

Global Pharma R&D Overview

MARKET INSIGHTS SERIES

Situation analysis & Perspectives

December 2025

The following examples of recent major drug innovations – amongst many others – illustrate their benefits in terms of clinical efficacy and quality of life

Impact of drug innovation on Healthcare (1/2)

Examples of recent major drug innovations



Chronic hepatitis C infection

- **Hepatitis C virus** causes inflammation which can lead to cirrhosis or cancer
- Direct-acting antivirals (DAAs) have shown to be effective for all **HCV** types, in combination with ribavirin or interferon
- Sovaldi, the first DAA launched, is a **definitive cure** with **few side effects**
- The treatment has proven to be effective in **>90% of patients** vs. 50 to 70% for the previous treatments
- The drug has paved the way for **global eradication** of the hepatitis C virus



Spinal Muscular Atrophy (SMA)

- SMA is a **rare neuromuscular disease**, extremely physically disabling or even fatal depending on the type
- Zolgensma, by a **single injection**, allows to overcome the deficiency of the gene responsible for the disease
- The therapy is indicated in **children under 2 years of age**, and **~4,000 patients** have received it worldwide
- Clinical trials demonstrated a **95% survival rate**
- Data in **pre-symptomatic patients** showed a **100% survival rate**



Covid-19 infection

- From 2020 to 2025, ~760 million of **Covid-19 infections** have been reported and **>7 million deaths**
- **mRNA vaccines** deliver a synthetic messenger RNA sequence that encodes a viral antigen which triggers both humoral (antibody) and cell-mediated (T-cell) immunity
- To date, >13 billion doses have been administered worldwide, **drastically reducing hospitalizations and severity of symptoms**
- Covid-19 **vaccination averted ~2.5 million deaths** and contributed to **~15 million life-years saved**

The following examples of recent major drug innovations – amongst many others – illustrate their benefits in terms of clinical efficacy and quality of life

Impact of drug innovation on Healthcare (2/2)

Examples of recent major drug innovations



KEYTRUDA
(pembrolizumab)

OPDIVO
(nivolumab)

Oncology

- **Yervoy (ipilimumab)**¹ was the **first checkpoint inhibitor** to enter the market in 2011, **followed by Keytruda**² (pembrolizumab) and **Opdivo**² (nivolumab) in 2014³
- **Checkpoint inhibitors** treat several cancers by **stimulating** the patient **anti-tumor immunity**
- High **benefits** vs. chemotherapies or targeted non-immunotherapies have been shown, **incl. overall survival** in:
 - Metastatic melanoma
 - Metastatic NSCLC⁴
 - Head & Neck cancer

Sunlenca
(lenacapavir) injection

yeztugo
(lenacapavir) injection 15mL

HIV treatment & prophylaxis

- **~41 million people worldwide** were living with **HIV** at the end of 2024
- **Lenacapavir** is a first-in-class capsid inhibitor, administered **twice a year**
- In 2022, it was approved under **Sunlenca** name **for patients resistant to prior HIV treatments**
- When added to usual drugs, Sunlenca has shown a meaningful **decrease** in **viral load** for **87.5% of patients**
- In 2025, it was approved under **Yeztugo** name for pre-exposure prophylaxis (**PRoP**), showing a **99.9% efficacy rate**

HEMLIBRA
emicizumab-kxwh 150 mg/mL
injection for subcutaneous use

Hemophilia A

- **Hemophilia A** is a **rare genetic disorder** affecting **~400,000 people** worldwide
- **Hemlibra** is a bispecific mAb⁵ indicated for Hemophilia A (with or without factor VIII inhibitors) that was launched in 2017
- Compared with prior standard of care, **Hemlibra**:
 - Substantially **reduces bleeding risk**, incl. in **hard-to-treat patients** (those with factor VIII inhibitors)
 - Is approved from **newborns to adults**
 - Is more **patient-friendly** (e.g., SC injection⁶, less frequent injections⁷)

Sources: R Ferrara et al., Cochrane Database Sys. Rev. (2021) – E. De Clercq, ¹ CTLA-4 inhibitor – ² PD-1 inhibitors – ³ Since then, other checkpoint inhibitors like the PD-L1 inhibitors Tecentriq (atezolizumab), Bavencio (avelumab) and Imfinzi (durvalumab) entered the market – ⁴ Non-Small Cell Lung Cancer – ⁵ Monoclonal Antibody that mimics the factor VIII function – ⁶ Subcutaneous vs. intravenous injection – ⁷ Once-weekly, every two weeks, or even once every four weeks, depending on patient needs

2024 top selling drugs include three metabolic diseases drugs,
two oncology drugs and two inflammatory diseases drugs

Top 10 worldwide pharmaceutical drugs (2024)

#	Brand	Molecule	Therapeutic Class	Company	WW Product Sales (USD B)		
					2023	2024 ¹	2023-2024 growth
1	Keytruda	Pembrolizumab	Oncology	MSD + Ono Pharmaceutical	25.0	29.5	+17.9%
2	Eliquis	Apixaban	Cardiovascular / Hematology	BMS + Pfizer	19.0	20.7	+9.2%
3	Ozempic	Semaglutide	Metabolic diseases	Novo Nordisk	13.9	17.5	+25.8%
4	Dupixent	Dupilumab	Inflammatory diseases	Sanofi + Regeneron	11.5	14.1	+22.1%
5	Biktarvy	Bictegravir + emtricitabine + tenofovir alafenamide	HIV ¹ disease	Gilead + Yuhan	11.9	13.5	+13.3%
6	Jardiance	Empagliflozin	Metabolic / Cardiovascular	Boehringer Ingelheim + Eli Lilly	10.8	12.4	+15.0%
7	Skyrizi	Risankizumab	Inflammatory diseases	AbbVie	7.8	11.7	+50.9%
8	Darzalex	Daratumumab	Oncology	J&J + Genmab	9.8	11.7	+19.8%
9	Mounjaro	Tirzepatide	Metabolic diseases	Eli Lilly	5.1	11.5	+123.5%
10	Stelara	Ustekinumab	Immunology	J&J	10.9	10.4	-4.6%

The top 10 selling products in 2030 should be dominated by metabolic diseases drugs, including anti-obesity drugs

Top 10 worldwide pharmaceutical drugs (2030 estimates)

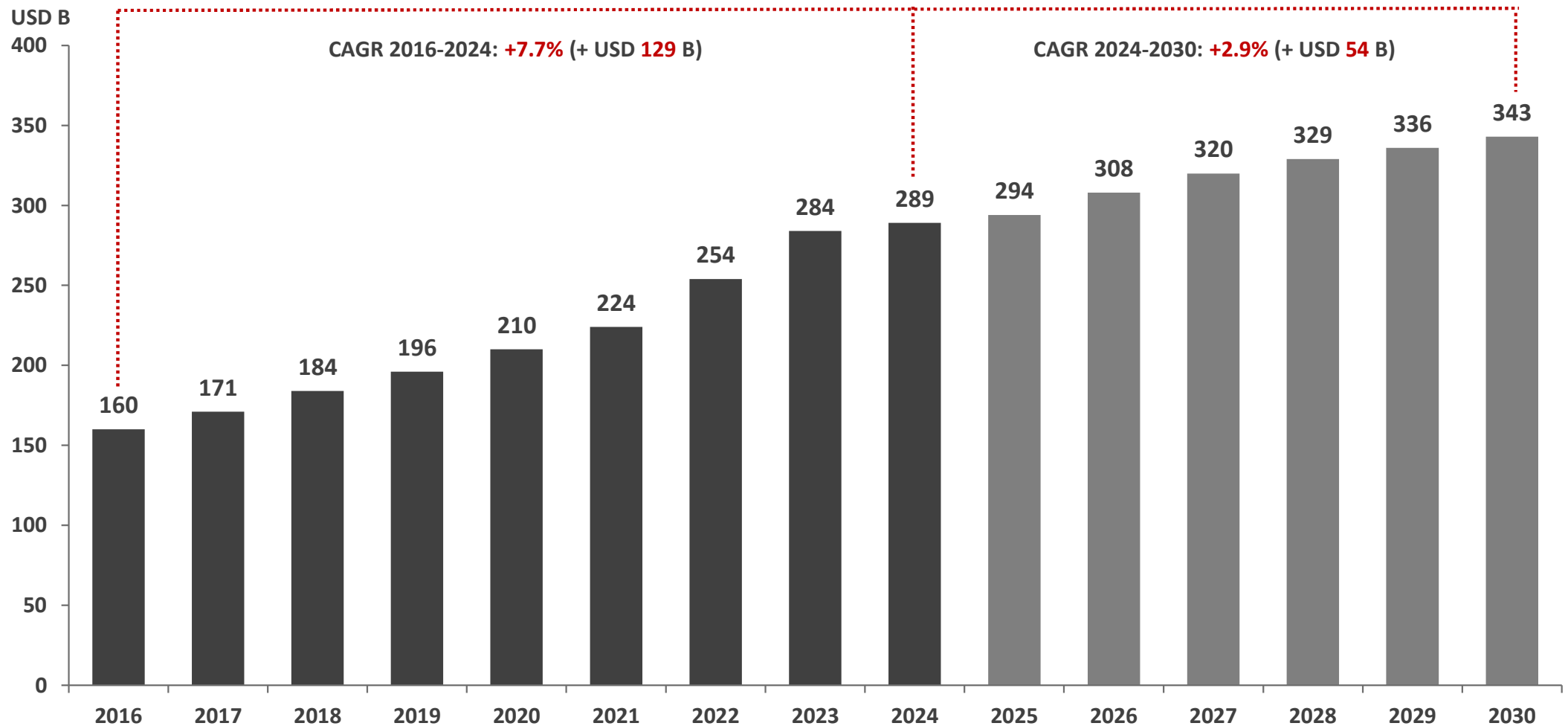
#	Brand	Molecule	Therapeutic Class	Company	WW Product Sales (USD B)			Market status in 2025
					2024	2030 ²	CAGR ³	
1	Mounjaro	Tirzepatide	Metabolic diseases	Eli Lilly	11.5	36.2	+21.1%	Marketed
2	Skyrizi	Risankizumab	Inflammatory diseases	AbbVie	11.7	26.6	+14.7%	Marketed
3	Zepbound	Tirzepatide	Metabolic diseases	Eli Lilly	4.9	25.5	+31.6%	Marketed
4	Dupixent	Dupilumab	Inflammatory diseases	Sanofi + Regeneron	14.1	25.1	+10.1%	Marketed
5	Ozempic	Semaglutide	Metabolic diseases	Novo Nordisk	17.5	24.4	+5.7%	Marketed
6	Wegovy	Semaglutide	Metabolic diseases	Novo Nordisk	8.4	18.1	+13.6%	Marketed
7	Keytruda	Pembrolizumab	Oncology	MSD + Ono Pharmaceutical	29.5	16.9	-8.9%	Marketed
8	Darzalex	Daratumumab	Oncology	J&J + Genmab	11.7	16.6	+6.0%	Marketed
9	Biktarvy	Bictegravir + emtricitabine + tenofovir alafenamide	HIV ¹ disease	Gilead + Yuhan	13.5	15.7	+2.5%	Marketed
10	Cagrisema	Cagrilintide + semaglutide	Metabolic diseases	Novo Nordisk	0.0	15.2	N/A	Not marketed

Sources: "World Preview", Evaluate (Jul. 2025) – Smart Pharma Consulting estimates

¹ Human Immunodeficiency Virus – ² Estimates – ³ Compound annual growth rate

The R&D spending should increase until 2030 but at a slower pace (+2.9% CAGR¹) than over the 2016 – 2024 period (+7.7% CAGR), reflecting the more focused strategy of pharma companies

Worldwide pharmaceutical R&D spending (2016 – 2030)



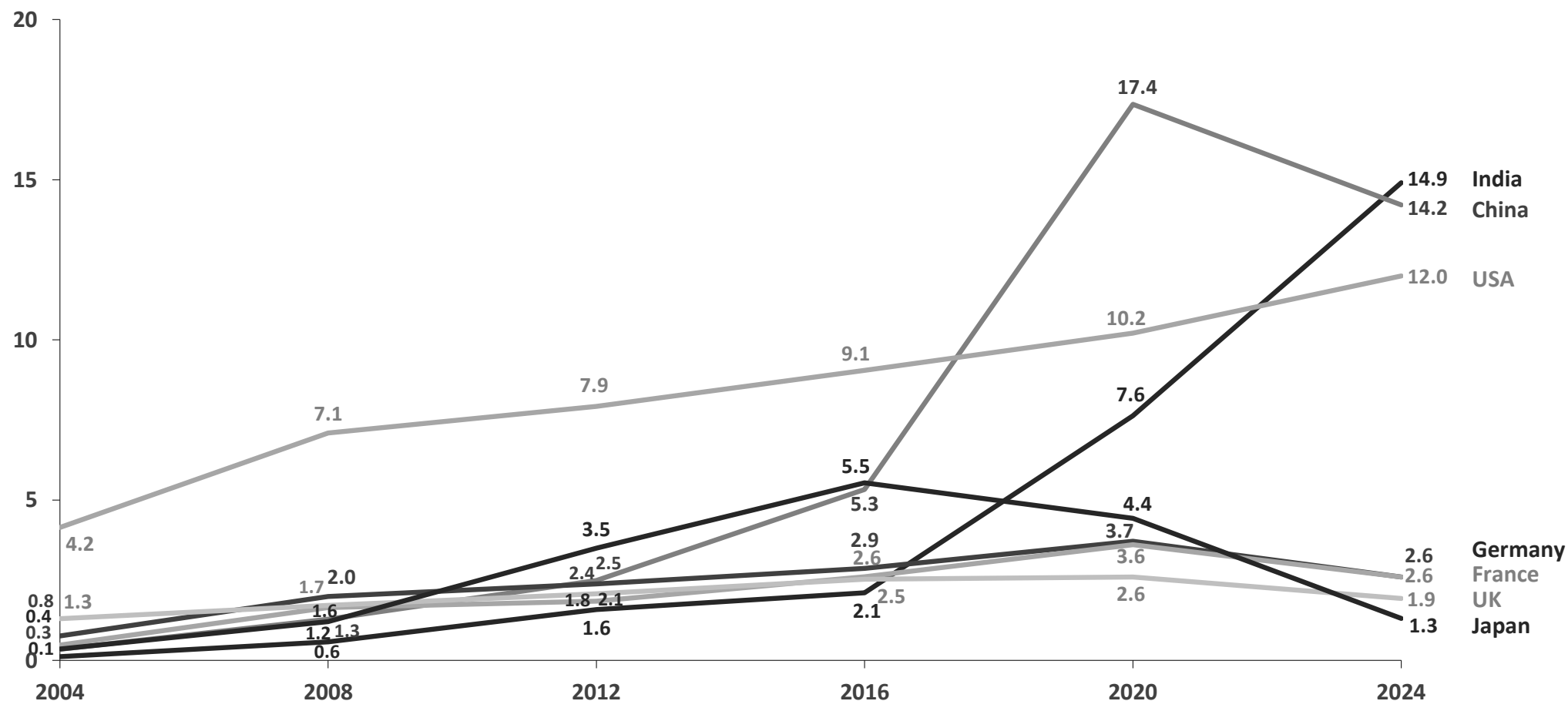
Sources: "World Preview", Evaluate (Jul. 2025) – Smart Pharma Consulting analyses

¹ Compound annual growth rate

The number of clinical trials in India and China has risen sharply since 2016, surpassing the USA and demonstrating their ambition to become major players in the R&D field

Evolution of the distribution of clinical trials by country (2004 – 2024¹)

Number of on-going clinical trials (in thousands)



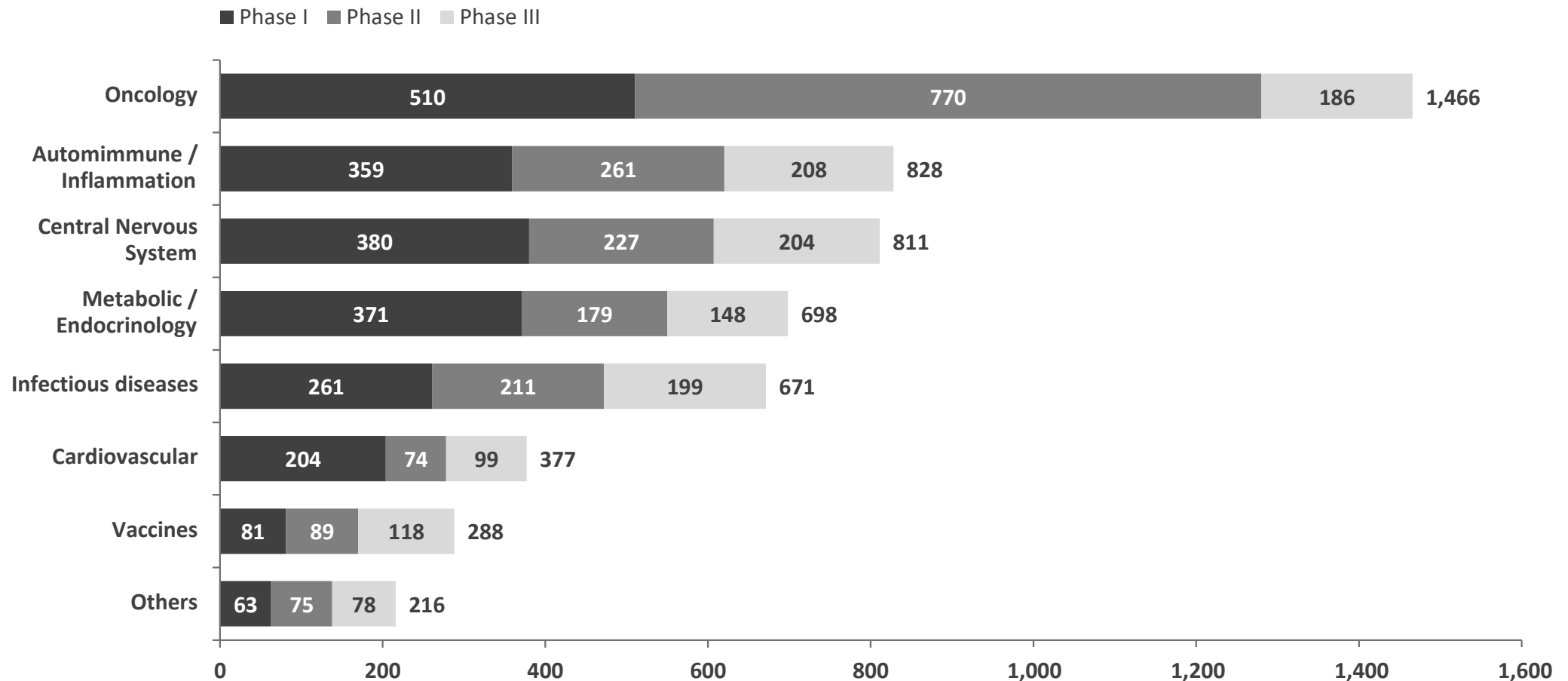
Sources: WHO observatory (Dec. 2024) – Smart Pharma Consulting analyses and estimates

¹ 2024 data estimated based on data as of June 2024

Oncology is by far the therapeutic area with the most ongoing clinical trials, but the ones with the most advanced (Phase III) trials are the autoimmune and CNS areas

Distribution of clinical trials by therapeutic area and phase (2024)

Distribution of industry-sponsored clinical trials completed by therapeutic area and phase



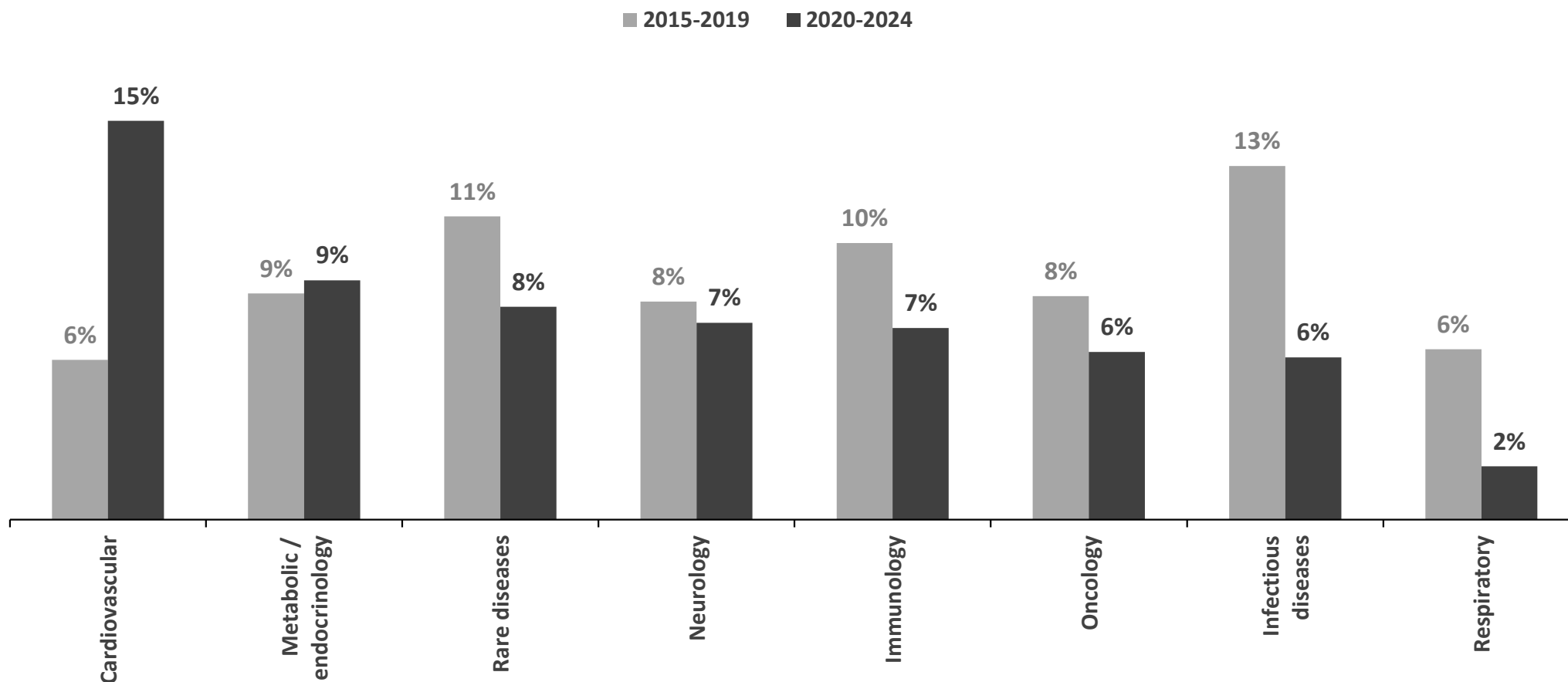
Sources: "Annual Completed Clinical Trials", Citeline Trialtrave (Feb. 2025)—Smart Pharma Consulting analyses

Note: Phase II includes Phase I/II and II, Phase III includes Phase II/III and III

Probability of success varies considerably across therapeutic areas with, over 2020-2024, cardiovascular that replaced infectious diseases as the most successful area

R&D success rate by therapeutic area (2015 – 2024)

% of composite success¹ by therapeutic area



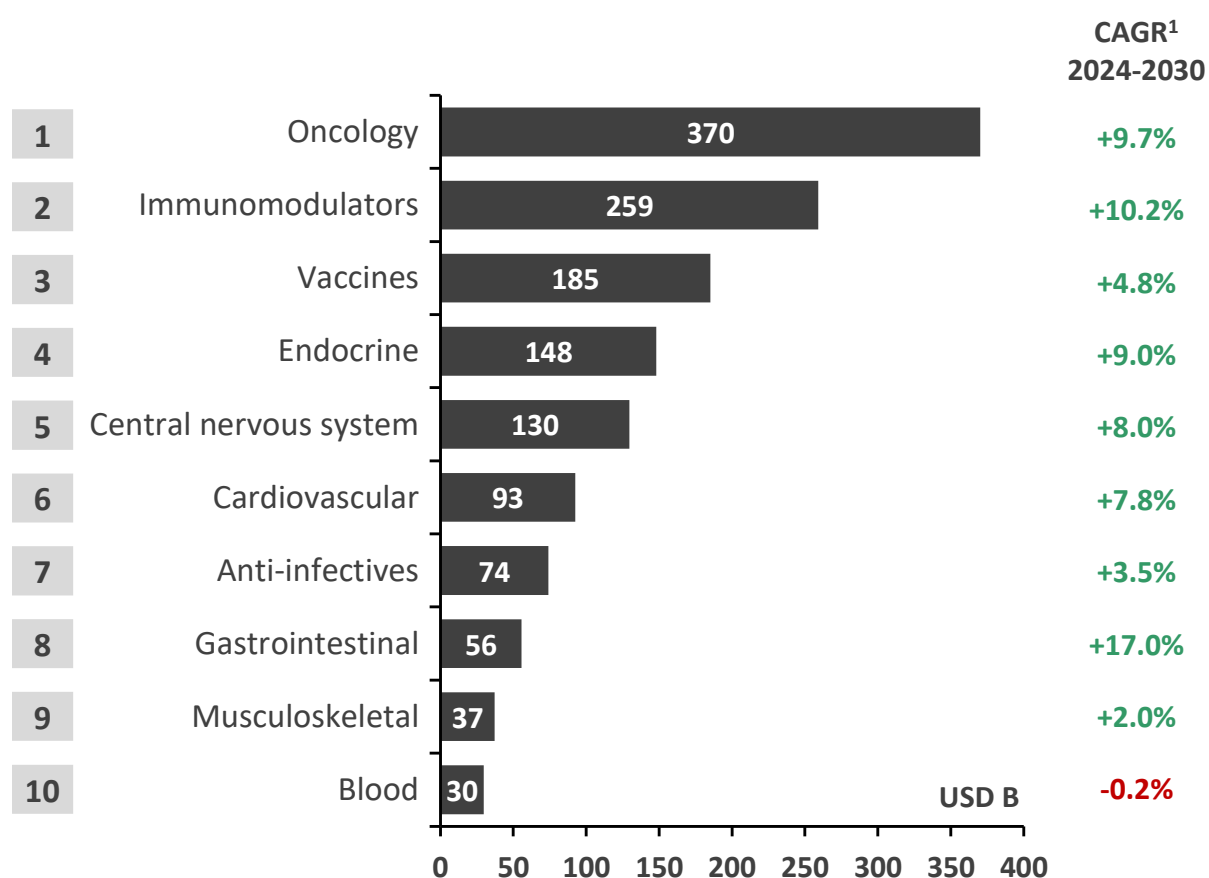
Sources: “Global trends in R&D”, IQVIA Institute (Mar. 2025) – Smart Pharma Consulting analyses

¹ Composite success = Phase I x Phase II x Phase III x Regulatory submission successes

Gastrointestinal, oncology and endocrine drugs should grow strongly until 2030, driven by advances in personalized medicines, anti-obesity and anti-diabetes drugs

Top 10 therapeutic areas (2024 – 2030)

Estimated 2030 sales per therapeutic area (USD B)



- The 2030 therapeutic area forecasts confirm the trend foreseeing the steadily increasing weight of **specialty products**, and the recent rise of **obesity drugs**
- **Oncology** prevails as the leading therapeutic area and will be notably driven by the growth of **targeted therapies**, **precision medicine** and **CAR-T cell therapy**
- **Gastrointestinal drugs**, including **obesity drugs**, will have the market highest 2024-2030 CAGR, driven by the increasing global prevalence of obesity, the multiple products already commercialized and in development, and the rising awareness of authorities, healthcare professionals and patients about the disease and its related risks
- Similarly, **diabetes** prevalence is rising and the increasing number of diabetes drugs at affordable prices should favor the market growth, and thus the endocrine market

Among the 10 highest potential drugs expected in 2025, six are already FDA-approved for the US market and two should be marketed by small biopharmaceutical companies

Biggest potential drugs expected in 2025 (2030 sales estimates)

#	Brand name	Molecule	Indication	Company	FDA approval (US market)	2030 sales estimates (USD B)
1	Alyftrek	Vanzacaftor tezacaftor + deutivacaftor	Cystic fibrosis	Vertex Pharmaceuticals	FDA-approved (Dec. 2024)	8.3
2	Datroway	Datopotamab deruxtecan (Dato-DXd)	Breast and lung cancers	Daiichi Sankyo + AstraZeneca	FDA-approved (Jan. 2025 ¹)	5.9
3	Journavx	Suzetrigine	Acute and neuropathic pain	Vertex Pharmaceuticals	FDA-approved (Jan. 2025)	2.9
4	(no brand name yet)	Aficamten	Hypertrophic cardiomyopathy	Cytokinetics	<i>Under review (target: Dec. 2025)</i>	2.8
5	Brinsupri	Brensocatib	Non-cystic fibrosis bronchiectasis	Insmmed	FDA-approved (Aug. 2025)	2.8
6	(no brand name yet)	Tolebrutinib	Multiple sclerosis	Sanofi	<i>Under review (target: Dec. 2025)</i>	1.4
7	(no brand name yet)	Mazdutide	Type II Diabetes and obesity	Lilly + Innovent	<i>Under review</i>	1.3
8	(no brand name yet)	Depemokimab	Severe allergic asthma	GSK	<i>Under review</i>	1.2
9	MenABCWY	Meningococcal A, B, C, W-135 and Y bacteria	Meningococcal A, B, C, W-135 and Y vaccine	GSK	FDA-approved (Feb. 2025)	1.2
10	IMAAVY	Nipocalimab-aahu	Myasthenia gravis and other autoimmune diseases	Johnson & Johnson	FDA-approved (Apr. 2025)	1.2

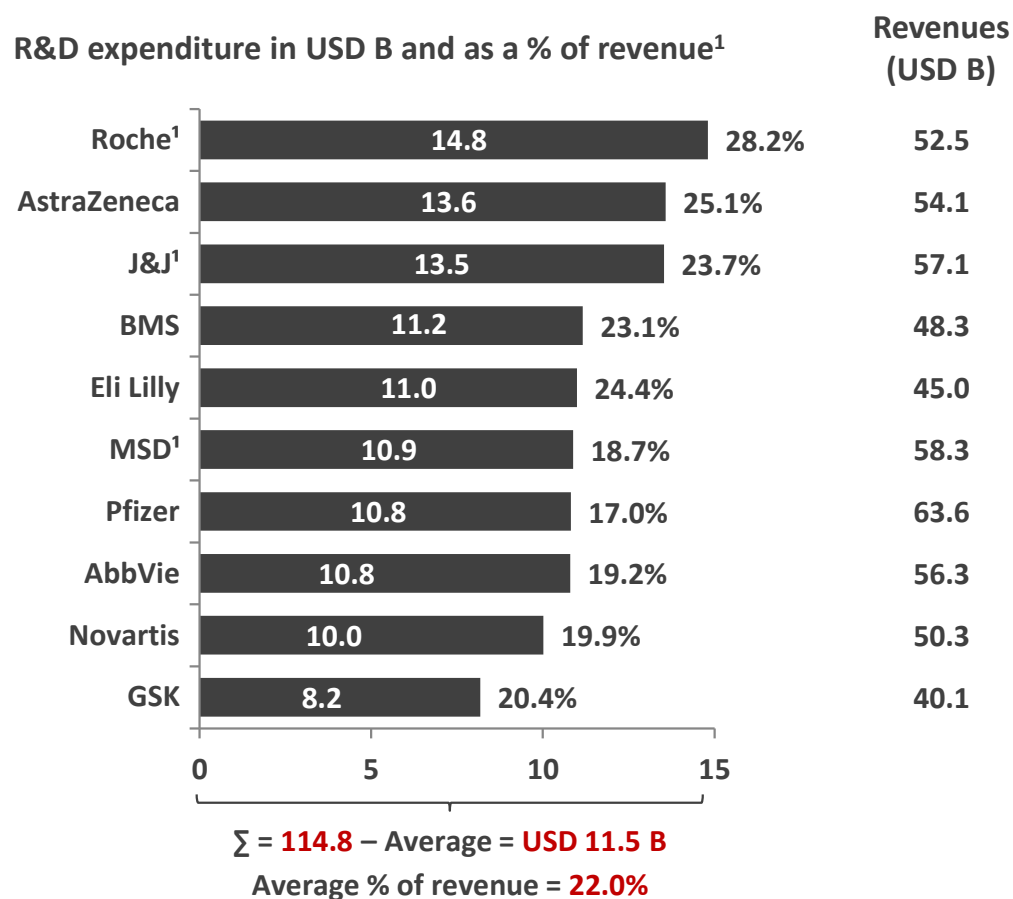
Sources: Fierce Pharma & Evaluate (Jan. 2025) – FDA (Dec. 2025) – Companies' press releases (Dec. 2025) – Smart Pharma Consulting analyses

¹ Approved for breast cancer and under review for lung cancer

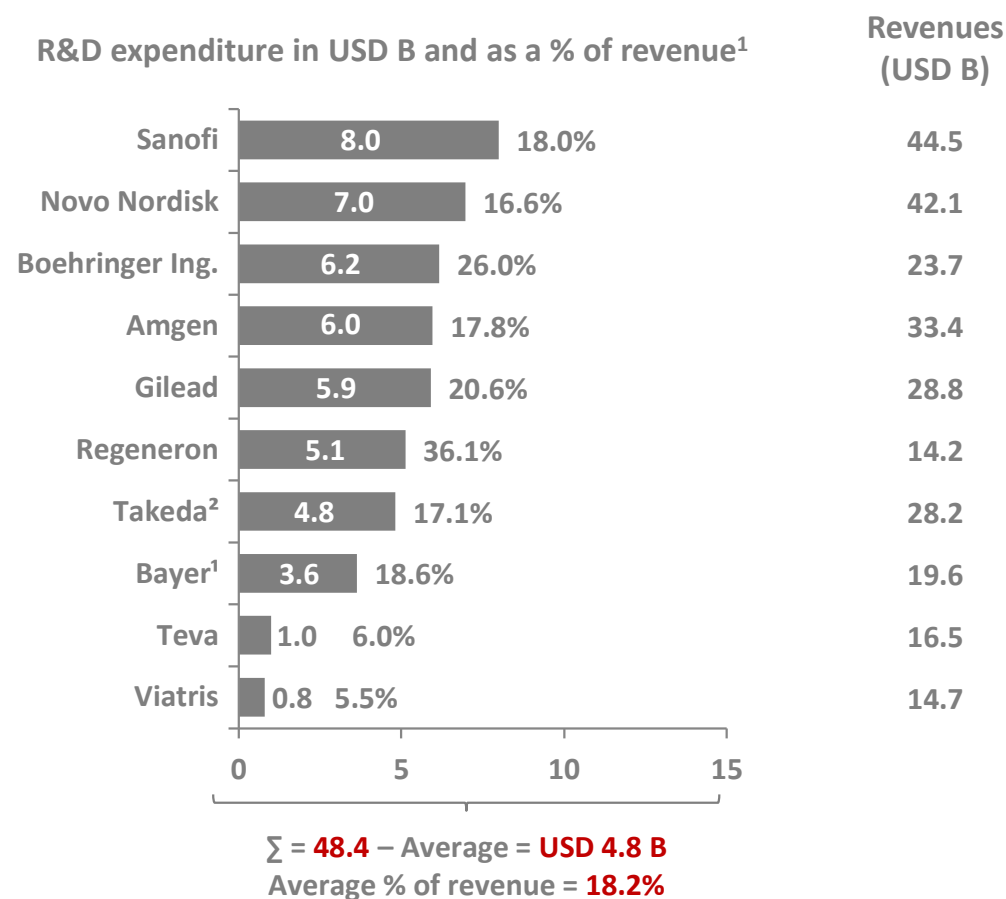
Tier-one pharma companies have spent 2.4 times more for R&D in absolute value than tier-two pharma companies, and 3.8 points more as a percentage of their revenues

Top 20 pharma companies – R&D expenditure (2024)

Tier-one



Tier-two



Almost all top pharma companies investing in R&D have candidates in oncology and immunology, and to a lesser extent in CNS, endocrinology, anti-infectives, cardiovascular and vaccines

Pharma companies' R&D priorities by therapeutic area (2025) – (1/2)

Human Rx-bound drugs & Vaccines strategic segment

Pharma company	2024 R&D (USD B)	# of R&D candidates	Oncology	Immunology	CNS	Endocrinology / Metabolic	Cardio-vascular	Anti-infectives	Vaccines	Others
 Roche	14.8	109	+++	+	+					
 AstraZeneca	13.6	198	+++	+			+			
 Johnson & Johnson	13.5	103	+++	++	+					
 Bristol Myers Squibb	11.2	89	++	+	+					+ Hematology
 Lilly	11.0	86	++	+	+	++				
 MSD	10.9	50	++					+	+	
 Pfizer	10.8	101	+++	++					+	+ Internal medicine
 abbvie	10.8	58	++	+	++					+ Esthetic medicine
 NOVARTIS	10.0	102	++	++	+		+			
 GSK	8.2	79	++	++				++		

Legend: +++: ≥ 50% of candidates in the pipeline // ++: 20%-49% of candidates // +: 10%-19% of candidates

Sources: R&D portfolios and Corporate communication of pharma companies (as of Nov. 2025) – Smart Pharma Consulting analyses

Tier-two pharma companies align their R&D investment with their specific areas of expertise (e.g., endocrinology for Novo Nordisk, inflammatory for Amgen or Takeda)

Pharma companies' R&D priorities by therapeutic area (2025) – (2/2)

Human Rx-bound drugs & Vaccines strategic segment

Pharma company	2024 R&D (USD B)	# of R&D candidates	Oncology	Immunology	CNS	Endocrinology / Metabolic	Cardio-vascular	Anti-infectives	Vaccines	Others
 sanofi	8.0	93	+	++	+				+	+ Rare diseases
 novo nordisk	7.0	38				+++	+			+ Hematology
 Boehringer Ingelheim	6.2	49	++	+	+		++			
 AMGEN	6.0	50	++				+			++ Inflammatory
 GILEAD	5.9	55	++					++		+ Inflammatory
 REGENERON	5.1	53	++	+		++				++ Hematology
 Takeda	4.8	49	+		+					+++ Inflammatory Plasma
 BAYER	3.6	31	++		+		++			
 teva	1.0	9 ¹	+	+	++		+			+ Inflammatory
 VIATRIS™	0.8	0 ¹								+++ ²

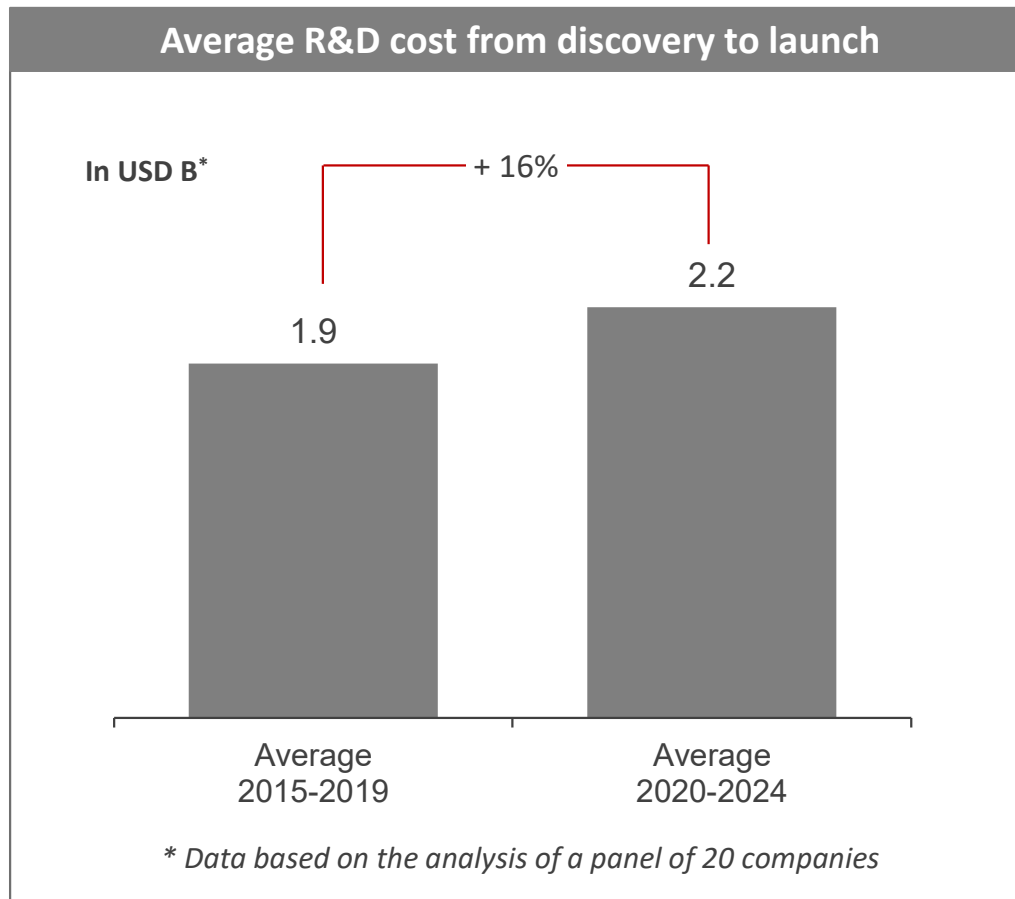
Legend: +++: ≥ 50% of candidates in the pipeline // ++: 20%-49% of candidates // +: 10%-19% of candidates

Sources: R&D portfolios and Corporate communication of pharma companies (as of Nov. 2025) – Smart Pharma Consulting analyses

¹ Innovative medicines only (i.e., excluding biosimilars and generics) – ² Biosimilars and/or generics

Drug development costs an average USD 2.2 B per asset, driven by complex science, costly trials, high failure rates and new technology investments, despite efforts to improve R&D efficiency

Evolution of drug R&D costs



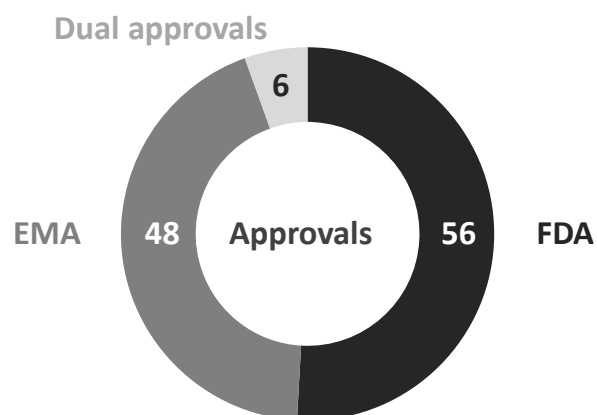
- Despite **yearly fluctuations**, the average annual R&D cost from the 2015-2019 period to the 2020-2024 period **increased by 16%**, driven by:
 - **Research complexity** for drugs indicated in diseases like Alzheimer's, cancers or rheumatoid arthritis
 - Increasingly rigorous **clinical trials** required by health authorities to demonstrate efficacy and safety...
 - ... inducing a high **failure rate**
 - Significant upfront investment in **new technologies** such as AI and gene therapies
- In addition, broader **economic pressures** (incl. inflation and taxes) push overall costs higher
- If R&D cost control **efficiency** is improving with the deployment of AI and GenAI from drug discovery to drug filing, it remains a **high-risk** and **capital-intensive** endeavor

The EMA generally approves therapies after FDA authorization, particularly for extending indications of previously approved treatments

Market access of new drugs (Jan. - Sep. 2025)

New drugs approvals in the USA and Europe (2025)

Number of approvals in **Europe** (by the **EMA**¹) and/or the **USA** (by the **FDA**²) between January and September **2025**:



Drugs approved by both the EMA and the FDA on this period include:

- **New agents** (e.g., Datroway – Daiichi Sankyo for the treatment of breast cancer)
- **Indications extensions** (e.g., Nubeqa – Bayer for the treatment of prostate cancer³)

New drugs market access

- The fact that all newly approved drugs are **not introduced everywhere** depends on **several factors**:
 - Different **regulatory systems** and authorities require **distinct applications**, with different requirements and procedures
 - Even when there is a centralized approval procedure like in the EU, the approved drug is not necessarily introduced in all countries, as **local pricing** and **reimbursement policies** can make the launch unattractive
 - **Market potential** and **attractiveness** (e.g., **epidemiology**, **pricing policy**) are key factors in the decision of introducing a drug in a new country by the pharma company
 - New drugs are usually more expensive, which makes their introduction more difficult in **lower income countries**, where the budget for pharmaceutical products is lower

Pharma companies' strategy to enhance R&D efficiency is based on a reduced number of programs, increased external collaborations and accelerated acquisitions of biotech start-ups

Key strategic drivers to enhance pharma companies' R&D efficiency

Portfolio Optimization

- **Focus resources on a limited number of programs** in predefined strategic therapeutic areas considering:
 - The **market potential**
 - The level of **unmet needs** as valued by health authorities
 - **The probability of success**
 to improve “value per invested dollar”

Open Innovation & Partnerships

- **Collaborating with biotech start-ups and/or academic institutions** has shown **higher productivity** by:
 - Giving access to **multiple cutting-edge R&D programs**
 - **Avoiding investment** in infrastructures for **early phases**
 - **Sharing development costs** and risks
 - **Reducing time to market**

Acquisitions

- **Acquiring biotech start-ups** has become a strategic lever:
 - **Accelerating access to innovative platforms**¹
 - **Diversifying pipelines** without bearing the full cost and risk of early-stage research
 - **Shortening development timelines**
 - Bringing operational **synergies** (e.g., scale for clinical trials)
- **Acquisitions have accelerated** with deals in **oncology, immunology, rare diseases or innovative platforms**
 - Examples of biotech start-ups acquisitions in 2025**
 - **J&J** acquired **Halda Therapeutics** (oncology)
 - **Vertex** acquired **Alpine Immune** (immunology)
 - **Sanofi** acquired **Blueprint Medicines** (rare diseases)
 - **Novartis** acquired **Avidity Biosciences** (RNA-based drugs)

Pharma companies that integrate digital technologies, agile processes, and closely monitor their R&D activities, will lead in developing breakthrough therapies faster and more cost-effectively

Key operational drivers to enhance pharma companies' R&D efficiency

Artificial Intelligence (AI) & Machine Learning (ML) enablers

- AI-native platforms and cloud infrastructure can dramatically **shorten cycle times, improve data quality and success rates** by:
 - **Accelerating molecule discovery** (target-drug interaction prediction, lead compounds optimization, drug repurpose)
 - **Optimizing trial design** (predictive modeling enhancement and **data integration** with digital twins, *in silico* clinical trials and cloud platforms)
- Using patient recruitment platforms, digital biomarkers, wearable devices and digital endpoints to **gather real-time data**, reducing trial costs and patient burden
- Companies like Pfizer, Novartis or Sanofi demonstrate that AI-driven drug design and predictive analytics can compress timelines by up to 80%

Agile Organization

- Reducing bureaucratic layers by adopting centralized decision hubs and integrating scientific enables **faster portfolio prioritization and resource allocation**
- Applying a rigorous and early Go/No-Go decision-making process, based on robust data, **saves time and cost**

“AstraZeneca and Roche streamlined governance by consolidating committees and empowering cross-functional teams”

R&D efficiency monitoring

- To **optimize** the execution of R&D activities, its is essential to introduce **qualitative and quantitative KEIs**¹ such as²:
 - Cycle time from discovery to market launch
 - Overall success rate / attrition rate
 - R&D expenditure per approved NME³
- Key Performance Indicators (KPIs) measure the outcome:
 - Number of NMEs approved per period
 - Return on R&D investment (e.g., rNPV⁴)

Sources: Pharma Companies corporate communication (2025) – Unleash AI's potential, Deloitte (April 2024) – A. Schuhmacher, Drug Discovery Today (2025) – Smart Pharma Consulting analyses

¹ Key Execution Indicators which will enable to identify possible gaps and then address them, if required, are essential to enhance R&D productivity – ² Examples of indicators for illustrative purpose – ³ New Molecular Entities – ⁴ Risk-adjusted Net Present Value

Pharma companies face the dual challenge of containing the weight of their R&D cost while striving to accelerate the launch of drugs valued by health authorities and payers

Key takeaways

1. Pharma R&D has shown to play a major role to save life and improve quality of life of people who can access to innovations

2. Oncology, immunology, CNS¹ and endocrinology are the therapeutic areas concentrating the larger number of R&D projects

3. France and Germany are tied for 4th re. the number of clinical trials in 2024, far behind India, China and the USA

5. The top 20 pharma companies have spent an average of USD 8.2 B in R&D in 2024 (i.e., ~21% of their revenues)



4. Over the 2020-2024 period, the cardiovascular area showed the highest clinical trial success rate

6. Top pharma companies focus R&D investment in 2 or 3 therapeutic areas, mainly in oncology and immunology

7. To enhance R&D efficiency, pharma companies tend to focus their resources on fewer programs, increase external collaborations and/or start-ups acquisitions, while implementing an agile organization and increasingly using AI² & ML³

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

Market Insights Series

- This series provides practical tools and recommendations to enhance the efficacy and efficiency of the most important activities or processes in place within pharma companies
- Our tools and recommendations are based on both:
 - Our consulting experience in the pharma sector
 - Our research for innovative, pragmatic and useful solutions
- Each issue is designed to be read in less than 20 minutes and not to exceed 20 pages

Global Pharma R&D Overview

Situation analysis & Perspectives

- Drug innovation has contributed to extend life and improve the quality of life of people, offering a real added-value
- This paper reviews global R&D trends, priority therapeutic areas and top 20 pharma companies' R&D strategies
- Smart Pharma Consulting has also analyzed:
 - The key strategic drivers
 - The key operational driversto enhance pharma companies R&D efficiency

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)
 - Training activities for pharma executives
 - The publication of articles, booklets, books and expert reports
- Our publications can be downloaded from our website:
 - 43 articles
 - 74 position papers covering the following topics:

1. Market Insights	5. Marketing
2. Strategy	6. Sales Force Effectiveness
3. Market Access	7. Management & Trainings
4. Medical Affairs	
- Our research activities in pharma business management and our consulting activities have shown to be highly synergistic
- We remain at your disposal to carry out consulting projects or training seminars to help you improve your operations

Best regards

Jean-Michel Peny