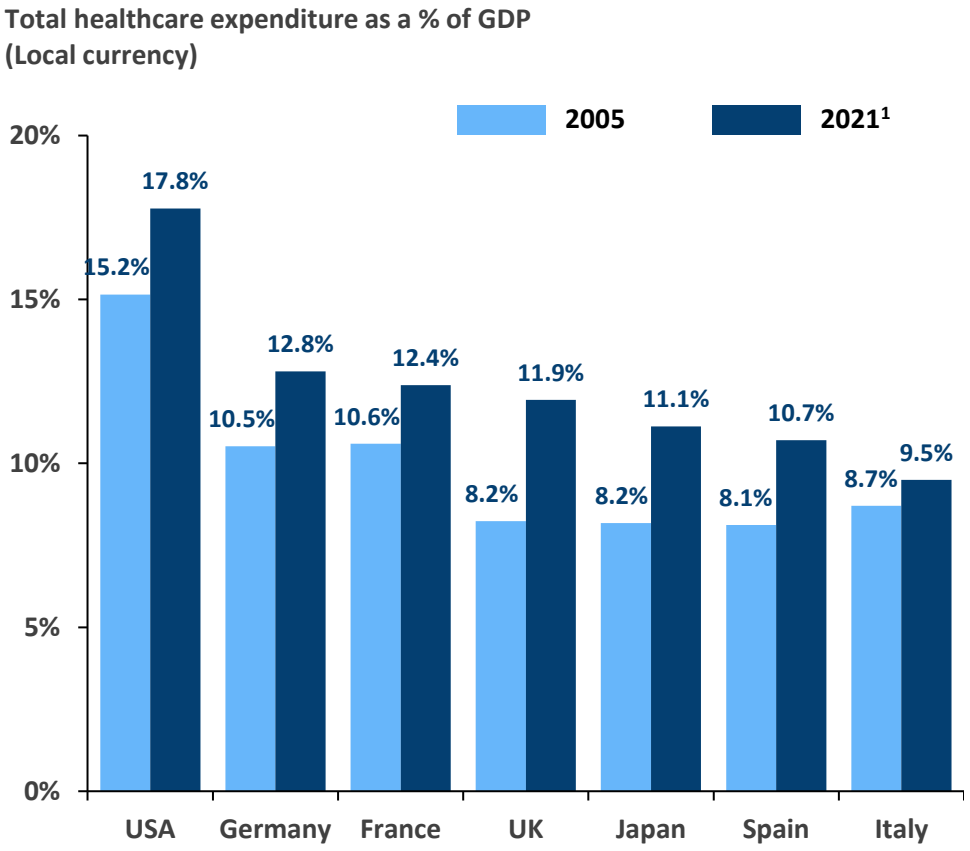



*Sources: Top 20 Rx pharma companies' 2021 and 2018 annual reports (2022 and 2019) – Forbes: The Global 2000 (May 2022 and 2019) – World economic outlook, IMF (October 2022 and 2018) – Smart Pharma Consulting analyses*

*[1] Top 30 for 2018 and top 20 for 2021 –*
*[2] Return on revenues = net profits / total revenues – [3] Compound annual growth rate*

# Healthcare expenditure should keep on growing faster than national economies due to demographic factors and willingness of citizens to have a better access to healthcare

## Healthcare expenditure as a percentage of GDP (2021)



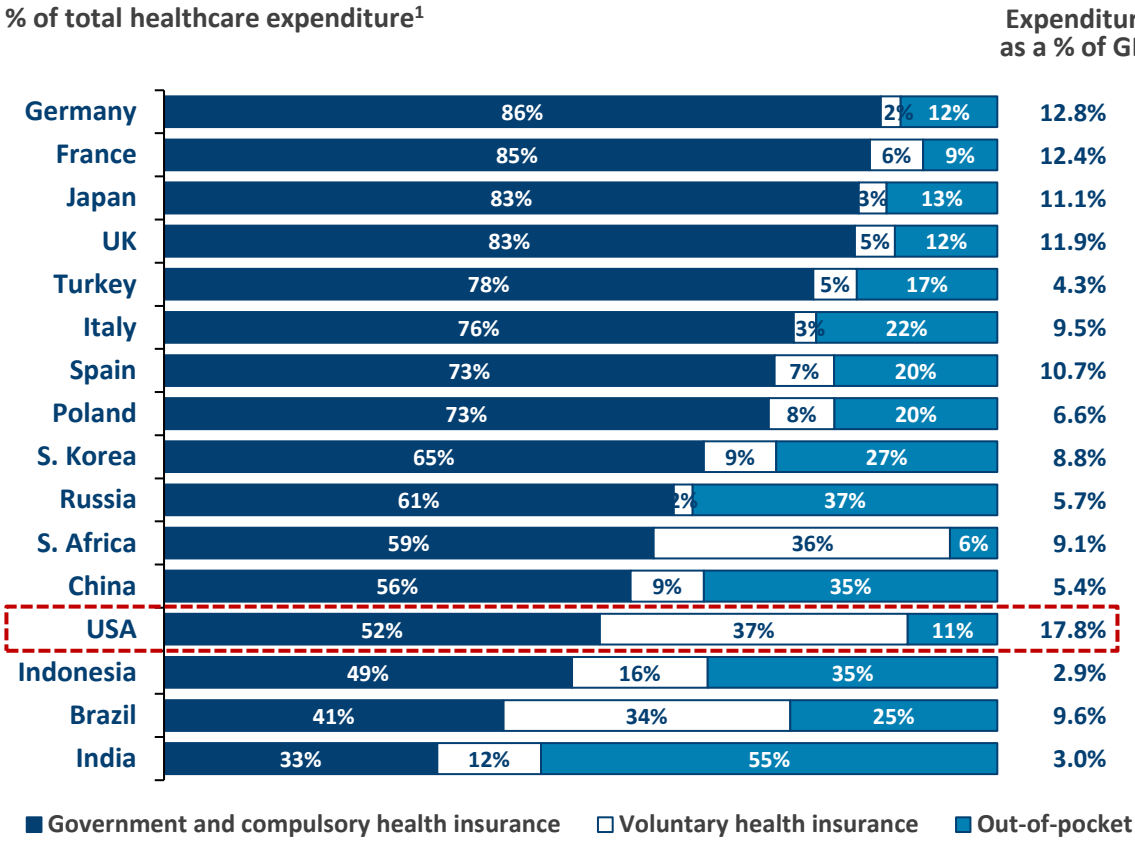

- **Healthcare expenditure** represents one of the **largest public spending** items in most developed economies:
  - 2nd (France, Germany, UK, USA and Spain)[2]
  - 3rd (Italy[3] and Japan[4])
- At best, governments and payers will manage to **slow down** the rise of healthcare expenditure as a percentage of GDP but **not to stop it**, unless they **initiate a hazardous rationing policy**
- There is **no optimal ratio** of spending over GDP
- This ratio primarily results from:
  - **National** economies
  - **Public health** conditions
  - **Governments'** investment prioritization
  - **Citizens'** willingness to seek for care
  - **Healthcare cost**

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

*[1] Provisional/Estimated value, excluding for Spain – [2] After social protection – [3] After social protection and general public services – [4] After social protection and economic affairs*

# Germany, France Japan and the UK ensure more than 80% of healthcare expenditure covering through a government and compulsory health insurance scheme

## Share of public spending in total healthcare expenditure (2021)



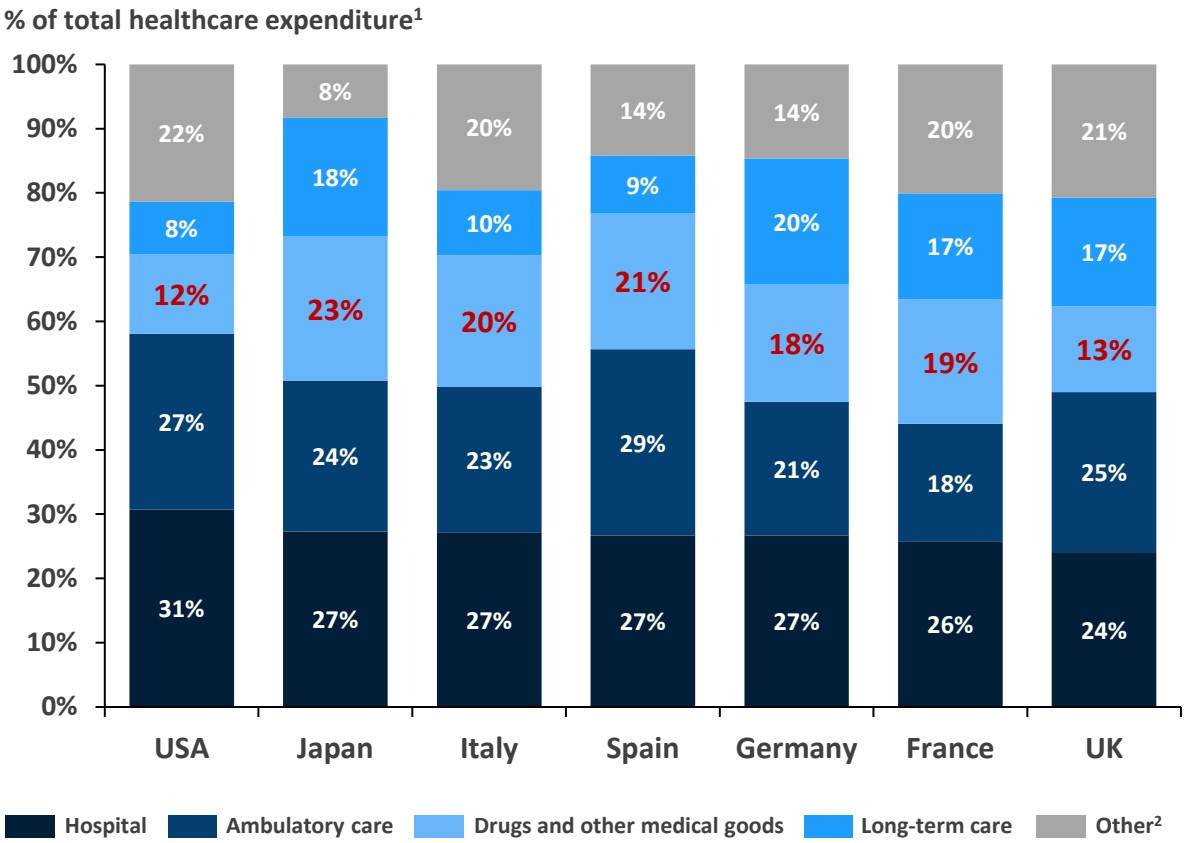

- **Germany** and **France** levels of **public spending** on healthcare are **amongst the highest**, showing a **highly protective** healthcare system
- As a result, "**out-of-pocket**" spending represents only **12%** and **9%** of total healthcare expenditure, respectively, in these two countries
- **USA public spending** share on healthcare is **much lower**...
- ...although this expenditure represents a larger share of GPD than in Germany and France (~18% vs. ~13 and 12%, respectively)

*Sources: World Bank and OECD databases (January 2023) – National Health Expenditure database: Centers for Medicare & Medicaid Services (January 2023) – Smart Pharma Consulting analyses*

[1] *Or latest data available*

# The cost of drugs is far behind that of hospital and ambulatory care, yet this segment is targeted by governments because it is technically and politically easier to control

## Breakdown of healthcare expenditure per country (2021)




- Drugs represent the **3rd largest source** of healthcare expenditure in most major developed countries
- Drugs are typically the **easiest segment** to apply **cost-containment** 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**

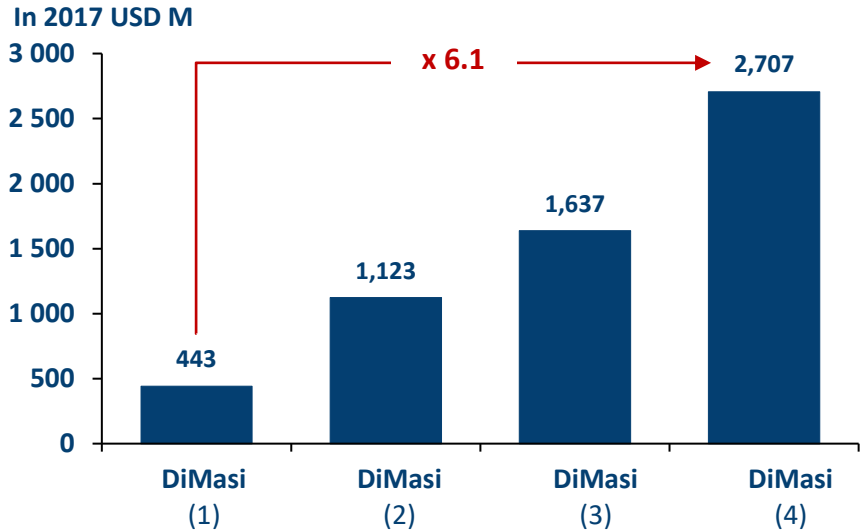
*Sources: OECD database (January 2023) – Center for Medicare & Medicaid Services (February 2023) – Smart Pharma Consulting analyses*

*[1] Or latest data available – [2] Other expenditures include ancillary services, preventive care and governance, healthcare system and financing administration*

# The analysis of four studies carried out with the same methodology shows that the development cost of new drugs has more than sextupled over the last three decades

## Evolution of R&D costs

**Estimated capitalized cost per approved new drug (pre-tax)**




*Note: For the sake of comparability, all values are adjusted to USD 2017 prices using data of the US GDP implicit price deflator from the US. Bureau of Economic Analysis. The GDP implicit deflator shows the rate of price change in the economy as a whole; being the ratio of GDP in current local currency to GDP in constant local currency*

- The increase of the **capitalized R&D costs per approved new drug**, between 1991 and 2016 is explained by:
  - **Growth of out-of-pocket costs**, especially clinical trial spending (x10.8 vs. x3.9 for preclinical spending)
  - **Decrease of the success rate** to reach approval from phase I (23% vs. 12%)
  - **Overall increase** of the used **cost of capital**
- However, these assumptions of cost of capital seem **overestimated** compared with available data from NYU[2] Stern School of Business for biotech products (9.2% for biotech and 7.7% for traditional pharma companies)

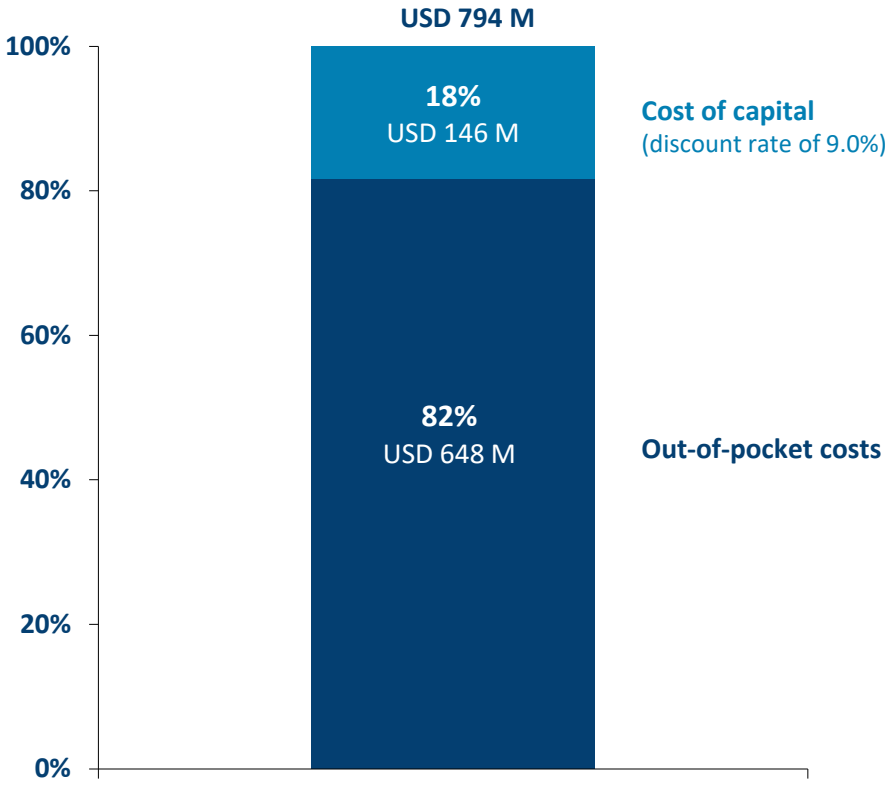
*Sources: DiMasi (1991) – DiMasi et al. (2003) – DiMasi, Grabowski (2007) – DiMasi (2016) – Cost of Capital, NYU Stern School of Business (January 2016) – Implicit price deflators for GDP, Bureau of Economic Analysis – Smart Pharma Consulting analyses*

*[1] Products with first testing in humans over the analyzed period – [2] New York University*

# This study, published in the JAMA Internal Medicine, estimates the median cost of developing a single cancer drug at USD 794 M, including a 9% per annum cost of capital

## R&D costs estimates for oncology drugs (2017)

**Estimated 2017 capitalized R&D cost per new cancer drug[1]**




- The **10 drugs** included in the study had a **medium development time** of **7.3 years**
- The **median cost of drug development** was estimated at:
  - **USD 648.0 M**
  - **USD 757.4 M** (with a 7% per annum cost of capital[2])
  - **USD 793.6 M** (with a 9% per annum cost of capital)
- With a median time of **4.0 years** since approval, the total revenues from sales of these 10 drugs since approval was **USD 67.0 B** compared with total **R&D spending** of **USD 7.2 B** (USD 9.1 B, including 7% cost of capital)

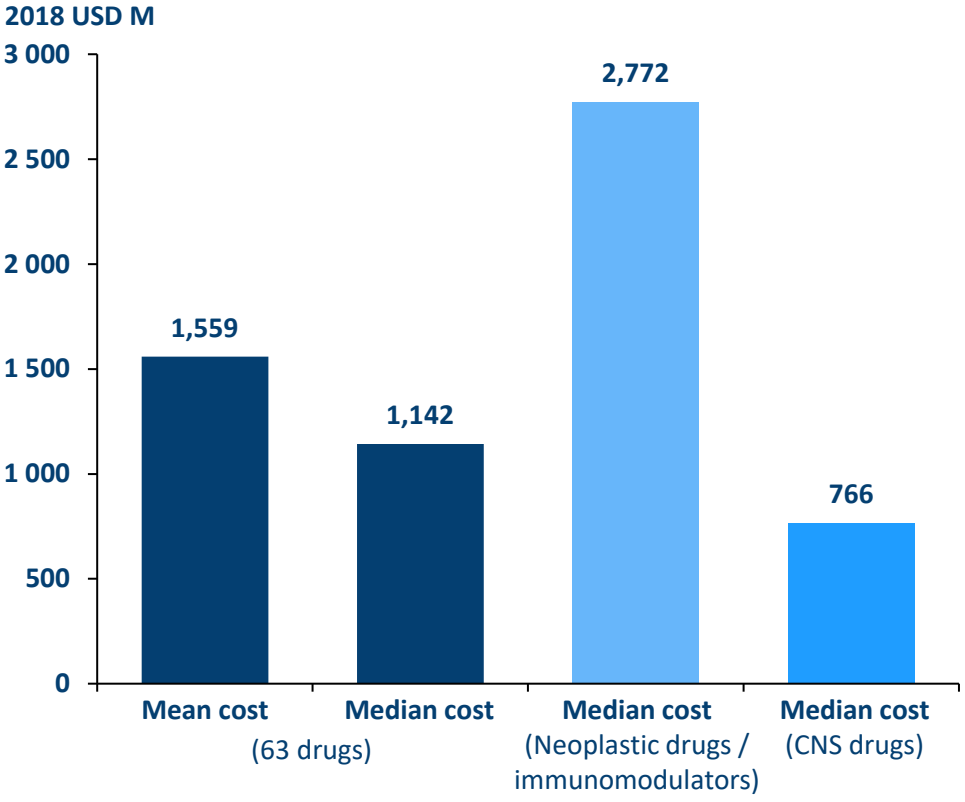
*Source: V. Prasad et al. in JAMA Internal Medicine (November 2017) – Smart Pharma Consulting analyses*

*[1] Cumulative R&D spending was estimated from initiation of drug development activity to date of approval – [2] Opportunity cost*

# This study confirms the important variability of R&D estimated costs, depending on the products analyzed, the calculation method and the underlying assumptions

## R&D costs estimates for drugs (2018)

**Estimated 2017 capitalized R&D cost per new drug[1]**




- The **mean cost of R&D** was estimated at **USD 1,559 M**…
- …and the **median R&D cost** at **USD 1,142 M**, after accounting for the costs of failed trials
- The median costs by therapeutic area ranged from:
  - USD 766 M for CNS drugs, to
  - USD 2,772 M for antineoplastic and immunomodulating drugs
- The R&D costs were capitalized at a real **cost of capital rate of 10.5%** per year

*Source: O. J. Wouters et al., JAMA (March 3, 2020), corrected on September 20, 2022 – Smart Pharma Consulting analyses*

*[1] Including the costs of failed trials ; data (mainly coming from US SEC, FDA database and ClinicalTrials.gov) were analyzed on 63 new products approved by the FDA between 2009 and 2018*

# Remicade, the first marketed anti-TNF agent, has revolutionized the management of autoimmune diseases by introducing biotherapies into the therapeutic arsenal

## Remicade (infliximab): Autoimmune diseases


### Drug history

- Infliximab, a **chimeric monoclonal antibody**, was discovered in 1989 by Jan Vilcek and Jungmin Le at New York School of Medicine
- They **collaborated** with **Centocor**, a biotech company, acquired by Johnson & Johnson in 1999, **to develop the drug**
- Infliximab (Remicade), is the **first anti-TNFα**, which obtained its initial **approval in 1998** followed by approval in another five adult and two pediatric chronic inflammatory conditions
- J&J entered into an **agreement with Schering-Plough**[1] to distribute the product in Europe, Russia and Turkey
- In 2017, Remicade was **ranked 4th** amongst **best-selling** prescription drugs of all time

### Impact on patients' life

- Remicade is indicated in **different autoimmune diseases** by directly addressing the inflammatory mechanism (e.g., IBD[2], rheumatoid arthritis, psoriasis)
- Before the 2000s, **conventional treatments** (e.g., methotrexate) were the only therapeutic option...
- ...and did not stabilize patients in the long term
- As a new treatment option, Remicade allowed to considerably improve patients' life with for example the:
  - Slowing down of the disease progression
  - Recovery of mobility
  - Decrease in joint pain

*Sources: Johnson & Johnson and MSD press releases – R. Melsheimer et al. in Biologics: Target and Therapy (2022) – Smart Pharma Consulting*

*[1] Acquired by MSD in 2009 – [2] Inflammatory bowel diseases (i.e., Crohn Disease, Ulcerative Colitis)*

# Gleevec is an extraordinary innovation, developed in a record time by Novartis, which allows to treat in a very effective way, chronic myeloid leukemia

## Gleevec[1] (imatinib): Chronic myeloid leukemia (CML)

NOVARTIS


### Drug history

- **Imatinib** (Gleevec) was discovered in the late 90s by scientists at **Ciba-Geigy**, that became Novartis after the merger with Sandoz in 1996
- The **first clinical trial** of Gleevec took place in **1998**, and showed **exceptional results**
- Novartis made the product **its priority**, despite the forecasted low business potential of the product, at that time
- Gleevec was **approved by the US FDA in 2001**, less than **3 years** after the first clinical trial…
- …which is significantly less than the standard development duration

### Impact on patients' life

- Imatinib, a **tyrosine kinase inhibitor**, is an oral therapy that directly targets the origin of CML
- Before imatinib, people with chronic myeloid leukemia had a **life expectancy** of four to five years after diagnosis
- Clinical results showed:
  - A complete hematological response in **98%** of patients
  - An overall survival rate of **89%** at 5 years (vs. 30% before Gleevec)
  - A relapse rate of only **17%**
- Gleevec is now used to treat other cancer types (e.g., skin cancer, digestive tract cancer)

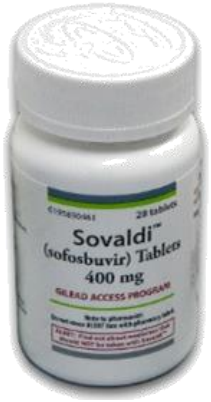
*Sources: Gleevec: The breakthrough in cancer treatment (2008) – Smart Pharma Consulting*

*[1] Also commercialized as Glivec, outside of the US*

# Sovaldi, approved at the end of 2013 and commercialized by Gilead Sciences, has revolutionized the care of hepatitis C, with a definitive cure in 12 to 24 weeks in over 90% of patients

## Sovaldi (sofosbuvir): Chronic hepatitis C infection

GILEAD




### Drug history

- Sofosbuvir was **discovered in 2007** by Michael Sofia, a Pharmasset scientist, and the drug was **first clinically tested in 2010**
- In 2011, **Gilead Sciences** bought **Pharmasset** for about **USD 11 B** and got the **FDA approval** in **December 2013**
- The **first year** of commercialization, Sovaldi sales exceeded **USD 10 B**
- **No generics** of Sovaldi are currently marketed...
- ...but **price reductions** have been agreed to **facilitate access** to the treatment

### Impact on patients' life

- **Hepatitis C virus** causes inflammation of the intestine which can lead to **serious consequences** (cirrhosis or cancer)
- The direct antiviral drug is effective for all **HCV** types, in association with ribavirin or interferon
- At one tablet per day for **12-24 weeks**, Sovaldi is a **definitive cure** with very few side effects
- The treatment has proven to be effective in **over 90% of patients**
- Previously, treatment strategies relied on strengthening the patient's immune system
- The drug has paved the way for **global eradication** of the hepatitis C virus

*Sources: Gilead press releases – HepCoalition website –*
*Hepatitis C treatment: a short history of Sofosbuvir and Sovaldi (2017) – Smart Pharma Consulting*

# Zolgensma, a gene therapy marketed by Novartis, but partly developed via public research, cures children with spinal muscular atrophy with a single injection

## Zolgensma (onasemnogene abeparvovec): Spinal Muscular Atrophy (SMA)

### Drug history

- Zolgensma gene therapy was **pre-clinically developed** by **Genethon**[1] and the **CNRS**[2]
- The clinical studies were delegated from 2013 onwards to the **US biotech AveXis**, which had the necessary financial resources
- In 2018, after the success of the clinical trials, Genethon and the CNRS **granted a license** to AveXis,...
- ...**acquired the same year** for **USD 8.7 B by Novartis** which finally obtained an FDA approval in 2019
- With a **price** of more than **USD 2 M per patient**, Zolgensma was the most expensive drug in the world at its launch

### Impact on patients' life

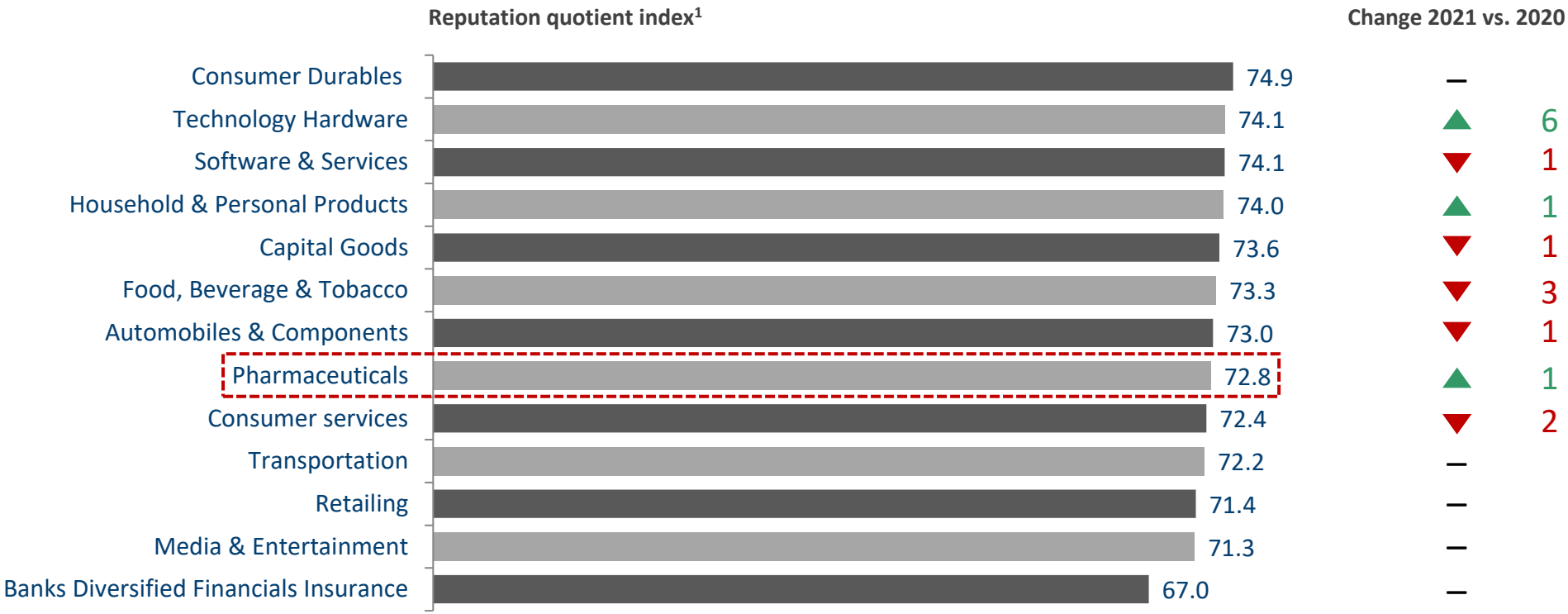
- SMA is a **rare neuromuscular disease**, extremely physically disabling or fatal depending on the type
- Zolgensma, by a **single injection,** allows to overcome the deficiency of the responsible gene for the disease
- The therapy is indicated in **children under 2 years of age** and to date, more than 2,300 patients have benefited from it worldwide
- Phase III clinical trial showed a **95% survival rate**, compared to 50% based on the natural history of the disease
- Data in **pre-symptomatic patients** showed a **100% survival rate**

*Sources: AFM Telethon website – Novartis press releases – Smart Pharma Consulting*

*[1] AFM Telethon laboratory, French association fighting against myopathies – [2] French national center for scientific research*

## If the pharma industry's role to fight the Covid-19 pandemic has contributed to improve its reputation, it is still behind consumer goods and tobacco, for reasons that are mainly structural

### Corporate reputation ranking by sector (2021)




*"Distrust of pharma companies stems from a belief that they have deviated from their mission of improving public health to focus on increasing profits"*

*Sources: 2021 Global RepTrak 100 Study – Smart Pharma Consulting analyses*

*[1] Based on 7 indicators: Products/Services, Innovation, Workplace, Governance, Citizenship, Leadership, Financial performance; and with score > 80 = Excellent/top Tier, 70-79 = Strong/Robust, 60-69 = Average/Moderate, 40-59 = Weak/Vulnerable, < 40 = Poor/Bottom Tier*

# While pharma companies contribute to save and improve health of billions of people, they are regularly and heavily criticized by stakeholders for the manner they accomplish their mission

## Drivers of pharma companies' reputation (1/2)

**Main criticisms from different stakeholders (e.g., governments, HCPs, media, citizens)**

- High drug costs limiting access to the wealthiest countries and social classes
- Massive profits (~32%)[1] to enrich shareholders
- Aggressive patent protection strategies, limiting access to innovative medicine
- Unethical practices to influence the prescription of HCPs
- Lack of transparency (e.g., drug pricing, clinical study results, collaborations with KOLs, etc.)


Mission: contribution to prolong life, to improve health and wellbeing of people by developing drugs and vaccines

*Sources: Smart Pharma Consulting analyses*

[1] *Expressed in EBITDA (Earnings before interest, taxes, amortization and depreciation) as a percentage of sales*

## There is a mismatch between the pharma companies' mission, their corresponding activities and the way they implement them

### Drivers of pharma companies' reputation (2/2)


Pharma companies claim that their **mission** consists in **improving** and **extending people's lives** by offering products and related services


**Actions** enabling to accomplish their mission are **not well-known**, nor **well-understood** by stakeholders, which **lead** to **distrust** and **suspicion**


If **stakeholders** agree with pharma companies' mission…
… they **consider** that corresponding **actions are not fully in line**

*Sources: Smart Pharma Consulting analyses*

# Pharma companies will remain very profitable, despite increasing price pressure and R&D costs, while their reputation could improve by raising awareness about their breakthrough drugs

**Pharma Market Attractiveness**

- Pharma companies' **profitability should decline** by end of 2027, but will **remain highly profitable**, provided they keep on improving their operational and organizational efficiency

**Drug Price Pressure**

- Knowing that **payors** will keep on **increasing** drug **price** pressure, pharma companies should negotiate a "**Drug Price Stability Pact**" based on various criteria such as medico-economic value, commitment to invest in R&D, manufacturing, logistics, to safeguard employment

**R&D Cost of Drugs**

- **R&D cost varies** significantly from one source to another, due to **differences in therapeutic areas**, **methodologies** and **cost assumptions** used, ranging **from USD 0.8 to 2.7 Bn** per drug

**Impact of Drugs on people's life**

- **Pharma companies** contribute to **improve** and **extend people's life** by discovering and marketing **breakthrough drugs** (e.g., Remicade, Gleevec, Sovaldi, Zolgensma)

**Companies' reputation**

- To **improve** their **average reputation**, pharma companies should carry out **activities in line** with their **mission**, **be compliant** with the **code of ethics** and **communicate faithfully**

*Sources: Smart Pharma Consulting*

Smart Pharma
CONSULTING

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

## Five Insights about the Pharma industry

### Truths & Untruths

- Smart Pharma Consulting proposes to cover 5 key insights that are specific to the pharma market:
  1. Why is the pharma market so attractive?
  2. Why will the pressure on drug price intensify?
  3. What is the R&D cost of drugs?
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  5. Why do pharma companies have a poor reputation?

## 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
  - 64 position papers covering the following topics:
    1. Market Insights
    2. Strategy
    3. Market Access
    4. Medical Affairs
    5. Marketing
    6. Sales Force Effectiveness
    7. Management & Trainings
- 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

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