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This document proposes a review of global pharma trends by 2025 and an analysis of top 20 pharma companies' performance and strategies

Introduction

Smart Pharma Consulting proposes to address the following issues:



What is the structure of the global pharma market and how should it evolve by 2025?



What has been the recent performance of the top 20 pharma companies worldwide?



What are the current portfolio strategies of the top 20 pharma companies worldwide?

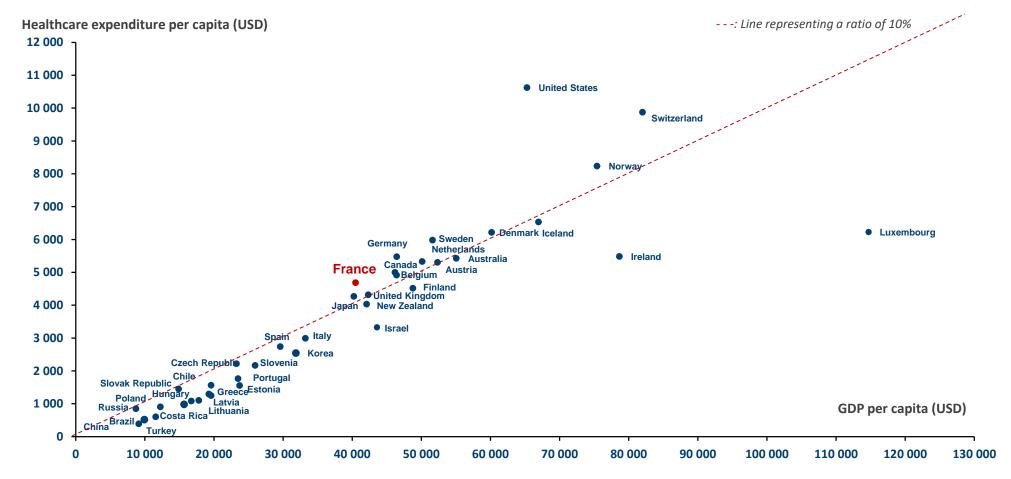


What have been the objectives pursued by the top 20 pharma companies in their recent M&A deals?



Healthcare expenditure and GDP¹ per capita are highly related and the ranking² of France (#15 and #19 respectively) shows that healthcare is a key national priority

Relation between GDP and healthcare expenditure per capita (2018*)

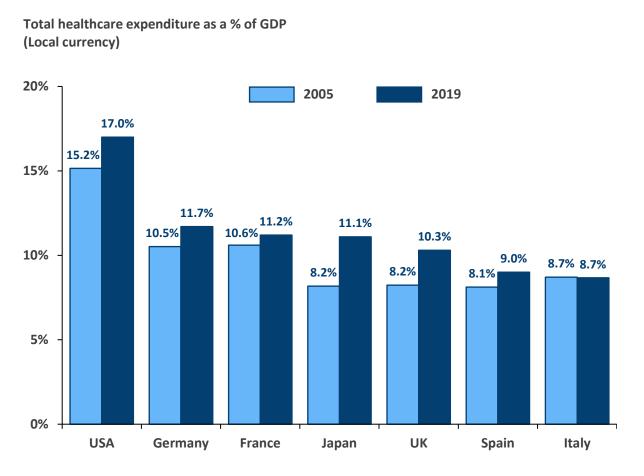


Sources: World Bank database (March 2021) -Smart Pharma Consulting analyses



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

Healthcare expenditure as a percentage of GDP (2019*)

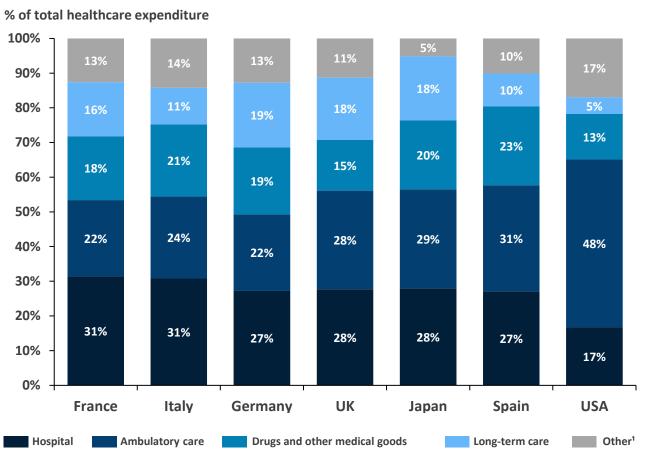


- Healthcare expenditure represents one of the largest public spending items in most developed economies: 1st (USA), 2nd (France, Germany, Japan and UK)¹ and 3rd (Italy and Spain)²
- At best, governments and payers will manage to slow down the rise of healthcare expenditure as a percentage of GDP but not to stop it
- There is no optimal ratio of healthcare expenditure over GDP
- This ratio primarily results from:
 - Public health conditions
 - Governments' investment prioritization
 - Citizens' willingness to seek for care
 - Healthcare cost



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 (2019*)



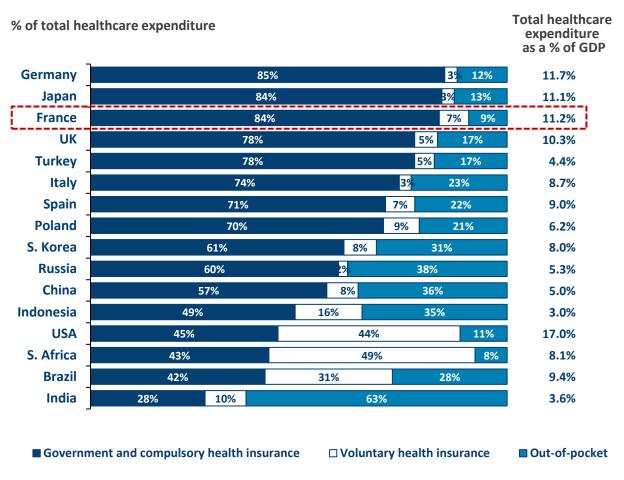
- Drugs represent the 3rd largest source of healthcare expenditure in most major developed countries
- Drugs are typically the easiest segment to apply cost-containment measures on, as decisions are:
 - Made by payers (either public and/or private), with a limited bargaining power of suppliers
 - Much better accepted by citizens than restriction measures on the other segments
 - Practically easy to implement
- However, to significantly contain the raise of total healthcare costs, governments need to apply costoptimization measures on all healthcare segments, irrespective of their relative importance

Sources: OECD database (March 2021) – Smart Pharma Consultina analyses



France is one of the countries where the percentage of "out-of-pocket" spending to cover the healthcare expenditure is the lowest

Share of public spending in total healthcare expenditure (2019*)



- With 11.2% of its GDP spent in healthcare, France belongs to the countries allocating the largest share of their resources
- Its level of public spending on healthcare is amongst the highest, just behind Germany and Japan, showing a highly protective healthcare system
- All the French citizens benefit from a public health insurance and 95% of them have a complementary private healthcare insurance, which is compulsory, since the 1st of January 2016, for all employees, irrespective of the size of their company
- As a result, "out-of-pocket" spending represents only 9% of total healthcare expenditure



The key drivers and limiters of the global pharmaceutical market by the end of 2025, as well as their probable impact on sales trends, are well identified and should remain stable

Global pharmaceutical market drivers and limiters (2020 – 2025)



- Population increase and ageing
- Better access to medicines in emerging markets (e.g., BRICS¹, Mexico, Turkey, etc.) as a result of an increasing GDP per capita
- 3 Strong development of generics market (access to a larger number of people, especially in lower income countries), and to a lesser extent of biosimilars
- Strong demand from patients / PAGs² for more effective and better tolerated new drugs



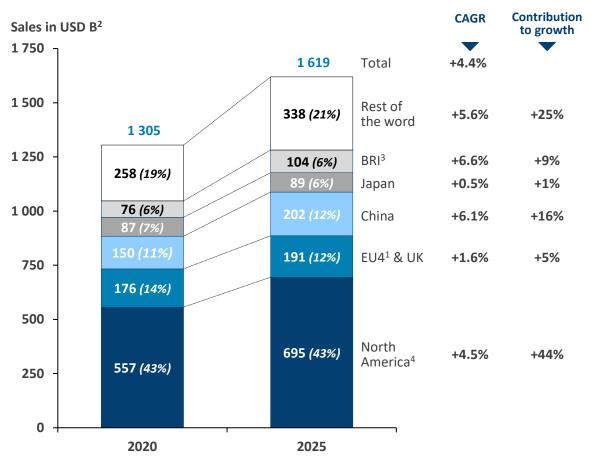


- Decreasing R&D productivity of pharma companies re. breakthrough innovations
- Increasing barriers to market access and stronger pressure on price from payers (governments, HMOs, patients, etc.), exacerbated by a tougher economic environment
- Increasing competition of nonreimbursed drugs by medical devices and food supplements
- Intensification of competition from generic and biosimilar drugs



Sales of EU4¹ & UK 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 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
- EU4 & UK 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 in the world
- North America (of which the USA accounts from 41%) 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
- ~75% of the global pharmaceutical market profits which have been generated by the USA in 2020, should reach ~80% in 2025

Sources: IQVIA Institute (April 2021) – Smart Pharma Consulting estimates



By 2025, the French Pharma market is expected to step back from the 5th to the 6th place at the global level and remain at the 2nd place in Europe

Global pharmaceutical market ranking in value¹ (2015 – 2020 – 2025)

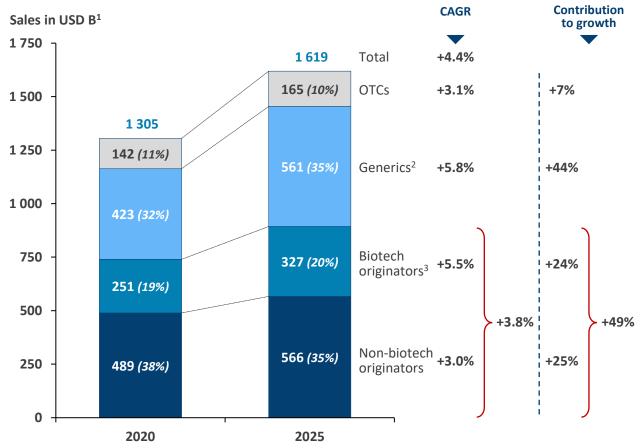
Rank	2015		2020		2025	CAGR 2020 – 2025	
1	USA		USA		USA	++	
2	China		China		China	+++	
3	Japan		Japan		Japan	+	
4	Germany		Germany		Germany	++	
5	France		France		Brazil	++++	
6	Italy		Italy	\longrightarrow	France	+	
7	UK		UK		Italy	++	
8	Spain		Brazil		UK	++	
9	Canada		Spain		India	++++	
10	Brazil		Canada		Russia	++++	
11	India		India		Spain	++	
12	South Korea		Russia		Canada	++	
13	Russia		South Korea		South Korea	+++	
14	Australia		Australia		Turkey	++	04.00
15	Saudi Arabia		Mexico		Mexico	++	CAGR 2020 – 2025
16	Mexico		Saudi Arabia		Australia	++	
17	Poland		Poland		Saudi Arabia	++	++++ → ≥8% +++ → 6 - 7.9%
18	Switzerland		Turkey		Poland	++	++ → 3 – 5.9%
19	Belgium		Belgium		Belgium	++	+ → <0 - 2.9%
20	Netherlands		Taiwan		Egypt	+++	2 10 2.5%

Sources: IQVIA Institute (April 2021) – Smart Pharma Consulting estimates



All the business segments of the pharma market will be affected by the Covid-19 crisis through a strong price pressure over the 2020-2025 period

Global pharmaceutical market by strategic segment (2020 – 2025)



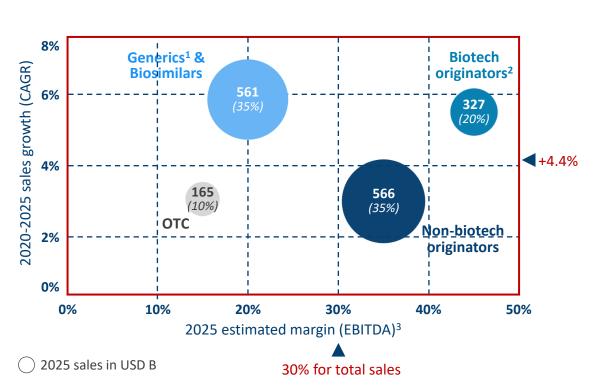
- OTCs, which should remain the smallest segment of the global pharma market, has been significantly affected by the Covid-19 crisis in 2020, especially during lockdown periods. OTCs should grow at a lower pace than the other market segments, due to their stronger sensitivity to the economic environment
- Generics and biosimilars should continue to grow in volume due to patent expiries, but pressure on prices should intensify on this market segment
- Biotech originators should become the main driver of innovation in the next 5 years
- Non-biotech originators should be less dynamic, due to generics competition and the maturity of most of the brands. However, they should remain the largest segment of the global pharma market

Sources: IQVIA Institute (April 2021) – Smart Pharma Consulting estimates



By 2025, the sales growth of the pharma market should be essentially driven by generics and biotech originators, but pharma companies should lose two points of profitability

Global pharmaceutical market attractiveness by strategic segment (2020 – 2025)



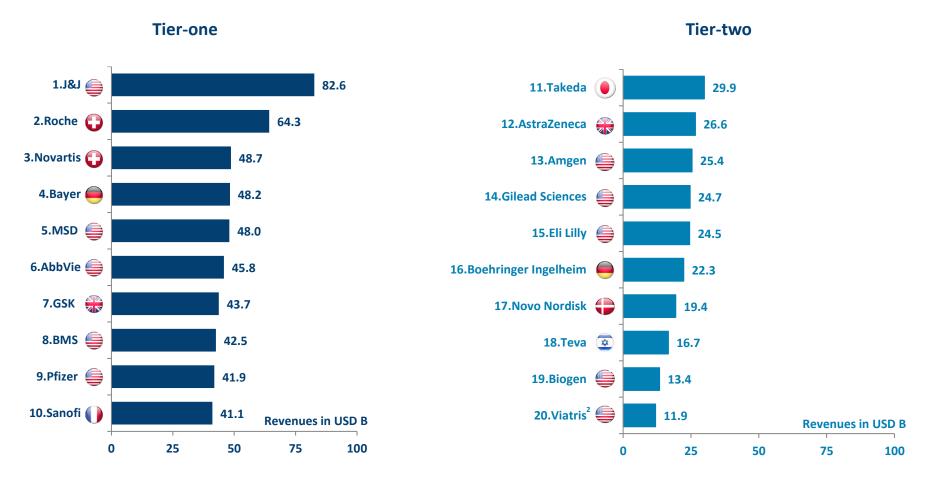
- By 2025, the global pharma market should reach USD 1,619 B and grow at a pace of +4.4% per year, i.e., 1.5 point of percentage above the forecasted worldwide economic growth, but 0.6 point below the pre-Covid-19 estimates
- The average EBITDA of the pharma industry should decrease from ~32% in 2020 to ~30% in 2025, mainly as a result of increasing price pressure
- In 2025, the average net profits of pharma companies are expected to be more than twice higher than the average of all other business sectors
- The biotech segment will remain very attractive but biosimilar competition will ramp up
- The OTC segment should be the least attractive

Worldwide economic growth – CAGR 2020-2025: +2.9%



The top 20 pharma companies based on all segments of activities¹ counts 10 companies from the USA, 8 from Europe, 1 from Japan and 1 from Israel

Top 20 pharma companies (2020) – All segments

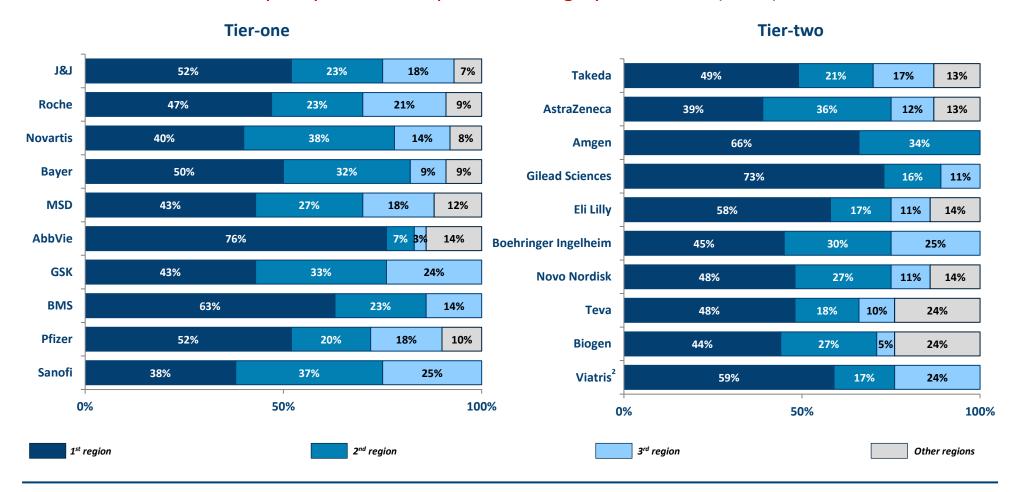


Sources: Companies annual reports (2020) – Pharmaceutiques (March 2021) – Smart Pharma Consulting analyses



Tier-two pharma companies tend to be less geographically diversified, with most of them generating half of their revenues in a single region

Top 20 pharma companies – Geographical areas (2020)

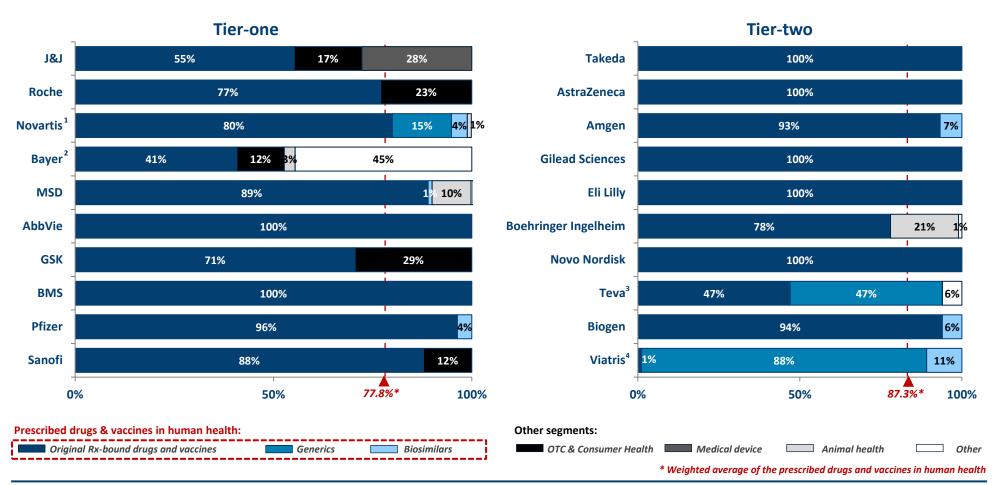


Sources: Companies annual reports (2020) – Smart Pharma Consulting analyses



In 2020, original Rx-bound drugs and vaccines segments were the main source of revenue for most big pharma companies

Top 20 pharma companies – Strategic segments coverage (2020)

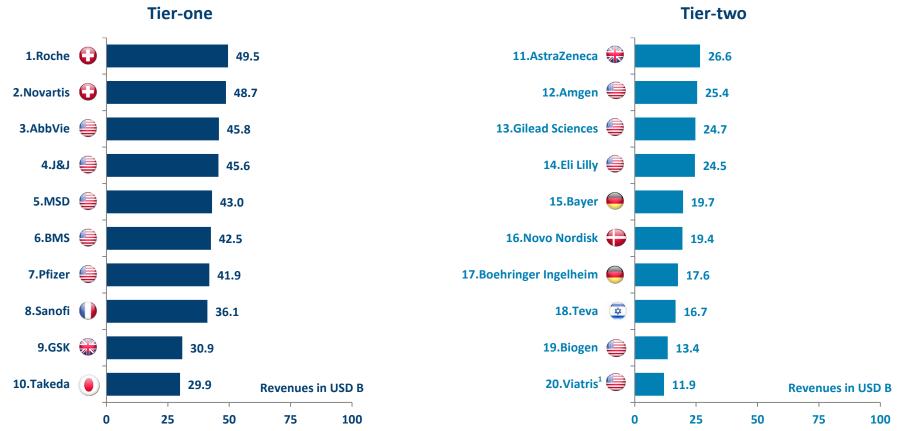


Sources: Companies annual reports (2020) – Smart Pharma Consulting analyses 1 Including Sandoz: Novartis division of generics and biosimilars $-^{2}$ Other includes Crop Science specialized in chemicals (fungicide, herbicide etc.) $-^{3}$ Generics segment including OTC products $-^{4}$ Including mature brands business of Pfizer Upjohn merged with Mylan since November 16, 2020



The top 20 pharma companies based on strategic drug & vaccines segments sales counts 10 companies from the USA, 8 from Europe, 1 from Japan and 1 from Israel

Top 20 pharma companies – Drugs & vaccines strategic segments (2020)

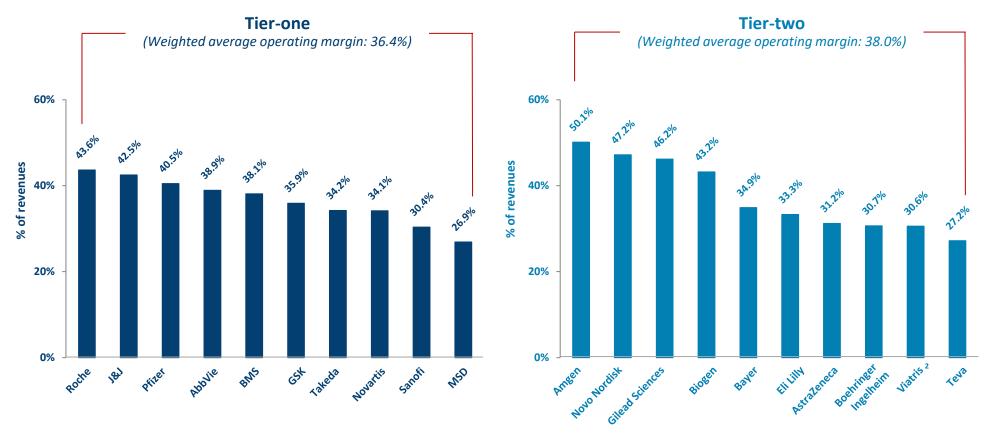


Note: panel of the 20 biggest pharma companies in terms of prescribed sales (drugs & vaccines) in human health in 2020 (excluding diagnostics, medical device, nutrition products and animal heath)



The 2020 average operating margin was higher for tier-two companies in comparison to tier-one companies, with a similar dispersion profile

Top 20 pharma companies – EBITDA¹ (2020)

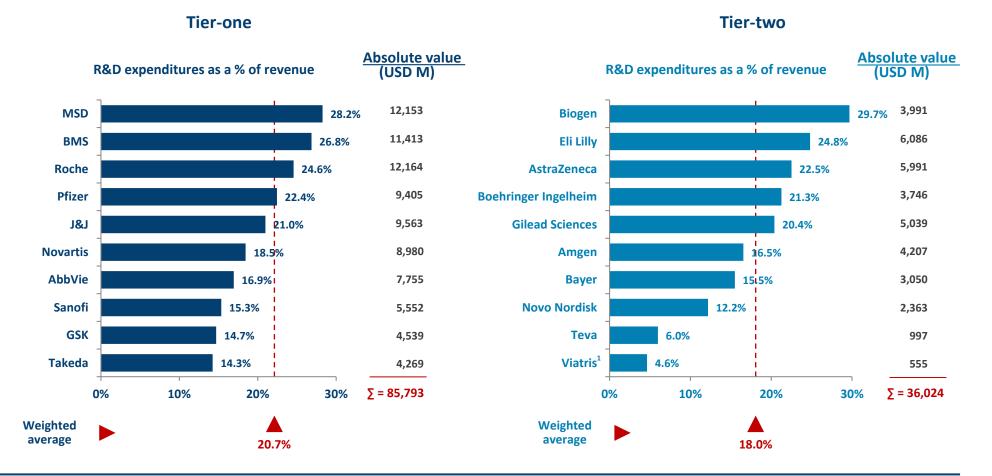


Note: panel of the 20 biggest pharma companies in terms of prescribed sales (drugs & vaccines) in human health in 2020 (excluding diagnostics, medical device, nutrition products and animal heath)



Tier-one pharma companies have spent two times more for R&D in absolute value than tier-two pharma companies and ~2.7 points more as a percentage of their revenues

Top 20 pharma companies – R&D expenditures (2020)



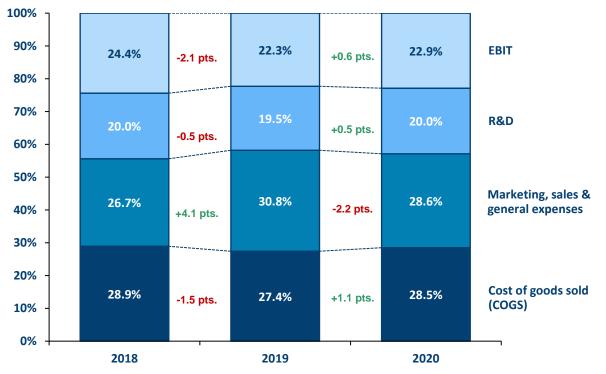
Sources: Companies annual reports (2020) – Smart Pharma Consulting analyses

In 2020, the weighted average operating result (EBIT) of the top 20 pharma companies reached ~23% of revenues, decreasing by 1.5 point of percentage vs. 2018

Top 20 pharma companies – Cost structure (2018 – 2020)

Cost structure as a percentage of total revenues

Weighted average of total revenues



- The analysis of the top 20 pharmaceutical companies in the world shows that their average profitability has slightly decreased by 1.5 point of percentage between 2018 and 2020
- This negative trend can be explained by:
 - The price pressure imposed by healthcare authorities
 - The loss of exclusivity of many blockbusters that has led to the intensification of generics and biosimilars competition
- With an average operating result of ~23% in 2020, the level of performance remains high, which is the Achilles heel of pharmaceutical companies when negotiating price and reimbursement of their drugs with governments and payers
- In 2020, Marketing, sales & general expenses were 43% higher than investment in R&D

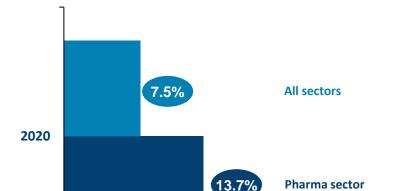
Note: panel of the 20 biggest pharma companies in terms of prescribed sales (drugs & vaccines) in human health in 2020 (excluding diagnostics, medical device, nutrition products and animal heath)



In 2020, the net profitability of the pharma sector outpaces by ~6.2 points of percentage the average profitability of all sectors

Profitability and sales dynamics of the pharma sector (2018 – 2020)

Net profitability in 2020 (Of top 20 Rx pharma companies and of the global economy)



Return on revenues¹ (weighted average)

15%

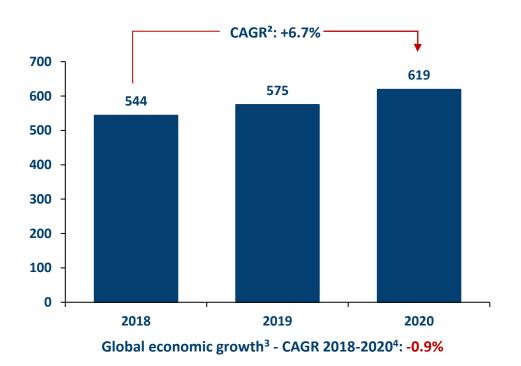
20%

25%

30%

10%

Market sales trend (Of top 20 Rx pharma companies)



Note: panel of the 20 biggest pharma companies in terms of prescribed sales (drugs & vaccines) in human health in 2020 (excluding diagnostics, medical device, nutrition products and animal heath)

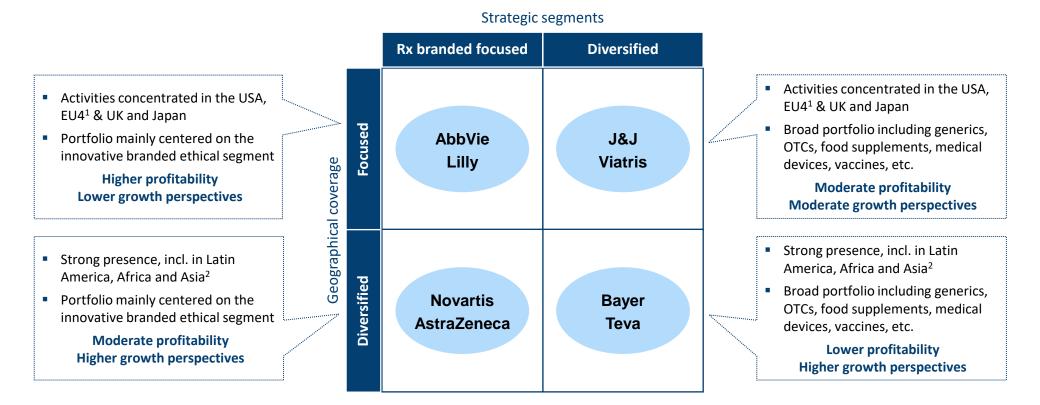
0%

5%



Best performers are focused on innovative Rx-bound drugs and generate an important share of their revenues from the USA, which is the most profitable and dynamic market

Development strategy matrix – Principles



Note: Rx branded focused: Prescribed drugs and vaccines \geq 75% of total product sales – Geographically focused: >50% of sales in a single geographical region (e.g., USA, Europe, Japan, etc.)

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Tier-one and tier-two companies are mainly focused on Rx branded segment, but tier-one companies are more geographically diversified

Pharma companies' development strategy (2020)

Tier-one

Strategic segments

		_	
		Rx branded Focused	Diversified
		abbvie	
deoglapliical covelage	Focused	ر ^{ال} Bristol Myers Squibb	Johnson Johnson
		₹ Pfizer	
	Diversified	Roche	BAYER BAYER E R
ב ב ב		NOVARTIS	R
		MSD	gsk
		SANOFI	

Tier-two

Strategic segments

		Rx branded Focused	Diversified	
Geographical coverage	Focused	AMGEN Lilly GILEAD	₩ VIATRIS ⁻¹	
	Diversified	AstraZeneca Biogen Boehringer Ingelheim novo nordisk Takeda	teva	

Note: Rx branded focused: Prescribed drugs and vaccines $\geq 75\%$ of total product sales - Geographically focused: >50% of sales in a single geographical region (e.g., USA, Europe, Japan, etc.)



Most of the recent M&A operations have been carried out to strengthen pharma companies position on their core strategic segments

Major M&A operations (2016 – 2020)

Acquirer	Acquired	Strategic objectives			
Acquirei	(> USD 2.0 B)	Diversification	Strengthening	Expansion	
181	 Actelion (Pulmonary arterial hypertension) Momenta pharmaceuticals (Biotechnology) Auris Health (Medical device) Abbott Medical Optics (Products for dry & irritated eyes) 		V V	<i>V V</i>	
Roche	Sparks Therapeutics (Gene therapies)	✓			
Novartis	 Advanced Accelerator Applications (Oncology) AveXis (Gene therapies, rare diseases) Endocyte (Cancer and inflammatory diseases) The medicine company (Critical care) 		\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \		
Bayer	Monsanto (Chemical & agricultural biotechnology) Asklepios Biopharmaceutical (Gene therapies for genetic disorders)	✓	✓		
MSD	Antelliq (Animal health)		√		
Abbvie	Stemcentrx (Oncology) Allergan (Branded pharmaceuticals)	✓	V		
GSK	Tesaro (Oncology) Stiefel (Dermatology)	✓	√		
BMS	IFM Therapeutics (Cancer immunotherapies) Celgene (Oncology) MyoKardia (Rare cardiovascular disease)	~	<i>Y Y Y</i>		

Acquirer	Acquired	Strategic objectives			
Acquirei	(> USD 2.0 B)	Diversification	Strengthening	Expansion	
Pfizer	Pfizer - Medivation (Oncology) - Anacor (Anti-inflammatory) - ArrayBiopharma (Oncology)		V V		
Boehringer Ingelheim (Consumer healthcare business of the company) Bioverativ (Rare blood disorders) Ablynx (Immunotherapies) Principia BioPharma (Oral therapies in immunology & oncology) Synthorx (Biotechnology)		~	<i>Y Y Y</i>		
Takeda = Ariad Pharmaceuticals (Oncology) Shire (Rare diseases, US-based)			√ √	√	
AstraZeneca - Acerta Pharma (Cancer and autoimmune diseases) - Alexion Pharmaceuticals (Rare disease, US-based)			<i>Y</i>		
Amgen	Amgen • Otezla (Dermatology)		✓		
Gilead Sciences - Kite Pharma (Cancer immunotherapies) - Forty Seven (Cancer immunotherapies) - Immunomedics (Cancer treatment)			V V		
Eli Lilly	Loxo Oncology (Oncology)		✓		
Boehringer Ingelheim	Merial (Animal health business of Sanofi)		~		
Teva	Teva - Actavis Generics (Allergan generics) Rimsa (Latin America)		✓	V	
Viatris	Viatris • Meda (OTC, Emerging markets) • Upjohn (Pfizer's established medicines)		✓	✓	

Note: Diversification means entering new strategic segments/balancing minor segments – Strengthening means reinforcing major strategic segments – Expansion means geographical coverage

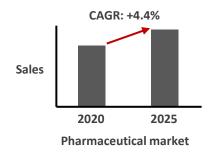
Sources: Companies annual reports (2020) – Smart Pharma Consulting analyses



The global pharmaceutical market should keep on growing at a pace of 4.4% p.a. by 2025, but pharma companies' profitability would be impacted by strong price cuts

Conclusion (1/2)

Global pharma market 2020-2025 perspectives



The global pharma market should reach USD 1,619 B in 2025, representing a +4.4% CAGR over the 2020-2025 period

- North America should continue to weigh for 43% of the global pharma market in value and should generate ~80% of the global pharmaceutical market (vs. ~75% in 2020)
- EU4¹ & UK countries should see their weight in the global pharma market drop by 2 points from 14% to 12% due to stringent cost containment measures
- All the business segments will be affected by the pandemicsinduced economic crisis, resulting into strong price pressure

Top 20 pharma companies Performance & Strategies

EBITDA ²	37% of sales	EBIT ³	~23% of sales	R&D	~20% of sales

Strategic segments

		Rx branded focused	Diversified		
		abbvie AMGEN	a-l		
geograpiiicai coverage	Focused	ر ^{ااا} Bristol Myers Squibb Lilly	Johnson Johnson		
		₹ Pfizer	⊚ VIATRIS″		
abnic		AstraZeneca Biogen	BA		
geog	Diversified	Boehringer Ingelheim Roche	BAYER BAYER TEVO		
	Dive	U NOVARTIS SMSD	gsk		
		SANOFI Takeda			

¹ France, Germany, Italy and Spain − ² Earnings before interest, taxes, amortization and depreciation − ³ Earnings before interest and taxes



To improve their performance, pharma companies tend to refocus on therapeutic areas with high potential for growth (e.g., rare diseases, oncology, gene and cellular therapies)

Conclusion (2/2)

- In recent years, mega-deals aiming at increasing pharma companies' size and/or strengthening their economies of scale have come to an end
- Pharma companies rather seek to refocus their assets on secondary-care therapeutic areas with high potential for growth:
 - Rare diseases (e.g., acquisition of Shire by Takeda or of Alexion by AstraZeneca, etc.)
 - Oncology (e.g., merger of Celgene and BMS, acquisition of Stemcentrx by AbbVie and partnership of the latter with Genmab, etc.)
 - Gene and cellular therapies (e.g., partnership of Biogen with Sangamo, etc.)

- Top-pharma companies increasingly seek to acquire promising early-stage development biotechs with the aim to add complementary platforms and technologies...
- ... and tend to foster their collaborations with other pharma companies, notably in the Covid-19 context (e.g., Pfizer / BioNTech, GSK / Sanofi, AstraZeneca / Oxford University, etc.)
- Conversely, divestments are made in other areas (e.g., separation by Pfizer of its Upjohn mature brands division merged with Mylan into the new Viatris, rethinking by Sanofi of its core activities, sale by GSK of its Consumer Healthcare division)



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

The 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 new issue is designed to be read in 15 to 20 minutes and not to exceed 25 pages

Issue #19

Top 20 pharma companies

Performance & Strategies

This paper proposes a review of global pharma trends by 2025 and an analysis of the top 20 pharma companies' performance and strategies

Global Pharma Market – 2020-2025 perspectives

- International healthcare expenditure
- Global pharma market

Top 20 pharma companies – Performance & Strategies

- 2020 performance
 - All strategic segments
 - Drugs & vaccines only
- Portfolio strategies
- M&A operations

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 - The publication of articles, booklets, books and expert reports
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 - 11 position papers in the "Best-in-Class Series"
 - 18 position papers in the "Market Insights Series"
 - 10 position papers in the "Smart Manager Series"
 - 10 position papers in the "Smart Tool Series"
- Our research activities in pharma business management and our consulting activities have shown to be highly synergistic
- We hope that this new publication will be useful for you
- We remain at your disposal to carry out consulting projects or training seminars to help you improve your operations

Best regards

Jean-Michel Peny